Programma voorjaarsvergadering 19 en 20 maart 2015
NH Conference Centre Koningshof Veldhoven

NEDERLANDSE VERENIGING VOOR GASTROENTEROLOGIE

Sectie Gastrointestinale Endoscopie
Netherlands Society for Parenteral and Enteral Nutrition
Sectie Neurogastroenterologie en Motiliteit
Sectie Experimentele Gastroenterologie
Sectie Gastrointestinale Oncologie
Sectie Inflammatoire Darmziekten IBD
DEGH-Meeting
Sectie Kinder-MDL
V&VN MDL

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

NEDERLANDSE VERENIGING VOOR GASTROINTESTINALE CHIRURGIE

NVGIC Nederlandse Vereniging voor GastroIntestinale Chirurgie

NEDERLANDSE VERENIGING VAN MAAG-DARM-LEVERARTSEN

MDL

INHOUDSOPGAVE **pag**

Tijdstippen diverse vergaderingen tijdens voorjaarsvergadering:

Nederlandse Vereniging voor Gastroenterologie	19 maart, 11.30 uur – Brabantzaal
Sectie Kinder MDL	19 maart, 11.45 uur – Zaal 81
NVMDL i.o	19 maart, 12.00 uur – zaal 63-64
Vergadering Sectie Inflammatoire Darmziekten	19 maart, 15.00 uur – Brabantzaal
Nederlandse Vereniging voor Hepatologie	19 maart, 15.00 uur – Baroniezaal

INHOUDSOPGAVE **pag**

Tijdstippen diverse ledenvergaderingen tijdens voorjaarsvergadering:

Nederlandse Vereniging van Maag-Darm-Leverartsen	21 maart, 08.00 uur – Zaal 81-82-83
V & VN MDL	21 maart, 11.45 uur – Beneluxhal

Belangrijke mededeling
over de aanwezigheid van farmaceutische industrieën

Aan alle deelnemers aan de voorjaarsvergadering op 19 en 20 maart 2015

De Nederlandse Vereniging voor Gastroenterologie kent een jarenlange samenwerking met de farmaceutische industrie. De vereniging stelt de farmaceutische industrie in de gelegenheid aanwezig te zijn bij de wetenschappelijke vergaderingen met een stand. Mede hierdoor kan de vereniging haar wetenschappelijke bijeenkomsten organiseren.

De Geneesmiddelenwet zegt dat - onder strikte voorwaarden - de farmaceutische industrie alleen reclame mag maken voor receptgeneesmiddelen voor personen die bevoegd zijn om dergelijke geneesmiddelen voor te schrijven. Alle andere personen (inclusief bijvoorbeeld verpleegkundigen, endoscopie-assistenten en biochemici) worden beschouwd als “publiek”. De farmaceutische industrie mag geen reclame maken voor receptgeneesmiddelen voor publiek.
De Nederlandse Vereniging voor Gastroenterologie is een wetenschappelijke vereniging voor personen die beroepsmatig betrokken zijn bij zorg, onderwijs en onderzoek ten behoeve van patiënten met maag-, darm- en leveraandoeningen. Dat betekent dat ook personen die geen arts zijn, lid van de NVGE zijn. De aanwezigheid van artsen, niet-artsen en farmaceutische industrieën tijdens de voorjaarsvergadering kan de NVGE ongewild in aanraking brengen met de inspectie voor de gezondheidszorg, sectie reclametoezicht, en daarmee in diskrediet worden gebracht. Dat willen wij uiteraard voorkomen.

In verband met de Gedragscode Geneesmiddelenreclame van de CGR en de aan het NVGE-congres verbonden expositie van farmaceutische producten, medische instrumenten en voedingsmiddelen, zal bij uw congresregistratie via de NVGE-website worden gevraagd naar uw bevoegdheid om medicijnen voor te schrijven.

Alle congresdeelnemers dragen verplicht een congresbadge waarop behalve de naam ook beroep/functie staat aangegeven. Farmaceutische standhouders benaderen uitsluitend congresdeelnemers die de bevoegdheid hebben om receptgeneesmiddelen voor te schrijven of ter hand te stellen. Om dit extra te verduidelijken zal tijdens het voorjaarscongres worden gekozen voor verschillende kleuren congresbadges.

Uit het bovenstaande volgt dat aanwezige reclame-uitingen en merkproductinformatie van farmaceutische industrieën alleen gericht zijn op personen die bevoegd zijn om de betreffende geneesmiddelen voor te schrijven. Wij maken u erop attent dat het voor niet-artsen dan ook niet is toegestaan de stands van de aanwezige farmaceutische industrieën te bezoeken.

De NVGE en farmaceutische industrie (sponsoren) vertrouwen erop u met bovenstaande voldoende te hebben geïnformeerd.

Het bestuur van de NVGE

VOORWOORD

Hierbij treft u het volledige programma aan van het voorjaarscongres op 19 en 20 maart in NH Conference Center Koningshof te Veldhoven. Zoals gebruikelijk wordt ons congres vooraf gegaan door het cursorisch onderwijs op woensdag 18 maart, waarvan u het programma aantreft op bladzijde 6 en 7.

Hoogtepunt tijdens het voorjaarscongres is de *Tytgat Lecture*, die op donderdag om 17.30 uur gepland staat in de Brabantzaal. Dr Martin Blaser, Director van het Human Microbiome Program, en Professor aan de New York University Langone Medical Center in New York komt hiervoor naar Veldhoven. Zijn laboratorium is beroemd vanwege het onderzoek naar de rol van de microbiota in gezondheid en ziekte, en zijn verhaal zal voor een breed publiek inspirerend zijn. Wij zijn ook verheugd dat hij voorafgaand aan de Tytgat-Lecture een DEGH sessie zal voorzitten.

In het voorjaar is er traditioneel veel aandacht voor onderzoekers, met een groot aantal uiteenlopende abstract sessies. Het DEGH programma is zowel op donderdag als vrijdag in de Baronie zaal. De heelkunde abstracts zijn donderdag morgen in de Parkzaal, parallel aan het NVGIC symposium in het Auditorium, dat gefocust is op benigne en maligne colorectale pathologie. Op donderdag zijn de IBD en motiliteitsabstracts gepland. Tijdens de plenaire sessie worden de *MLDS Onderzoeksprijs 2014* en de *NVGE Research Award 2015* uitgereikt door prof. dr. P. Fockens en prof. dr. K.K. Krishnadath als voorzitters van de respectievelijke jury's.

Op vrijdag morgen zijn er naast de abstractsessie symposia van de sectie endoscopie en voeding. Om 11.30 uur is een state af the art lecture door dr. F. Vleggaar over EUS gepland, gevolgd door een kort minisymposium *Radiologie Update* met als gastsprekers prof. dr. E.F.I. Comans (over PET CT), dr. M. van Leeuwen (over het onderscheid tussen auto-immuun pancreatitis en pancreascarcinoom) en prof. dr. J. Stoker (over CT colonografie). Op vrijdagmiddag gaat het symposium van de Sectie Gastrointestinale Oncologie over surveillance door de MDL-arts. Op vrijdag in de Beneluxzaal wordt door de Vereniging Verpleegkundigen en Verzorgenden Nederland MDL (V&VN MDL) een eigen programma met lezingen verzorgd, met na de lunch een keuze uit twee subsessies.

Tijdens het congres zijn er weer twee Meet the Expert sessies. Een sessie over poliepectomie wordt verzorgd door prof. dr. P. Fockens en prof. dr. B.L.A.M. Weusten. De andere sessie over functionele buikklachten wordt verzorgd door prof. dr. A.A.M. Masclee en dr. L.A. van der Waaij.

Wij wensen u een plezierig congres!

Dr. J.J. Keller, secretaris NVGE
Dr. K. van der Linde, bestuurslid NVGE

Woensdag 18 maart 2015

Cursorisch onderwijs in maag-darm-leverziekten **Auditorium**

Cursuscommissie

Prof. dr. U.H.W. Beuers, voorzitter, MDL-arts, AMC, Amsterdam
Mevr. dr. C.M. Bakker, MDL-arts, Atrium MC, Heerlen
Drs. K. van Hee, aios MDL
Dr. J. Heisterkamp, chirurg, St. Elisabeth Ziekenhuis, Tilburg
Dr. P.J.F. de Jonge, aios MDL
Mevr. dr. A.M.J. Langers, MDL-arts, LUMC, Leiden
Dr. B. Oldenburg, MDL-arts, UMC Utrecht
Mevr. dr. R.E. Pouw, aios MDL
Dr. J. Vecht, MDL-arts, Isala Klinieken, Zwolle
Dr. B.J. Veldt, MDL-arts, Reinier de Graaf Gasthuis, Delft
Dr. R.A. de Vries, MDL-arts, VUmc, Amsterdam
Dr. P.J. Wahab, MDL-arts, Rijnstate Ziekenhuis, Arnhem

Pancreatitis

Voorzitters: Prof. dr. U.H.W. Beuers, Dr. P.J.F.de Jonge

14.30 – 14.35 Inleiding

14.35 – 14.55 Etiologie van de acute en chronische pancreatitis
Mevr. dr. Y.C.A. Keulemans (MUMC)

15.00 – 15.20 Diagnose en therapie van de acute pancreatitis
Dr. M.G.H. Besselink (AMC)

15.25 – 15.45 Endoscopische interventie bij complicaties van pancreatitis
Dr. J.W. Poley (EMC)

15.50 – 16.10 Chirurgische behandeling, complicaties en pijnbestrijding bij chronische pancreatitis
Mevr. prof. dr. M.A. Boermeester (AMC)

16.15 – 16.35 Pauze

Woensdag 18 maart 2015

Cursorisch onderwijs in maag-darm-leverziekten **Auditorium**

Dunne darm I

Voorzitters: Dr. C.M. Bakker, Dr. R.A. de Vries

16.35 – 16.55 Glutenvrij dieet in Nederland – zin en onzin
Prof. dr. C.J.J. Mulder (VUmc)

17.00 – 17.20 Kleine en grote beesten in de dunne darm
Dr. B. Oldenburg (UMCU)

17.25 – 17.45 De dunne darm in beeld brengen
Dr. S.J.B. van Weyenberg (LUMC)

17.50 – 18.10 Bariatrische chirurgie: techniek, resultaten en complicaties
Drs. I.M.C. Janssen (Arnhem)

18.15 – 18.35 Pauze

Dunne darm II

Voorzitters: Dr. P.J. Wahab

18.35 – 18.55 Acute, 'acute on chronic' en chronische darmischemie
Prof. dr. J.J. Kolkman (Enschede)

19.00 – 19.25 Short bowel syndroom, totale parenterale voeding en darmtransplantatie
Prof. dr. G. Dijkstra (UMCG)

19.30 Einde cursus, diner, borrel

De cursuscommissie verwacht van de MDL-artsen i.o. dat ze de Cursus Klinische Hepatologie (NVH) tijdens de Dutch Liver Week éénmaal bezoeken in het tweede deel van de MDL-opleiding (jaar vier tot zes).
Op het cursorisch onderwijs zijn conform de eisen van het Centraal Register Kort Beroepsonderwijs leveringsvoorwaarden van toepassing. Informatie vindt u op de onderwijspagina van www.mdl.nl en www.nvge.nl.

Programma donderdag 19 maart 2015

Donderdag	Brabantzaal	Baroniezaal	Auditorium	Parkzaal
08.45 - 09.30	Ontvangst en koffie	Ontvangst en koffie	Ontvangst en koffie	Ontvangst en koffie
09.30 – 11.30	Vrije voordrachten Sectie Inflammatoire Darmziekten *pagina 10*	Carreer Development sessie (aanvang 09.00) *pagina 23* DEGH-meeting (aanvang 10.30) *pagina 23*	Symposia NVGIC: - Benigne colorectaal - Colorectaal techniek *pagina 19* Innovation room: zaal 82- 83	Vrije voordrachten Nederlandse Vereniging voor Gastrointestinale Chirurgie (aanvang 09.30) *pagina 27*
11.30 - 12.00	Ledenvergadering NVGE		Geen programma i.v.m. ALV van de NVGE	Geen programma i.v.m. ALV van de NVGE
12.00 - 13.00	Lunch in expositiehal	Lunch in expositiehal	Lunch in expositiehal	Lunch in expositiehal
13.00 – 15.00	Vrije voordrachten Sectie InflammatoireDarmziekten *pagina 12*	DEGH-meeting *pagina 24*	Symposia NVGIC: - Bevolkingsonderzoek - Maligne colorectaal *pagina 20*	Vrije voordrachten Ned. Vereniging voor Gastroenterologie *pagina 29*
15.00 - 15.30	Theepauze	Theepauze + ALV NVH	Theepauze	Theepauze
15.30 - 17.00	Vrije voordrachten Sectie Gastrointestinale Endoscopie *pagina 15*	DEGH-meeting *pagina 26*	Voordracht prof. dr. J.W. Milsom, New York Vervolg symposium Maligne colorectal *pagina 21*	Vrije voordrachten Sectie Neuro-gastroenterologie en Motiliteit *pagina 31*
17.00 - 17.30	Voordrachten President Select - *pagina 17*			
17.30 – 17.50	Prijsuitreikingen: MLDS Award NVGE Research Award			
17.50 – 18.00	Uitreiking Leerboek MDL			
18.00 – 18.30	Tytgat lecture door Prof. dr. M.J. Blaser, New York *pagina 18*			
18.30 - 19.30	Borrel in expositiehal			
19.30 - 22.00	Diner Genderzaal			
22.00 - 01.00	Borrel / Muziek in foyer			

Donderdag	Zaal 80 – Meet the expert - Functionele buikklachten	Zaal 81 – Meet the expert - Poliepectomie
13.00 – 14.00 14.00 – 15.00	Groep 1 - volgeboekt Groep 2 – volgeboekt *pagina 33*	Groep 1 - volgeboekt Groep 2 – volgeboekt *pagina 33*

Programma vrijdag 20 maart 2015

Vrijdag	Brabantzaal	Baroniezaal	Auditorium	Parkzaal
08.30 – 09.30	Ontvangst en koffie	Ontvangst en koffie	Ontvangst en koffie	Ontvangst en koffie
09.30 – 11.00	Symposium Voeding en Endoscopie van de Sectie Gastrointestinale Endoscopie *pagina 34*	Posterrondes DEGH zaal 19 en 20, aanvang 09.00 met ontbijt *pagina 40*	Vrije voordrachten Sectie Gastrointestinale Oncologie *pagina 37*	Vrije voordrachten Ned. Vereniging voor Gastroenterologie *pagina 47*
11.00 - 11.30	Koffiepauze	Koffiepauze	Koffiepauze	Koffiepauze
11.30 - 13.00	Vrije voordrachten Sectie Gastrointestinale Endoscopie *pagina 34*	DEGH-meeting *pagina 44*	State of the Art lecture Dr. F. Vleggaar *pagina 39* Radiologie symposium *pagina 39*	Vrije voordrachten Sectie Gastrointestinale Oncologie *pagina 49*
13.00 – 14.00	Lunch expositiehal	Lunch expositiehal	Lunch expositiehal	Lunch expositiehal
14.00 – 15.30	Symposium: Diagnostiek en surveillance voor de MDL-arts *pagina 36*	DEGH-meeting *pagina 46*	Vrije voordrachten Ned. Vereniging voor Gastroenterologie en Gastrointestinale Chirurgie -pagina	Vrije voordrachten Ned. Vereniging voor Gastroenterologie *pagina 51*
15.30 – 16.00	Limburgfoyer	Limburgfoyer	Limburgfoyer	

Programma vrijdag 20 maart 2015
V&VN MDL en NESPEN

Vrijdag	Beneluxhal	Zaal 52	Zaal 80
09.00 – 12.30	09.45 - ALV V&VN MDL Plenair ochtendprogramma V&VN MDL *pagina 57*		Voordrachten NESPEN, om 11.00 uur gevolgd door Symposium Darmfalen *pagina 53*
12.45	Lunch in expo		Lunchbuffet bij de zaal 12.30 uur
13.45 – 15.30	Middagprogramma V&VN *pagina 58*	Parallel programma Lever- en IBD-verpleegkundigen *pagina 58*	Symposium dietetiek en onderzoek, thema: voeding en bewegen *pagina 55* Presentaties eigen onderzoek *pagina 56*
15.30	Einde programma	Einde programma	Einde programma

Vrije voordrachten Sectie Inflammatoire Darmziekten — Brabantzaal

09.00 Registratie, koffie

Voorzitters: I.A.M. Gisbertz en C.J. van der Woude

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

09.30 Comparison of disease phenotype in 35,128 European and 4,686 non-European IB patients in the international IBD genetic consortium cohorts (p.62)

R.K. Weersma[1], C.W. Lees[2], S. Ng[3] on behalf of the International IBD Genetics Consortium, [1]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [2]GI Unit, Western General Hospital, Edinburgh, United Kingdom, [3]Institute of Digestive Disease, State Key Laboratory of Digestive Diseases, Medicine and Therapeutics, Chinese University of Hong Kong, China

09.40 Epidemiology and characteristics of inflammatory bowel disease in a large population-based cohort in the Netherlands (p.63)

E.J. de Groof[1,2], N.G.M. Rossen[1], B.D. van Rhijn[1], E.P.M. Karregat[1], K. Boonstra[1], I. Sadal[1], P.J. Kingma[3], A.H.J. Naber[3], J.H.M. van den Brande[3], R.C. Mallant-Hent[4], M.W. Mundt[4], G. D'Haens[1], C.Y. Ponsioen[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dept of Surgery, Academic Medical Center, Amsterdam, [3]Dept of Gastroenterology and Hepatology, Tergooi Hospitals, Hilversum and Blaricum, [4]Dept of Gastroenterology and Hepatology, Flevohospital, Almere, The Netherlands

09.50 Disease course, phenotype, and medication use in elderly-onset Crohn's disease patients - A Dutch population-based IBD cohort study (p.64)

S.F.G. Jeuring[1,2], T.R.A. van den Heuvel[1,2], M.P. Zeegers[3,4], W.H. Hameeteman[1], M.J.L. Romberg-Camps[5], L.E. Oostenbrug[6], A.A.M. Masclee[1,2], D.M.A.E. Jonkers[1,2], M.J. Pierik[1,2], [1]Division of Gastro-enterology and Hepatology, Maastricht University Medical Center+, Maastricht, The Netherlands [2] School for Nutrition, Toxicology and Metabolism (NUTRIM), Maastricht University Medical Center, Maastricht, The Netherlands, [3]Dept of Complex Genetics, Cluster of genetics and Cell Biology, Maastricht University Medical Center, Maastricht, The Netherlands, [4]Dept of Epidemiology and Public Health, University of Birmingham, Birmingham, United Kingdom, [5]Dept of Internal Medicine and Gastroenterology, Orbis Medical Center, Sittard-Geleen, The Netherlands, [6]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center, Heerlen, The Netherlands

10.00 Increased cancer risk in Dutch Crohn's disease patients: results from a population based cohort (p.65)

D.S.J. Wintjens[1], T.R.A. van den Heuvel[1], S.F.G. Jeuring[1], W.H. Hameeteman[1], L.E. Oostenbrug[2], M.J.L. Romberg-Camps[3], A.A.M. Masclee[1], M.P. Zeegers[4,5], D.M.A.E. Jonkers[1], M.J. Pierik[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Center, The Netherlands, [2]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Atrium Medical Center, The Netherlands, [3]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Orbis Medical Center, The Netherlands, [4]Dept of Complex Genetics, Cluster of Genetics and Cell Biology, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center,

Maastricht, The Netherlands, [5]Dept of Epidemiology and Public Health, University of Birmingham, Birmingham, United Kingdom

10.10 Baseline characteristics and datamodel from a nationwide standardized inflammatory bowel disease collection by all university medical centers in the Netherlands: the IBD Parelsnoer Institute (p.66)

L.M. Spekhorst[1,2], F. Imhann[1,2*], A.A. van Bodegraven[3], N.K.H. de Boer[3], G. Bouma[3], E.A Festen[1,2], H.H. Fidder[4], G.R.A.M. D'Haens[5], F. Hoentjen[6], D.W.Hommes[7], D.J. de Jong[6], M. Lowenberg[5], A.E. van der Meulen[7], B. Oldenburg[4], M.J. Pierik[8], P.C. Stokkers[9], C.J. van der Woude[10], G. Dijkstra[1^], R.K. Weersma[1^], *Both authors contributed equally to this work, ^Shared last author, Parelsnoer Institute[#] , On behalf of the Dutch Initiative on Crohn and Colitis (ICC), [1]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, [2]Dept of Genetics University of Groningen and University Medical Center Groningen, [3]Dept of Gastroenterology and Hepatology, VU University Medical Center, [4]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, [5]Dept of Gastroenterology and Hepatology, Academic Medical Center, [6]Dept of Gastroenterology and Hepatology, University Medical Center St. Radboud, [7]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, [8]Dept of Gastroenterology and Hepatology, University Medical Center Maastricht, [9]Dept of Gastroenterology and Hepatology, St Lucas Andreas Ziekenhuis, Amsterdam, [10]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, The Netherlands*

10.20 Smoking is associated with extra-intestinal manifestations in inflammatory bowel disease (p.67)

M. Severs[1], S.J.H. van Erp[13], G. Dijkstra[3], M.E. van der Valk[1], M.J. Mangen[2], M. Leenders[1], A.A. van Bodegraven[4], H.H. Fidder[1], D.J. de Jong[5], M. Pierik[6], C.J. van der Woude[7], M.J. RombergCamps[8], C.H. Clemens[9], J.M. Jansen[10], N. Mahmmod[11], P.C. van de Meeberg[12], C.Y. Ponsioen[14], C.J. Bolwerk[15], J.R. Vermeijden[16], P.D. Siersema[1], A.E. van der Meulen-de Jong[13], B. Oldenburg[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Julius Centre for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, [3]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [4]Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, [5]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [6]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [7]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [8]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [9]Dept of Gastroenterology and Hepatology, Diaconessenhuis, Leiden, [10]Dept of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, [11]Dept of Gastroenterology and Hepatology, Antonius Hospital, Nieuwegein, [12]Dept of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, [13]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [14]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [15]Dept of Gastroenterology and Hepatology, Reinier de Graaf Groep, Delft, [16]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, The Netherlands

10.30 Identification of genetic and clinical risk factors for hidradenitis suppurativa in inflammatory *bowel disease* (p.68)

L.M. Spekhorst1,2, I.C. Janse3, M. Koldijk3, A. Vich Vila2, R.K. Weersma1, G. Dijkstra1, B. Horváth3, 1Dept of Gastroenterology, 2Dept of Genetics and 3Dept of Dermatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

10.40 Drug repositioning in inflammatory bowel disease by using genetic information (p.69)

V. Collij[1], E.A.M. Festen[1], R. Alberts[1], R.K. Weersma[1], [1]University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

10.50 Genetic polymorphisms in IBD determine response to treatment (p.70)
V.J.A.A. Nuij[1], M.P. Peppelenbosch[1], C.J. van der Woude[1], G.M. Fuhler[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

11.00 Disease specific differences in intestinal microbiota between pediatric-IBD and healthy control (p.71)
E.F.J. de Groot[1], N.K.H. de Boer[1], M.A. Benninga[3], A.E. Budding[4], A.A. van Bodegraven[5], P. Savelkoul[4], T.G.J. de Meij[2], [1]Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, [2]Dept of Pediatric Gastroenterology, VU University Medical Center, Amsterdam, [3]Dept of Pediatric Gastroenterology, Academic Medical Center, Amsterdam, [4]Dept of Medical Microbiology and infection control, VU University Medical Center, Amsterdam, [5]Dept of Gastroenterology and Hepatology, ORBIS Medical Center, Sittard, The Netherlands

11.10 Incidence and severity of pre-pouch Ileitis: a distinct disease entity or a manifestation of refractory pouchitis? (p.72)
S. Sahami[1,2], M.A. Samaan[3], D.C. de Jong[1], S.M. Morgan[3], G.R. van den Brink[1], M. Lowenberg[1], C.I. Ponsioen[1], C.J. Buskens[2], P.J. Tanis[2], A. de Buck van Overstraeten[4], A. D'Hoore[4], W.A. Bemelman[2], G.R. D'Haens[1], [1]Dept of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands, [3]Dept of Gastroenterology, University College Hospital London, London, United Kingdom, [4]Dept of Surgery, University Hospital Leuven, Leuven, Belgium

11.20 **MLDS-voordracht**
Faecal Microbiota Transplantation in ulcerative colitis: a randomised controlled trial. (p.73)
N. Rossen[1], S. Fuentes[2], M. van der Spek[1], J. Tijssen[3], J. Hartman[2], Ann Duflou[1], L. Mathus- Vliegen[1], W. de Vos [2,4], E. Zoetendal[2], G. D'Haens[1], C. Ponsioen[1]. [1]Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam. [2]Department of Cardiology, Academic Medical Centre, Amsterdam, The Netherlands. [3]Laboratory of Microbiology, Wageningen University, the Netherlands. [4]Departments of Bacteriology & Immunology and Veterinary Biosciences, University of Helsinki, Finland.

11.30 Korte ledenvergadering Nederlandse Vereniging voor Gastroenterologie

12.00 Lunch in expositiehal

Vrije voordrachten Sectie Inflammatoire Darmziekten — Brabantzaal

Voorzitters: G. Dijkstra en R.L. West

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

13.00 Non-trough IFX concentrations reliably predict trough levels and accelerate dose adjustment in Crohn's disease (p.74)
D.R. Hoekman[1], M. Lowenberg[1], R.A. Mathot[2], G.R. D'Haens[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Hospital Pharmacy, Academic Medical Center, Amsterdam, The Netherlands

13.10 Antibodies to infliximab, body weight and low serum albumin levels increase clearance of infliximab, a population pharmacokinetic study in 324 IBD patients (p.75)

J.F. Brandse[1], D.R. Mould[2], Y.K. Ashruf[1], O.S. Smeekes[1], M. Löwenberg[1], C.Y. Ponsioen[1], G.R. van den Brink[1], G.R. D'Haens[1], [1]Dept of Gastroenterology, The Netherlands, [2]Projections Research Inc., Phoenixville, United States of America

13.20 Elevated 6-methylmercaptopurine metabolites assessed shortly after thiopurine therapy initiation are associated with hepatotoxicity in inflammatory bowel disease patients (p.76)

D.R. Wong[1], M.J.H. Coenen[2], L.J.J. Derijks[3], C.J. van Marrewijk[2], S.H. Vermeulen[2,4], A.L.M. Verbeek[4], B. Franke[2,6], H-J. Guchelaar[7], D.J. de Jong[8], L.G.J.B. Engels[9], P.M. Hooymans[1], On behalf of the TOPIC study group, [1]Dept of Clinical Pharmacy and Toxicology, Orbis Medical Center, Sittard-Geleen, [2]Dept of Human Genetics, Radboud University Medical Center, Nijmegen, [3]Dept of Clinical Pharmacy, Máxima Medical Center, Veldhoven, [4]Dept for Health Evidence, Radboud University Medical Center, Nijmegen, [5]Dept of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute of Pharmaceutical Sciences, Utrecht University, Utrecht, [6]Dept of Psychiatry, Radboud University Medical Center, Nijmegen, [7]Dept of Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, [8]Dept of Gastroenterology, Radboud University Medical Center, Nijmegen, [9]Dept of Gastroenterology, Orbis Medical Center, Sittard-Geleen, The Netherlands

13.30 Azathioprine and 6-mercaptopurine are equally effective in thiopurine naïve IBD patients (p.77)

M.M.T.J. Broekman[1], M.J. Coenen[8], B. Franke[7,8], L.J. Derijks[2], S.H. Vermeulen[3,8], D.R. Wong[4], O.H. Klungel[5], A.L. Verbeek[3], P. Hooymans[4], H. Scheffer[8], H.J. Guchelaar[6], C.J. van Marrewijk[8], D.J. de Jong[1], [1]Dept of Gastroenterology, Radboud University Medical Center, Nijmegen, [2]Dept of Clinical Pharmacy, Máxima Medical Center, Veldhoven, [3]Dept for Health Evidence, Radboud University Medical Center, Nijmegen, [4]Dept of Clinical Pharmacy and Toxicology, Orbis Medical Center, Sittard-Geleen, [5]Dept of Pharmacoepidemiology and Pharmacotherapy, Utrecht University, Utrecht, [6]Dept of Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, [7]Dept of Psychiatry, Radboud University Medical Center, Nijmegen, [8]Dept of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands

13.40 Short term prevalence of nodular regenerative hyperplasia of the liver in IBD patients treated with allopurinol-thiopurine combination therapy (p.78)

M.L. Seinen[1], D.P. van Asseldonk[1], N.K. de Boer[1], G. Bouma[1], C.J. Mulder[1], E. Bloemena[2], A.A. van Bodegraven[1,3], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Pathology, VU University Medical Center, Amsterdam, [3]Dept of Internal Medicine, Gastroenterology, and Geriatrics, Orbis Medical Center, Sittard-Geleen, The Netherlands

13.50 Development of a patient reported disease activity score to screen for mucosal inflammation in inflammatory bowel disease (p.79)

M.J. de Jong[1], J.H.R.J. Degens[1], T.R.A. van den Heuvel[1], M. Romberg-Camps[2], B. Winkens[3], T. Markus[4], A.A.M. Masclee[1], A. van Tubergen[5], D.M.A.E. Jonkers[1], M.J. Pierik[1], [1]Dept of Gastroenterology, Maastricht University Medical Center, Maastricht, [2]Dept of Gastroenterology, Orbis Medical Center, Maastricht, [3]Dept of Methodology and Statistics, Maastricht University, Maastricht, [4]CCUVN, Woerden, [5]Dept of Reumatology, Maastricht University Medical Center, Maastricht, The Netherlands

14.00 Long-term disease outcome of Crohn's disease in the biological era – Results from a Dutch population-based IBD cohort (p.80)

S.F.G. Jeuring[1,2], T.R.A. van den Heuvel[1,2], M.P. Zeegers[3,4], W.H. Hameeteman[1], M.J.L. Romberg-

Camps5, L.E. Oostenbrug6, S.O. Breukink7, L.P.S. Stassen7, A.A.M. Masclee1,2, D.M.A.E. Jonkers1,2, M.J. Pierik1,2, 1Division of Gastroenterology-Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands, 2School for Nutrition, Toxicology and Metabolism (NUTRIM), Maastricht University Medical Center, Maastricht, The Netherlands, 3Dept of Complex Genetics, Cluster of genetics and Cell Biology, Maastricht University Medical Center, Maastricht, The Netherlands, 4Dept of Epidemiology and Public Health, University of Birmingham, Birmingham, United Kingdom, 5Dept of Internal Medicine and Gastroenterology, Orbis Medical Center, Sittard-Geleen, The Netherlands, 6Dept of Internal Medicine and Gastroenterology, Atrium Medical Center, Heerlen, The Netherlands, 7Dept of General Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

14.10 Lower long-term colectomy rates with IFX than with CsA treatment in moderate to severe UC (p.81)

N.W. Duijvis[1], A. ten Hove[1], C. Ponsioen[2], G.R. van den Brink[1,2], A. te Velde[1], G.R.A.M. D'Haens[2], M. Löwenberg[2], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

14.20 Healthcare expenditures for inflammatory bowel disease peak in patients with a short disease duration (p.82)

M. Severs[1], M.E. van der Valk[1], M.J. Mangen[2], M. Leenders[1], G. Dijkstra[3], A.A. van Bodegraven[4], H.H. Fidder[1], D.J. de Jong[5], M. Pierik[6], C.J. van der Woude[7], M.J. Romberg-Camps[8], C.H. Clemens[9], J.M. Jansen[10], N. Mahmmod[11], P.C. van de Meeberg[12], A.E. van der Meulen-de Jong[13], C.Y. Ponsioen[14], C.J. Bolwerk[15], J.R. Vermeijden[16], P.D. Siersema[1], B. Oldenburg[1], COIN study group - Dutch Initiative on Crohn and Colitis, [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Julius Centre for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, [3]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [4]Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, [5]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, [6]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [7]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [8]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [9]Dept of Gastroenterology and Hepatology, Diaconessenhuis, Leiden, [10]Dep of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, [11]Dept of Gastroenterology and Hepatology, Antonius Hospital, Nieuwegein, [12]Dept of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, [13]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [14]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [15]Dept of Gastroenterology and Hepatology, Reinier de Graaf Groep, Delft, [16]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, The Netherlands

14.30 Evolution of IBD-related costs over two years of follow up: increase of anti-TNF α therapy related costs with a decline of hospitalization costs (p.83)

M.E. van der Valk[1], M.J.J. Mangen[1], M. van der Have[1], M. Severs[1], G. Dijkstra[2], A.A. van Bodegraven[3,4], H.H. Fidder[2], D.J. de Jong[5], M. Pierik[7], C.J. van der Woude[8], M. Romberg-Camps[4], C.H.M. Clemens[6], J.M. Jansen[15], P.C. van de Meeberg[9], M. Mahmmod[10], A.E. van der Meulen - de Jong[11], C.Y. Ponsioen[12], C. Bolwerk[13], J.R. Vermeijden[14], P.D. Siersema[1], M. Leenders[1], B. Oldenburg[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [3]Dept of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, [4]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [5]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [6]Dept of Gastroenterology and Hepa tology, Diaconessenhuis, Leiden, [7]Dept of Gastroenterology and Hepatology, Maastricht, University Medical Center, Maastricht, [8]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, [9]Dept of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, [10]Dept of Gastroenterology and Hepatology, Antonius Hospital, Nieuwegein, [11]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [12]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [13]Dept of Gastro

enterology and Hepatology, Reinier de Graaf Group, Delft, [14]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [15]Dept of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gastuis, Amsterdam, The Netherlands

14.40 Fertility in IBD women is comparable to fertility in non-IBD controls (p.84)

A. de Lima[1], M. van Amelsfort[1], E.A.P. Steegers[-2], C.J. van der Woude[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Obstetrics and Gynecology, Erasmus University Medical Center, Rotterdam, The Netherlands

14.50 Long term outcome of children born to IBD mothers - Preliminary result from a multicenter retrospective study in the Netherlands (p.85)

S.L. Kanis[1], A. de Lima[1], Z. Zelinkova[1], G. Dijkstra[2], R.L. West[3], R.J. Ouwendijk[4], N.K.H. de Boer[5], A.E. van der Meulen[6], M.J. Pierik[7], L.E. Oostenbrug[8], M. Romberg-Camps[9], G.L. Bodelier[10], B. Oldenburg[11], F. Hoentjen[12], R. Beukers[13], J.M. Jansen[14], C.J. van der Woude[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University, Erasmus Medical Center, Rotterdam, [2]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, [3]Dept of Gastroenterology and Hepatology, Sint Franciscus Gasthuis, Rotterdam, [4]Dept of Gastroenterology and Hepatology, Ikazia Hospital, Rotterdam, [5]Dept of Gastroenterology and Hepatology, Free University, Free University Medical Center, Amsterdam, [6]Dept of Gastroenterology and Hepatology, Leiden University, Leiden University Medical Center, Leiden, [7]Dept of Gastroenterology and Hepatology, Maastricht University, Maastricht University Medical Center, Maastricht, [8]Dept of Gastroenterology and Hepatology, Atrium Medical Center, Heerlen, [9]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [10]Dept of Gastroenterology and Hepatology, Amphia Hospital, Breda, [11]Dept of Gastroenterology and Hepatology, Utrecht University, University Medical Center Utrecht, Utrecht, [12]Dept of Gastroenterology and Hepatology, Radboud University, Radboud Medical Center, Nijmegen, [13]Dept of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht, [14]Dept of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

15.00 Ledenvergadering Sectie Inflammatoire Darmziekten
Theepauze expositiehal

Vrije voordrachten Sectie Gastrointestinale Endoscopie — Brabantzaal

Voorzitters: Y. Keulemans en J.W. Poley

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

15.30 Persistent low-grade dysplasia in Barrett's esophagus identifies patients at higher risk for esophageal adenocarcinoma: a Dutch nationwide cohort study (p.86)

C. Kestens[1], G.J.A. Offerhaus[2], J.W.P.M. van Baal[1], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

15.40 Detection of lesions in dysplastic Barrett's esophagus: are expert endoscopists doing a better job than community endoscopists? (p.87)

D.W. Schölvinck[1,2], K. van der Meulen[1], J.J.G.H.M. Bergman[2], B.L.A.M. Weusten[1,2], [1]Dept of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

15.50 First results on visualization of esophageal adenocarcinoma with VEGF-guided near infrared fluorescent endoscopy (p.88)

E. Hartmans[1], P.B. Garcia-Allende[2], F.T.M. Peters[1], J.J.J. Tjalma[1], H. de Jong[3], M. Linssen[4], M. Koller[5], A. Jorritsma-Smit[4], R. Bijlsma[1], J.H. Kleibeuker[1], G.M. van Dam[5], V. Ntziachristos[2], W.B. Nagengast[1], [1]Dept of Gastroenterology and Hepatology, [4]Dept of Clinical Pharmacy and Pharmacology, and [5]Dept of Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [2]Chair for Biological Imaging & Institute for Biological and Medical Imaging, Technical University of Munich and Helmholtz Center Munich, Munich, Germany, [3]Dept of Pathology, University of Utrecht, University Medical Center Utrecht, Utrecht, The Netherlands

16.00 Quantitative analysis of volumetric laser endomicroscopy of histologically correlated images potentially identifies early neoplasia in Barrett's esophagus (p.89)

A. Swager[1], D.M. de Bruin[2], D.J. Faber[2], B.L. Weusten[1], S.L. Meijer[3], J.J. Bergman[1], T.G. van Leeuwen[2], W.L. Curvers[4], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Biomedical Engineering and Physics, and [3]Dept of Pathology, Academic Medical Center, Amsterdam, [4]Dept of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, The Netherlands

16.10 Exploring diagnostic and therapeutic implications of endoscopic mucosal resection in EUS-staged T2 esophageal adenocarcinoma (p.90)

A.W. Gotink[1] , M.C.W. Spaander[1] , P. Didden[1] , B.P.L. Wijnhoven[2] , M.J. Bruno[1] and A.D. Koch[1] ,[1] Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam [2] Department of Surgery, Erasmus MC, University Medical Center Rotterdam

16.20 Differences in missed adenoma types comparing standard colonoscopy with "behind folds visualizing" techniques – a pooled analysis of three randomized back-to-back tandem colonoscopy studies (p.91)

E.C. Brand[1], V.K. Dik[1], M.G.H. van Oijen[1,2], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

16.30 Significant risk of post-colonoscopy colorectal cancer due to incomplete adenoma resection: results nationwide population-based cohort study (p.92))

H.J.M. Pullens[1,2], T.D.G. Belderbos[1*], M. Leenders[1], M.E.I. Schipper[3], M.G.H. van Oijen[1,4], P.D. Siersema[1], *Both authors contributed equally tot this work, [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [3]Dept of Pathology, University Medical Center Utrecht, Utrecht, [4]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*

16.40 Endoscopic resection of high-risk T1 colorectal carcinoma prior to surgical resection has no adverse effect on long-term outcomes (p.93)

A. Overwater[1], M.G.H. van Oijen[1], A. van den Blink[1], B.W.M. Spanier[2], T.C.J. Seerden[3], H.J.M. Pullens[4], W.H. de Vos tot Nederveen Cappel[5], G.J.A. Offerhaus[6], D.J. Bac[7], M. Kerkhof[8], K. Kessels[9], P.D. Siersema[1], M.A.G. Elferink[10], M.M. Lacle[6], L.M.G. Moons[1], Dutch T1 CRC Working Group, [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Rijnstate, Arnhem, [3]Dept of Gastroenterology and Hepatology, Amphia Hospital, Breda, [4]Dept of Gastroenterology and Hepatology, Meander, Medical Center, Amersfoort, [5]Dept of Gastroenterology and Hepatology, Isala, Zwolle, [6]Dept of Pathology, University Medical Center Utrecht, Utrecht, [7]Dept of Gastroenterology and Hepatology, Gelderse Vallei, Ede, [8]Dept of Gastroenterology and Hepa-

tology, Groene Hart Hospital, Gouda, [9]Dept of Gastroenterology and Hepatology, Flevo Hospital, Almere, [10]Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands

16.50 Patients with an endoscopic resection of a polyp containing carcinoma in situ or intramucosal carcinoma have a higher risk of postcolonoscopy colorectal cancer (p.94)

K. Kessels[1,2], M.A.G. Elferink[3], M.G.H. van Oijen[1], G.J.A. Offerhaus[4], M.M. Lacle[4], P.D. Siersema[1], L.M.G. Moons[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Flevo Hospital, Almere, [3]Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, [4]Dept of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

Voordrachten President Select — Brabantzaal

Voorzitter: J.J. Keller en P.D. Siersema

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

17.00 A randomized comparison of degradable esophageal stent versus dilation therapy for patients with recurrent benign esophageal strictures: 6-month results (DESTINY study) (p.95)

D. Walter[1], M.W. van den Berg[2], M.M. Hirdes[1], F.P. Vleggaar[1], A. Repici[3], E.C. Ferrara[3], P.H. Deprez[4], B.L. Viedma[5], L. Lovat[6], B.L. Weusten[7], R. Bisschops[8], E.E. O'Leary[9], J.E. van Hooft[2], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherland, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands, [3]Dept of Gastroenterology and Hepatology, IRCCS Humanitas, Milano, Italy, [4]Dept of Gastroenterology and Hepatology, Clinique Universitaire Saint Luc, Bruxelles, Belgium, [5]Dept of Gastroenterology and Hepatology, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain, [6]Dept of Gastroenterology and Hepatology, University College London, London, United Kingdom, [7]Dept of Gastroenterology, St. Antonius Hospital, Nieuwegein, The Netherlands, [8]Dept of Gastroenterology, University Hospitals Leuven, Leuven, The Netherlands, [9]MED Institute, Inc, West Lafayette, IN, United States of America

17.10 Complement factor C3 aggravates nonalcoholic steatohepatitis in mice (p.96)

F. Segers[1], N. van Best[1], C. Hodin[1], S.W.M. Olde Damink[1], A. Driessen[2], J.W. Greve[1,3], W.A. Buurman[1], S. Rensen[1, 1] Department of Surgery, Maastricht University Medical Center, Maastricht, [2]Department of Pathology, Maastricht University Medical Center, Maastricht; [3]Department of Surgery, Atrium Medical Center Parkstad, Heerlen, The Netherlands

17.20 Dose-escalating placebo-controlled study with allogeneic bone marrow-derived mesenchymal stem cells for the treatment of refractory perianal fistulas in Crohn's disease (p.97)

I. Molendijk[1], B.A. Bonsing[2], H. Roelofs[3], K.C.M.J. Peeters[2], M.N.J.M. Wasser[4], G. Dijkstra[5], C.J. van der Woude[6], R.A. Veenendaal[1], J.J. Zwaginga[3], H.W. Verspaget[1], W.E. Fibbe[3], A.E. van der Meulen-de Jong[1], D.W. Hommes[1,5], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Surgery,[3]Dept of Immuno-hematology and Blood Transfusion, and [4]Dept of Radiology, Leiden University Medical Center, Leiden, The Netherlands, [5]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [6]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands, [7]Division of Digestive Diseases, University of California, Los Angeles, USA.

Donderdag 19 maart 2015

Prijsuitreikingen **Brabantzaal**

17.30 **Uitreiking MLDS-Award voor beste onderzoek in 2014**
door Prof. dr. P. Fockens en mevr. M. Verasdonck, directeur MLDS
de uitreiking wordt gevolgd door een korte voordracht.

17.40 **Uitreiking NVGE Gastrointestinale Research Award 2014**
door de voorzitter van de jury, prof. dr. K.K. Krishnadath
gevolgd door erevoordracht door de prijswinnaar

Leerboek MDL **Brabantzaal**

17.50 **Overhandiging Leerboek Maag-, Darm- en Leverziekten**
door prof. dr. E.J. Kuipers aan de voorzitters van de NVMDL en NVGE, prof. dr. A.A.M. Masclee en prof. dr. P.D. Siersema.

State of the art lecture **Brabantzaal**

Voorzitter: P.D. Siersema

18.00 **Tytgat lecture**
The role of the gut microbiota in health and disease
Prof. dr. M.J. Blaser, Professor of Microbiology,
Director, Human Microbiome Program, New York University Langone Medical Center

18.40 Einde programma, congresborrel in expositiehal.

20.00 Diner in Beneluxzaal

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

08.45 Registratie, koffie

Voorzitters: A.L.A. Bloemendaal en N.A.T. Wijffels

Benigne colorectaal

09.15 Bekkenbodempathologie vanuit chirurgisch perspectief
Dr. P.M. Verheijen, chirurg, Meander MC, Amersfoort

09.30 Trials in IBD surgery: on the border of surgery & medical treatment
Prof. dr. W.A. Bemelman, chirurg, Academisch Medisch Centrum, Amsterdam

09.45 Anti-adhesie studie
Dr. M.W.J. Stommel, chirurg, Radboudumc, Nijmegen

10.00 Innovation Room – zaal 82-83

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: R.M.P.H. Crolla en O. van Ruler

Colorectaal techniek

10.15 SILS TME
Dr. H.A. Prins, chirurg, Jeroen Bosch Ziekenhuis, Den Bosch

10.30 Trans-anale TME
Dr. J. Knol, chirurg, Hasselt, België

10.45 Trans-anale TME met de robot
Dr. E.C.J. Consten, chirurg, Meander MC, Amersfoort

Donderdag 19 maart 2015

11.00 COLOR III study group initiative; TaTME or lap TME; an international multicenter randomized trial
Dr. J.B. Tuynman, chirurg, VUmc Amsterdam

11.15 Lokale chirurgie tenzij
Dr. E.J.R. de Graaf, chirurg, Rijnmond, Noord-IJsselland

11.30 Einde programma
U kunt zich voor de NVGE ledenvergadering begeven naar de Brabantzaal aanvang 11.30 uur.

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie **Auditorium**

Voorzitters: J.M. Vogten en J.D.W. van der Bilt

Bevolkingsonderzoek

13.00 De introductie van het BVO Darmkanker in Nederland
Dr. W.M.U. van Grevenstein, chirurg, UMC Utrecht

13.15 Resultaten na 1 jaar BVO
Prof. dr. E. Dekker, MDL-arts, Academisch Medisch Centrum, Amsterdam

13.30 Impact van BVO op lokale praktijk; chirurg
Dr. A.A.W. van Geloven, chirurg, Tergooi Ziekenhuis, Hilversum

13.45 Impact van BVO op lokale praktijk; MDL
Dr. M.A.M.T. Verhagen, MDL-arts, Diakonessenhuis, Utrecht

14.00 Innovation Room – zaal 82-83

Symposium Ned. Vereniging voor Gastrointestinale Chirurgie — Auditorium

Voorzitters: W. van Gijn en A.W.K.S. Marinelli

Voordrachten in het Engels

Maligne Colorectaal

14.30 Systeemtherapie bij het gemetastaseerd colorectaal carcinoom; de CAIRO studies
Dr. M. Koopman, internist-oncoloog, UMC Utrecht

14.45 De rol van tumor biologie in de behandeling van het colon carcinoom; het gebruik van biomarkers en vaccins
Dr. E.C.M. Zeestraten, aios chirurgie, IJsselland ziekenhuis, Capelle aan den IJssel

15.00 Debulking chirurgie bij diffuus gemetastaseerd colorectaal carcinoom; de ORCHESTRA studie,
Prof. dr. C. Verhoef, chirurg, Erasmus MC, Rotterdam

15.30 **State of the art in colorectal surgery**
Prof. dr. J.W. Milsom, Chief of Colon and Rectal Surgery, New York - Presbyterian / Weill Cornell Medical Center, New York, USA.

Vervolg Symposium NVGIC — Auditorium

Voorzitters: M. van Det en C. Verhoef

Maligne Colorectaal

16.00 Laparoscopische leverchirurgie
Dr. M.G.H. Besselink, chirurg, Academisch Medisch Centrum Amsterdam

16.15 Hemostase bij laparoscopische leverresecties
Dr. R.M. van Dam, chirurg, Maastricht UMC

Donderdag 19 maart 2015

16.30 Naadlekkage: Chirurgie, schaam je niet en neem je verantwoordelijkheid,
Prof. dr. J.F. Lange, chirurg, Erasmus MC, Rotterdam

16.45 "DSCA; kwaliteitsverbetering en kostenreductie
W. van Dijk, adviseur X-IS

17.00 Einde symposium

Voor de President Select, de prijsuitreikingen, uitreiking Leerboek Maag-Darm-Leverziekten en de Tytgat-lecture door prof. dr. M.J. Blaser kunt u zich begeven naar de Brabantzaal

18.40 Einde programma, congresborrel in expositiehal.

20.00 Diner in de Beneluxhal.

Carreer Development sessie — Baroniezaal

Voorzitters: P.C.F. Stokkers en A.Y. Thijssen

09.00 Career Development sessie met panel discussie georganiseerd door de NVMDLi.o.

10.00 Sluiting

DEGH oral presentations — Baroniezaal

Voorzitters: E. Nieuwenhuis en E.H.H.M. Rings

10.30 Novel approaches in pediatrics for replacement of the diseased liver and gut: the clinical incentive, recent concepts and current challenges

Prof. dr. E.E.S. Nieuwenhuis, kinderarts-MDL, Universitair Medisch Centrum Utrecht en
Prof. dr. E.H.H.M. Rings, kinderarts-MDL, Erasmus MC/Sophia Kinderziekenhuis, Rotterdam

Voordrachten in het Engels, spreektijd 8 minuten, discussietijd 4 minuten

11.20 Induction of ER stress identifies Id2 as a potential esophageal stem cell marker (p.98)

S.L. Rosekrans[1], B. Baan[1], E.J. Westerlund[1], C.A.J. Puylaert[1], J. Heijmans[1], V. Muncan[1], G.R. van den Brink[1,2], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, the Netherlands, [2]Department of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, the Netherlands

11.32 Genetic variants of recipient PD-1 and donor PD-L1 affect risk of acute rejection after liver transplantation (p.99)

X-L. Shi[1], S. Mancham[1], B.E. Hansen[1], L.J.W. van der Laan[2], H.J. Metselaar[1], J. Kwekkeboom[1] , [1]Department of Gastroenterology and Hepatology, [2]Department of Surgery, Erasmus MC – University Medical Center, Rotterdam, The Netherlands

11.44 CMV primary infection is associated with donor-specific T-cell hyporesponsiveness and fewer late acute rejections after liver transplantation (p.100)

X. Shi[1,5], E.L.D. de Mare-Bredemeijer[1], Ö. Tapirdamaz[1], B.E. Hansen[1], Rogier van Gent[1], M.J.H. van Campenhout[1], S. Mancham[1], N.H.R. Litjens[2], M.G.H. Betjes[2], A.A. van der Eijk[3], Q. Xia[5], L.J.W. van der Laan[4], J. de Jonge[4], H.J. Metselaar[1], J. Kwekkeboom[1,] , [1]Department of Gastroenterology and Hepatology, [2]Department of Internal Medicine, [3]Department of Virology, [4]Department of Surgery, Erasmus MC - University Medical Center, Rotterdam, The Netherlands, [5]Department of Liver Surgery, Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China*

11.56 Lunchpauze

DEGH oral presentations — Baroniezaal

Voorzitters: Q. Pan en K.F.J. van de Graaf

13.00 Liver inflammation
Dr. Q. Pan, onderzoeker i.o., Erasmus MC, Rotterdam en dr. K.F.J. van de Graaf, assistant professor, Academisch Medisch Centrum, Amsterdam

Voordrachten in het Engels, spreektijd 8 minuten, discussietijd 4 minuten

13.20 Low soluble CD14 in neonates may prevent immune activation by Hepatitis B surface antigen (p.101)

N. van Montfoort[1], E. van der Aa[1], A. van den Bosch[1], H. Brouwers[1], H. Javanbakht[2] and A. Woltman[1], [1]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, The Netherlands, [2]Infectious Diseases Discovery & Translational Area, Roche Innovation Center Basel Switzerland

13.32 Long-term therapy-induced viral clearance in chronic HCV does not lead to normalization of the intrahepatic T cell compartment (p.102)

M. Spaan[1], M.A.A. Claassen[1,2], H.L.A. Janssen[1,3], R.J. de Knegt[1], A. Boonstra[1], [1]Department of Gastroenterology and Hepatology, [2]Department of Internal Medicine, Infectious Diseases Unit, Erasmus MC University Hospital, Rotterdam, The Netherlands. [3]Department of Gastroenterology and Hepatology, University Health Network, Toronto Western Hospital, Canada

13.44 NK Cell Characteristics in Chronic Hepatitis B Patients are Associated with HBsAg Clearance After Combination Treatment with Peginterferon Alfa-2a And Adefovir (p.103)

F. Stelma[1,2], A. de Niet[1,2], R.B. Takkenberg[1], L. Jansen[1,2], H.L.A. Janssen[3], M.J. Tempelmans Plat-Sinnige[2], N.A. Kootstra[2], E.M.M. van Leeuwen[2], and H.W. Reesink[1,2], [1]Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Experimental Immunology, Academic Medical Center, Amsterdam, The Netherlands. [3]Department of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands; Toronto Centre for Liver Disease, Toronto Western & General Hospital, University Health Network, Toronto, Canada.

13.56 IgG4+ B-cell receptor clones in peripheral blood distinguish IgG4-associated cholangitis/autoimmune pancreatitis from primary sclerosing cholangitis (p.104)

L.M. Hubers[1,2], M.E. Doorenspleet[3,4]*, E. Culver[5,6], L.J. Maillette de Buy Wenniger[1,2], P.L. Klarenbeek[3,4], S.F. van de Graaf[2], J. Verheij[7], T. van Gulik[8], F. Baas[9], E. Barnes[5,6,10], N. de Vries[3,4], U. Beuers[1,2], [1]Gastroenterology and Hepatology, [2]Tytgat Institute of Liver and Intestinal Research, [3]Clinical Immunology and Rheumatology, [4]Laboratory of Experimental Immunology, Academic Medical Center, Amsterdam, Netherlands; [5]Translational Gastroenterology Unit, John Radcliffe Hospital, [6]NDM, Oxford University, Oxford, United Kingdom; [7]Pathology, [8]Experimental Surgery, [9]Genome Analysis, Academic Medical Center, Amsterdam, Netherlands, [10]Oxford NIHR Biomedical Research Center, Oxford University, Oxford, United Kingdom; *Contributed equally*

14.08 KIR ligand HLA-C2 is associated with immune activity and response to Peginterferon and Adefovir in HBeAg-positive chronic hepatitis B patients (p.105)

L..Jansen[1,2], F. Stelma[1,2], M.J. Tempelmans Plat-Sinnige[2], R.B. Takkenberg[1], E.M.M. van Leeuwen[2], N.A. Kootstra[2], H.W. Reesink[1,2], [1]Department of Gastroenterology and Hepatology, Academic Medical Center, [2]Department of Experimental Immunology, Academic Medical Center, Amsterdam, The Netherlands

Battle — Baroniezaal

Voorzitter: R.K. Weersma

14.20 Battle Basale Junior Onderzoekers Prijs SEG
Battle beste leverpublicatie van de NVH

15.00 Theepauze en ledenvergadering NVH

Donderdag 19 maart 2015

DEGH oral presentations — Baroniezaal

Voorzitters: H. Smidt en W.J. Wiersinga

Special guest: M.J. Blaser

Voordrachten in het Engels, spreektijd 8 minuten, discussietijd 4 minuten

15.30 Antibiotics, microbiota and the immune response
Dr. W.J. Wiersinga, internist, Academisch Medisch Centrum, Amsterdam

15.55 The intestinal microbiota in GI diseases: bridging the gap from composition to functionality
Prof. dr. H. Smidt, hoogleraar Microbiële ecologie, Wageningen Universiteit

16.20 Large-scale Case-Control Study Identifies Relations between the Microbiome and Disease Duration and Activity in Crohn's Disease and Ulcerative Colitis (p.106)
Imhann F.[1], Vich Vila A.[1], Bonder M.J.[2], Spekhorst L.M.[1], Festen E.A.M.[1], Dekens J.A.M.[2,3], Van Dullemen H.M.[1], Ter Steege R.[1], Van Sommeren S.[1], Tigchelaar E.F.[2,3], Cenit M.C.[2], Franke L.[2], Fu J.[2], Dijkstra G.[1], Huttenhower C.H.[6], Gevers D.[5], Xavier R.J.[4,5], Wijmenga C.[2,3], Zhernakova A.[2,3], Weersma R.K.[1], [1]Department of Gastroenterology and Hepatology, University Medical Center Groningen, the Netherlands, [2]Department of Genetics, University Medical Center Groningen, the Netherlands, [3]Top Institute Food and Nutrition, Wageningen, the Netherlands [4] Massachusetts General Hospital, Boston, USA, [5]Broad Institute of Harvard and MIT, Boston, USA, [6]Harvard School of Public Health, Harvard University, Boston, USA

16.32 Gut microbiota and lipid metabolism in humans (p.107)
J. Fu[1,2], M.J. Bonder[1], M.C. Cenit[1], E. Tighchelaar[1], M. Hofker[2], L. Franke[1], C. Wijmenga[1], A. Zhernakova[1], [1]Department of Genetics, UMCG, University of Groningen, [2]Department of Pediatrics, UMCG, University of Groningen

16.44 The influence of a short term gluten free diet on the human gut microbiome (p. 108)
M.J. Bonder[1], X. Cai[3*], E.F. Tigchelaar[1,2*], G. Trynka[1,4], M.C. Cenit[1], B. Hrdlickova[1], H. Zhong[3], D. Gevers[4], C. Wijmenga[1,2], Y Wang[3#], A. Zhernakova[1,2#], [1]Department of Genetics, University of Groningen, UMCG, the Netherlands. [2]TIFN, Wageningen, the Netherlands. [3]BGI-Shenzhen, 518083, China. [4]Broad Institute of MIT and Harvard, Cambridge, MA, USA.*

16.56 Einde programma

18.00 **Tytgat lecture – Brabantzaal**
The role of the gut microbiota in health and disease
Prof. dr. M.J. Blaser, Professor of Microbiology, Director, Human Microbiome Program, New York University Langone Medical Center

Nederlandse Vereniging voor Gastrointestinale Chirurgie — Parkzaal

Voorzitters: J. Omloo en E. Wassenaar

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

09.30 Early postoperative progression to solid foods is safe in Roux-en-Y gastric bypass procedure: a review of 936 patients (p.109)

C.M.J. Theunissen[1], J.K. Maring[1], N.J.C. Raeijmaekers[2], I.S. Martijnse[1], B.S. Langenhoff[1], [1]Dept of Surgery and [2]Dept of Nutrition, Elisabeth - TweeSteden Hospital, Tilburg, The Netherlands

09.40 Serious Postoperative Complications Affect Early Recurrence After Cyto-reductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis (p.110)

G.A. Simkens[1], T.R. van Oudheusden[1], M.D. Luyer[1], S.W. Nienhuijs[1], G.A. Nieuwenhuijzen[1], H.J. Rutten[1], I.H. de Hingh[1], [1]Dept of Surgical Oncology, Catharina Hospital, Eindhoven, [2]Dept of Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands

09.50 Molecular profile of young esophageal adenocarcinoma patients (p.111)

A.M.J. van Nistelrooij[1,2], R. Van Marion[1], K. Biermann[1], M.K. Casparie[3], J.J.B. van Lanschot[2], B.P.L. Wijnhoven[2], W.M.N. Dinjens[1], [1]Dept of Pathology and [2]Dept of Surgery, Erasmus MC Cancer Institute, Rotterdam, [3]Stichting PALGA, Utrecht, The Netherlands

10.00 SNPs associated with esophageal adenocarcinoma (p.112)

A.M.J. van Nistelrooij[1,2], H.A.G.M van der Korput[1], L. Broer[3], R. van Marion[1], M.I. van Berge Henegouwen[4], C.J. van Noesel[5], K. Biermann[1], V.M.C.W. Spaander[6], H.W. Tilanus[2], J.J.B. van Lanschot[2], A. Hofman[7], A.G. Uitterlinden[3,7], B.P.L. Wijnhoven[2], W.N.M. Dinjens[1], [1]Dept of Pathology, [2]Dept of Surgery, [3]Dept of Internal Medicine, [6]Dept of Gastroenterology and Hepatology, and [7]Dept of Epidemiology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, [4]Dept of Surgery, and [5]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands

10.10 Diffusion-weighted magnetic resonance imaging (MRI) for the prediction of response to neoadjuvant chemoradiotherapy in esophageal cancer (p.113)

P.S.N. van Rossum[1,2], A.L.H.M.W. van Lier[2], M. van Vulpen[2], O. Reerink[2], S.H. Lin[3], R. van Hillegersberg[1], J.P. Ruurda[1], G.J. Meijer[2], I.M. Lips[2], [1]Dept of Surgery, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Dept of Radiotherapy, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Dept of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston (Texas), USA.

10.20 The influence of sarcopenia and sarcopenic obesity on survival after major liver resection for colorectal liver metastases (p.114)

F. de Graaff[1,2], S. Mensink[2], M. Brusse-Keizer[3], D.E. Bouman[4], C.H. Slump[2], J.M. Klaase[1], [1]Dept of Surgery, Medisch Spectrum Twente, Enschede, [2]Faculty of Science and Technology, University of Twente, Enschede, [3]Medical School Twente, Medisch Spectrum Twente, Enschede, [4]Dept of Radiology, Medisch Spectrum Twente, Enschede, The Netherlands

10.30 Longterm quality of life after anastomotic leakage following colorectal surgery. A multicentre, case-matched cohort (p.115)

J.J. van den Broek1, D. Hogerzeil2, K. de Valk2, F. Daams3, J.F. Lange4, 1Medical Center Alkmaar, Alkmaar, 2Erasmus Medical Center, Rotterdam, 3VU Medical Center, Amsterdam, The Netherlands

10.40 Trends in patterns of care for resectable esophageal cancer in the Netherlands: a population based study (p.116)

M. Koëter[1], M. van Putten[2], R.H.A. Verhoeven[2], V.E.P.P. Lemmens[2,3], G.A.P. Nieuwenhuijzen[1], [1]Dept of Surgery, Catharina Hospital, Eindhoven, [2]Comprehensive Cancer Center South, Eindhoven, [3]Dept of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands

10.50 Effect of co-morbidity on the probability to receive definitive chemoradiotherapy or surgery and the impact on survival in esophageal cancer patients: a population-based study (p.117)

Z. Faiz[1], M. van Putten[2], R.H.A. Verhoeven[2], J.W. van Sandick[3], G.A.P. Nieuwenhuijzen[4], V.E. Lemmens[2], B.P.L. Wijnhoven[5], J.T.M. Plukker[1], [1]Dept of Surgery, University Medical Center Groningen, Groningen, [2]Netherlands Comprehensive Cancer Organization (IKNL), [3]Dept of Surgery, Dutch Cancer Institute - Antoni van Leeuwenhoek, [4]Dept of Surgery, Catharina Hospital, Eindhoven, [5]Dept of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

11.00 Survival after distal pancreatectomy for pancreatic ductal adenocarcinoma: a nationwide retrospective cohort study (p.118)

T. de Rooij[1], J.A. Tol[1], C.H. van Eijck[2], D. Boerma[3], B.A. Bonsing[4], K. Bosscha[5], R.M. van Dam[6], M.G. Dijkgraaf[7], M.F. Gerhards[8], H. van Goor[9], E. van der Harst[10], I.H. de Hingh[11], G. Kazemier[12], J.M. Klaase[13], I.Q. Molenaar[14], G.A. Patijn[15], H.C. van Santvoort[1], J.J. Scheepers[16], G.P. van der Schelling[17], E. Sieders[18], O.R. Busch[1], M.G. Besselink[1] for the Dutch Pancreatic Cancer Group, [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Surgery, Erasmus Medical Center, Rotterdam, [3]Dept of Surgery, St Antonius Hospital, Nieuwegein, [4]Dept of Surgery, Leiden University Medical Center, Leiden, [5]Dept of Surgery, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Surgery, Maastricht University Medical Center, Maastricht, [7]Clinical Research Unit, Academic Medical Center, Amsterdam, [8]Dept of Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, [9]Dept of Surgery, Radboud University Medical Center, Nijmegen, [10]Dept of Surgery, Maasstad Hospital, Rotterdam, [11]Dept of Surgery, Catharina Hospital, Eindhoven, [12]Dept of Surgery, VU University Medical Center, Amsterdam, [13]Dept of Surgery, Medisch Spectrum Twente, Enschede, [14]Dept of Surgery, University Medical Center Utrecht, Utrecht, [15]Dept of Surgery, Isala Clincs, Zwolle, [16]Dept of Surgery, Reinier de Graaf Gasthuis, Delft, [17]Dept of Surgery, Amphia Hospital, Breda, [18]Dept of Surgery, University Medical Center Groningen, Groningen, The Netherlands

11.10 First experience with laparoscopic pancreatoduodenectomy in the Netherlands (p.119)

M.W. Steen[1], M.F. Gerhards[1], S. Festen[1], [1]Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

11.20 Impact of upsizing percutaneous catheters in patients with suspected infected necrotizing pancreatitis (p.120)

J. van Grinsven[1,2], P. Timmerman[3], K.P. van Lienden[4], J.W. Haveman[3], D. Boerma[5], C.H. van Eijck[6], P. Fockens[1], H.C. van Santvoort[7], M.A. Boermeester[7], M.G. Besselink[7] for the Dutch Pancreatitis Study Group, [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dutch Pancreatitis Study Group, St. Antonius Hospital, Nieuwegein, [3]Dept of Surgery, University Medical Center Groningen, Groningen, [4]Dept of Radiology, Academic Medical Center, Amsterdam, [5]Dept of Surgery, St. Antonius Hospital, Nieuwegein, [6]Dept of Surgery, Erasmus Medical Center, Rotterdam, [7]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

11.30 Einde abstractsessie

Vrije voordrachten Ned. Vereniging voor Gastroenterologie — Parkzaal

Voorzitters: J. Hardwick en K.K. Krishnadath

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

13.00 Gamma-Delta T-Lymphocytes as diagnostic criterium in latent celiac disease (p.121)

P. Nijeboer[1], T. van Gils[1], R. Ooijevaar[1], H.J. Bontkes[2], C.J. Mulder[1], G. Bouma[1], [1]Dept of Gastroenterology, and [2]Dept of Pathology, VU University Medical Center, Amsterdam, The Netherlands

13.10 Medication-induced microscopic colitis: do recency and duration of use matter? (p.122)

B.P.M. Verhaegh[1,2], F. de Vries[3,4], A.A.M. Masclee[1,2], A. Keshavarzian[3], A. de Boer[3], P. Souverein[3], D.M.A.E. Jonkers[1,2], M.J. Pierik[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [2]NUTRIM, School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, [3]Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute of Pharmaceutical Sciences, Utrecht, [4]Clinical Pharmacology and Toxicology, Maastricht University Medical Center, Maastricht, The Netherlands

13.20 Incidence and treatment results of perianal and rectovaginal fistulizing Crohn's disease in a population-based cohort (p.123)

K.W.A. Göttgens[1], S.F.G. Jeuring[2,3], R. Sturkenboom[1], M.J.L. Romberg-Camps[4], G.L. Beets[1], L.E. Oostenbrug[5], L.P.S. Stassen[1], M.J. Pierik[2,3], S.O. Breukink[1], [1]Dept of Surgery, and [2]Division of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [3]School for Nutrition, Toxicology and Metabolism (NUTRIM), Maastricht UMC, Maastricht, [4]Dept of Internal Medicine and Gastroenterology, Orbis Medical Center, Sittard-Geleen, [5]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center, Heerlen, The Netherlands

13.30 Human splanchnic amino acid metabolism (p.124)

E.P.J.G. Neis[1,2], S.S. Rensen[1], H.M.H. van Eijk[1], M. Arts[1], S.W. Olde Damink[1], E.E. Blaak[2,3], C.H.C. Dejong[1,2], [1]Dept of Surgery, NUTRIM, Maastricht University, Maastricht, [2]Top Institute Food and Nutrition, Wageningen, [3]Dept of Human Biology, NUTRIM, Maastricht University, Maastricht, The Netherlands

13.40 Disease progression is a risk factor for colectomy in ulcerative colitis: 10-years of follow up in a tertiary care facility (p.125)

S. Sahami[1,2], K. Konté[1], C.J. Buskens[2], P.J. Tanis[2], M.L. Lowenberg[1], C.J. Ponsioen[1], G.R. van den Brink[1], W.A. Bemelman[2], G.R. D'Haens[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

13.50 Multiple in-hospitals transfers promote spread of Clostridium difficile infection in the hospital (p.126)

Y.H. van Beurden[1,2], O.M. Dekkers[3,4], A.M. Kaiser[1], M.K. Bomers[5], R. van Houdt[1], C.W. Knetsch[6], C.J.J. Mulder[2], C.M.J.E. Vandenbroucke-Grauls[1], [1]Dept of Medical Microbiology and Infection Control, [2]Dept of Gastroenterology and Hepatology, and [5]Dept of Internal Medicine, VU University Medical Center, Amsterdam, [3]Dept of Clinical Epidemiology, [4]Dept of Endocrinology and Metabolic Diseases, and [6]Dept of Medical Microbiology, Leiden University Medical Center, Leiden, The Netherlands

14.00 Clinical and genetic characterization of patients with graft-vs.-host disease after allogeneic hematopoietic cell transplantation suggests a role for JAK2, IL2RA and HLA-DRB1 (p.127)

S. van Sommeren[1,2], H.M. de Jonge[3], J. Kuball[4], L. te Boome[4], E. Vellenga[5], G. Huls[6], R.K. Weersma[1], [1]Dept of Gastroenterology, Univ. Medical Center Groningen, Groningen, [2]Dept of Genetics, Univ. Medical Center Groningen, Groningen, [3]Dept of Gastroenterology, Isala klinieken, Zwolle, [4]Dept of Hematology, University Medical Center Utrecht, Utrecht, [5]Dept of Hematology, Univ. Medical Center Groningen, Groningen, [6]Dept of Hematology, Radboud University Medical Center, Nijmegen, The Netherlands

14.10 Arabinoxylans show distinct prebiotic properties and may affect intestinal barrier function (p.128)

B. Salden[1], F.J. Troost[1], E. Wilms[1], F. Brüll[2], P. Truchado[3], T. Van de Wiele[3], S. Possemiers[3], A. Masclee[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, NUTRIM, Maastricht University Medical Center, Maastricht, The Netherlands, [2]BioActor BV, Maastricht, The Netherlands, [3]Laboratory of Microbial Ecology and Technology, Ghent University, Ghent, Belgium

14.20 Early detection of necrotizing enterocolitis by faecal volatile organic compounds analysis by electronic nose compared to the intestinal microbiota (p.129)

T.G.J. de Meij1, M.P.C. van der Schee2, M.E. van de Velde1, D.J.C. Berkhout1, A.E. Budding3, E.F.J. de Groot1, B.W. Kramer4, A.H. van Kaam5, M.M. van Weissenbruch6, P. Andriessen5, J.B. van Goudoever6, P.H.M Savelkoul3, H.J. Niemarkt4, N.K.H. de Boer7, 1Dept of Pediatric Gastroenterology, VU Medical Center, Amsterdam, 2Dept of Pediatric Pulmonology, Academic Medical Center, Amsterdam, 3Dept of Microbiology and Infection control, VU University Medical Center, Amsterdam, 4Dept of Neonatology, University Medical Center Maastricht, Maastricht, 5Dept of Neonatology, Academic Medical Center, Amsterdam, 6Dept of Neonatology, VU University Medical Center, Amsterdam, 7Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, The Netherlands

14.30 Colorectal cancer resections in the oldest old between 2011 and 2013 in The Netherlands (p.130)

N.M. Verweij[1], A.H.W. Schiphorst[1], A. Pronk[1], M.E. Hamaker[2], [1]Dept of Surgery, and [2]Dept of Geriatric Medicine, Diakonessenhuis, Utrecht, The Netherlands

14.40 **MLDS-voordracht**

Differential induction of mucosal tolerance in the small and large intestine (p.131)

S. Veenbergen[1], L.A. van Berkel[1], M. Fleur du Pré[1], J. He[2], Y. Simons-Oosterhuis[1], F. Luk[1], A.M. Mowat[3], B.L. Kelsall[2], J.N. Samsom. [1]Dept. of Pediatric Gastroenterology, Erasmus Medical Center - Sophia Children's Hospital, Rotterdam, The Netherlands. [2]Mucosal Immunobiology Section, Laboratory of Molecular Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, USA. [3]Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, UK.

14.50 **MLDS-voordracht**
Epithelial to mesenchymal transition is not a factor in biliary atresia related liver fibrosis (p.132)
C.M.G. Keyzer-Dekker[1], R.C. Lind[1], J.F. Kuebler[1], C. Petersen[1], M. Davenport[1], J.B.F. Hulscher[1], [1]University Medical Center Groningen, Groningen, The Netherlands

15.00 Theepauze,expositie

Vrije voordrachten Sectie Neurogastroenterologie en Motiliteit — Parkzaal

Voorzitters: J.M. Conchillo en A.J.P.M. Smout

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

15.30 Complications of botulinum toxin injections for treatment of esophageal motility disorders (p.133)
F.B. van Hoeij[1], J.E. Pandolfino[2], J.M. Sternbach[2], S. Roman[3], J.F. Tack[4], A.J.P.M. Smout[1], A.J. Bredenoord[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States of America, [3]Dept of Physiology, Hospices Civils de Lyon, Lyon 1 University, Lyon, France, [4]Dept of Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium

15.40 Esophagogastric junction distensibility in the management of achalasia patients: relation to treatment outcome (p.134)
F.G.M. Smeets[1,2], A.A.M. Masclee[1,2], D. Keszthelyi[1,2], E.T.T.L. Tjwa[3], J.M. Conchillo[1,2], [1]Division of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [2]NUTRIM, School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, [3]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands

15.50 Pediatric achalasia in The Netherlands: diagnosis, management, follow-up and quality of life (p.135)
R. Vrijlandt1, M. Smits1, M. van Lennep1, M. Benninga1, R. Houwen2, F. Kokke2, D. van der Zee3, H. Escher4, A. van den Neucker5, T. de Meij6, F. Bodewes7, J. Schweizer8, G. Damen9, M. van Wijk1, 1Dept of Pediatric Gastroenterology, Emma Child's Hospital, Academic Medical Center, Amsterdam, 2Dept of Pediatric Gastroenterology, Wilhemina Children's Hospital, University Medical Center Utrecht, Utrecht, 3Dept of Pediatric Surgery, University Medical Center Utrecht, Utrecht, 4Dept of Pediatric Gastroenterology, Sophia Children's Hospital, Erasmus Medical Center, Rotterdam, 5Dept of Pediatric Gastroenterology, Maastricht University Medical Center, Maastricht, 6Dept of Pediatric Gastroenterology, VU Medical Center, Amsterdam, 7Dept of Pediatric Gastroenterology, Beatrix Children's Hospital, University Medical Center Groningen, Groningen, 8Dept of Pediatric Gastroenterology, Willem-Alexander Child's hospital, University Medical Center Leiden, Leiden, 9Dept of Pediatric Gastroenterology, Radboud University Medical Center, Nijmegen, The Netherlands*

Donderdag 19 maart 2015

16.00 Esophageal epithelial barrier function in Non-Erosive Reflux Disease (NERD) patients: a barrier defect? (p.136)

N.F. Rinsma[1], R.M. Farré[2], F.J. Troost[1], M. Elizalde[1], A.A. Masclee[1], J.M. Conchillo[1], [1]Division of Gastroenterology and Hepatology, NUTRIM, Maastricht University Medical Center, Maastricht, The Netherlands, [2]Translational Research Center for Gastrointestinal Disorders, Catholic University Leuven, Belgium - Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, (Ciberehd), Instituto de Salud Carlos III, Spain

16.10 Brain processing of rectal sensation in children with functional defecation disorders and healthy controls (p.137)

I.J.N. Koppen[1], S.M. Mugie[1], M.M. van den Berg[2], P.F.C. Groot[3], L. Reneman[3], A.J. Nederveen[3], M.B. de Ruiter[3], M.A. Benninga[1], [1]Dept of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Emma Children's Hospital, Amsterdam, [2]Dept of Pediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, [3]Dept of Radiology, Academic Medical Center, Amsterdam, The Netherlands

16.20 Chait cecostomy catheter in adults for chronic obstipation: substantial morbidity and moderate functional results (p.138)

A.K.E. Elfrink[1], B. van den Heuvel[1], M. Ankersmit[1], P.F. Vollebregt[2], R.F. Felt-Bersma[2], J.B. Tuynman[1], W.J.H.J. Meijerink[1], [1]Dept of Surgery, and [2]Dept of Gastroenterology, VU University Medical Center, Amsterdam, The Netherlands

16.30 Utilising high-resolution colonic manometry to quantify dysmotility in children with slow transit constipation (p.139)

S. Kuizenga-Wessel[1], I.J.N. Koppen[1], M.A. Benninga[1], L. Wiklendt[2], P.G. Dinning[2,3], [1]Dept of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Emma Children's Hospital, Amsterdam, The Netherlands, [2]Human Physiology, Flinders University, Adelaide, SA, Australia, [3]Gastroenterology and Surgery, Flinders Medical Centre, Adelaide, SA, Australia

16.40 Yoga therapy for children with functional abdominal pain disorders; a randomized controlled trial (p.140)

J.J. Korterink[1,2], L. Ockeloen[2], M. Hilbink[3], M.A. Benninga[2], J.M. Deckers-Kocken[4], [1]Dept of Pediatrics, Jeroen Bosch Hospital, 's Hertogenbosch, [2]Dept of Pediatric Gastroenterology and Nutrition, Emma Children's Hospital, Academic Medical Center, Amsterdam, [3]Jeroen Bosch Academy, Jeroen Bosch Hospital, 's Hertogenbosch, [4]Kinderbuik&co, Bilthoven, The Netherlands

16.50 Laparoscopic ventral recto(vagino)pexy is a safe surgical procedure for elderly patients with a rectal prolapse or rectocele (p.141)

S.C.N. Plasschaert[1], E.J.R. de Graaf[1], M.M.M. Bruijninckx[1], M. Vermaas[1], P.G. Doornebosch[1], [1]Dept of Surgery, IJsselland Hospital, Capelle a/d IJssel, The Netherlands

17.00 Vervolg plenair programma in de Brabantzaal

Meet the expert sessie **Zaal 80**

Meet the expert sessie Functionele buikklachten*

Prof. dr. A.A.M. Masclee (MUMC)
Dr. L.A. van der Waaij (Martini Ziekenhuis Groningen)

groep 1: 13.00 – 14.00 uur

groep 2: 14.00 – 15.00 uur

** vanwege de grote belangstelling is deze sessie alleen toegankelijk voor deelnemers die zich hiervoor tevoren hebben ingeschreven*

Meet the expert sessie **Zaal 81**

Meet the expert sessie Poliepectomie*

Prof. dr. P. Fockens (AMC)
Prof. dr. B.L.A.M. Weusten (Antonius Ziekenhuis, Nieuwegein)

groep 1: 13.00 – 14.00 uur

groep 2: 14.00 – 15.00 uur

** vanwege de grote belangstelling is deze sessie alleen toegankelijk voor deelnemers die zich hiervoor tevoren hebben ingeschreven*

Symposium Sectie Gastrointestinale Endoscopie — Brabantzaal

Symposium Voeding en Endoscopie

Voorzitters: P. Didden en B.L.A.M. Weusten

09.30 Wat iedere endoscopist over sondevoeding moet weten
Mevr. M. van Asseldonk, MSc , diëtist Darmfalen Team Nijmegen Radboudumc, Nijmegen

09.45 Wanneer de maag, wanneer het duodenum?
Prof. dr. L. Mathus-Vliegen, MDL-arts, Academisch Medisch Centrum

10.05 Plaatsen van duodenumsondes: best practice
Prof. dr. B.J.M. Witteman, Gelderse Vallei, Ede

10.25 Help, een sondeprobleem!
M. Klos voedingsverpleegkundige, Gelre Ziekenhuis, Apeldoorn

10.40 Wanneer de transnasale route niet mogelijk / wenselijk is
J.F. Monkelbaan, MDL-arts, UMC Utrecht

11.00 Koffiepauze, expositie

Vrije voordrachten Sectie Gastrointestinale Endoscopie — Brabantzaal

Voorzitters: T.E.H. Römkens en R.C. Verdonk

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

11.30 Evaluation of the proximal serrated polyp detection rate as a valuable colonoscopy quality parameter (p.142)
J.E.G. IJspeert[1], S.C. van Doorn[1], B.A.J. Bastiaansen[1,2], P. Fockens[1,2], E. Dekker[1,2], [1]Dept of Gastro-enterology and Hepatology, Academic Medical Center, Amsterdam, [2]Procolo center for colonoscopy, Bergman Clinics, Amsterdam, The Netherlands

11.40 Development and validation of a classification system for optical diagnosis of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps (p. 143)

J.E.G. IJspeert[1], B.A.J. Bastiaansen[1], M.E. van Leerdam[2], J. Wang[3], S. van Eeden[4], S. Sanduleanu[5], E.J. Schoon[6], T. Bisseling[7], M.C. Spaander[8], N. van Lelyveld[9], M. Bigirwamungu-Bargeman[10], G.A. Meijer[11], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, [3]Dept of Clinical Epidemiology, Biostatistics and Bioinformatics, and [4]Dept of Pathology, Academic Medical Center, Amsterdam, [2]Dept of Gastroenterology and Hepatology, Netherlands Cancer Institute, Amsterdam, [5]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [6]Dept of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, [7]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [8]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [9]Dept of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, [10]Dept of Gastroenterology and Hepatology, Medical Spectrum Twente, Enschede, [11]Dept of Pathology, VU Medical Center, Amsterdam, The Netherlands

11.50 Measuring gaze patterns during colonoscopy: a useful tool to measure colon inspection? (p.144)

V.K. Dik[1], I.T.C. Hooge[2], M.G.H. Van Oijen[1,3], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Experimental Psychology and Helmholtz Institute, Utrecht University, Utrecht, [3]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

12.00 Colonoscopy with robotic steering and automated lumen centralization compared with conventional colonoscopy: results of a randomized in vitro pilot study (p.145)

H.J.M. Pullens[1,2], N. van der Stap[3,4], E.D. Rozeboom[3], M.P. Schwartz[1], F. van der Heijden[3], M.G.H. van Oijen[2,5], P.D. Siersema[2], I.A.M.J. Broeders[3,4], [1]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [2]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [3]Dept of Robotics and Mechatronics, University of Twente, Enschede, [4]Dept of Surgery, Meander Medical Center, Amersfoort, [5]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

12.10 Direct peroral cholangioscopic visualization can be helpful in differentiating benign and malign indeterminate bile duct lesions (p.146)

A.B. de Vries[1], K.T. Buddingh[4], A.S.H. Gouw[2], V.B. Nieuwenhuijs[3], R.K. Weersma[1], [1]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, [2]Dept of Pathology, University of Groningen, University Medical Center Groningen, Groningen, [3]Dept of Surgery, Isala, Zwolle, [4]Dept of Urology, Haga Ziekenhuis, Den Haag, The Netherlands

12.20 Endoscopic ultrasound-guided visualization of celiac ganglia and celiac ganglia neurolysis: results of a clinical cross-sectional and human cadaver study (p.147)

W.F.W. Kappelle[1], R.L.A.W. Bleys[2], A.J.M. Van Wijck[3], R. Stellema[3], P.D. Siersema[1], F.P. Vleggaar[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Anatomy, and [3]Dept of Anesthesiology, University Medical Center Utrecht, Utrecht, The Netherlands

12.30 A novel biodegradable non-covered self-expandable stent to treat pancreatic duct strictures in chronic pancreatitis; a pilot study (p.148)

D.L. Cahen[1], S.W. van der Merwe[2], J.W. Poley[1], M. J. Bruno[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Division of Gastroenterology and Hepatology, University Hospital Leuven, Belgium.

Vrijdag 20 maart 2015

12.40 Effects of radial and axial force of esophageal stents on occurrence of severe adverse events and recurrent dysphagia in patients with malignant dysphagia (p.149)
W.F.W. Kappelle[1], M.C.W. Spaander[2], M.J. Bruno[2], M. Leenders[1], M.M.C. Hirdes[1], F.P. Vleggaar[1], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands

12.50 Lunch, expositie

Symposium Sectie Gastrointestinale Oncologie — Brabantzaal

Voorzitters: J.J.G.H.M. Bergman en K.M.A.J. Tytgat

Diagnostiek en surveillance door de MDL-arts

14.00 Opening

14.05 Pancreasca
Dr. J.W. Poley, MDL-arts, Erasmus MC, Rotterdam

14.25 Methoden vroege ontdekking kanker
Dr. I. Lansdorp-Vogelaar, Maatschappelijke gezondheidzorg, Erasmus MC, Rotterdam

14.50 Achalasie
Dr. I. Leeuwenburgh, MDL-arts, St. Franciscus Gasthuis, Rotterdam

15.10 Maagkanker
Dr. A. Cats, MDL-arts, NKI Antoni van Leeuwenhoekhuis, Amsterdam

15.30 Nieuwe erfelijke CRC richtlijn
Dr. M.E. van Leerdam, MDL-arts, NKI Antoni van Leeuwenhoekhuis, Amsterdam

15.50 Einde symposium

Vrije voordrachten Sectie Gastrointestinale Oncologie — Auditorium

Voorzitters: M. Bigirwamungu en R.W.M. Schrauwen

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

09.30 Inleiding op het programma

09.40 FIT-based colorectal cancer screening: do we need to tailor screening for men and women? (p.150)

E.J. Grobbee[1], E.M. Stoop[1], T.R. de Wijkerslooth[2], I. Lansdorp-Vogelaar[3], P.M. Bossuyt[4], E. Dekker[2], E.J. Kuipers[1], M.C.W. Spaander[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [3]Dept of Public Health, Erasmus University Medical Center, Rotterdam, [4]Dept of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam, The Netherlands

09.50 Surgical resection for T1 colorectal carcinoma is associated with improved recurrence free survival (p.151)

T.D.G. Belderbos[1], F.N. van Erning[2], I.H.J.T. de Hingh[3], M.G.H. van Oijen[4], L.M.G. Moons[1], V.E.P.P Lemmens[2], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Eindhoven Cancer Registry, Eindhoven, [3]Dept of Surgery, Catharina Hospital, Eindhoven, [4]Dept of Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands

10.00 Lower risk of metastatic disease in pedunculated polyps containing T1 colorectal carcinoma compared to lateral spreading tumors (p.152)

A. van den Blink[1], A. Overwater[1], M.G.H. van Oijen[1], B.W.M. Spanier[2], T.C.J. Seerden[3], H.J.M. Pullens[4], W.H. de Vos tot Nederveen Cappel[5], G.J.A. Offerhaus[6], D.J. Bac[7], M. Kerkhof[8], K. Kessels[9], P.D. Siersema[1], M.M. Lacle[6], L.M.G. Moons[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Rijnstate, Arnhem, [3]Dept of Gastroenterology and Hepatology, Amphia Hospital, Breda, [4]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [5]Dept of Gastroenterology and Hepatology, Isala, Zwolle, [6]Dept of Pathology, University Medical Center Utrecht, Utrecht, [7]Dept of Gastroenterology and Hepatology, Gelderse Vallei, Ede, [8]Dept of Gastroenterology and Hepatology, Groene Hart Hospital, Gouda, [9]Dept of Gastroenterology and Hepatology, Flevo hospital, Almere, The Netherlands

10.10 Organ preservation for patients with a complete clinical response after neoadjuvant chemoradiotherapy for rectal cancer: Selection and follow-up (p.153)

M.H. Martens[1,2], L.A. Heijnen[1,2], M. Maas[2], D.M.J. Lambregts[2], L.P.S. Stassen[1], S.O. Breukink[1], J.W.A. Leijtens[3], C Hoff[4], R.G.H. Beets-Tan[2], G.L. Beets[1], [1]Dept of Surgery, and [2]Dept of Radiology, Maastricht University Medical Center, Maastricht, [3]Dept of Surgery, Laurentius Hospital, Roermond, The Netherlands

Vrijdag 20 maart 2015

10.20 Systemic treatment of patients with metachronous peritoneal carcinomatosis of colorectal origin (p.154)

T.R. van Oudheusden[1,2], Y.R. van Gestel[2], L. Razenberg[2,3], G.J. Creemers[3], V.E. Lemmens[2], I.H. de Hingh[1], [1]Dept of Surgery, and [3]Dept of Internal Medicine, Catharina Hospital, Eindhoven, [2]Dept of Research, Eindhoven Cancer Registry, Comprehensive Cancer Center The Netherlands (IKNL), Eindhoven, The Netherlands

10.30 Systematic assessment of quality of patient information on colorectal cancer screening on the internet (p.155)

E.H. Schreuders[1], E.J. Grobbee[1], E.J. Kuipers[1], M.C.W. Spaander[1], S.J.O. Veldhuyzen van Zanten[2], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [2]Division of Gastroenterology, University of Alberta Hospital, Edmonton, Alberta, Canada

10.40 Tolerability of neo-adjuvant chemoradiotherapy with capecitabine and surgical outcomes in patients aged 70 years or older with locally advanced rectal cancer (p.156)

L. Jacobs[1], E. van der Vlies[2], D. ten Bokkel Huinink[3], H.J. Bloemendal[4], P.D. Siersema[5], B.L.A.M. Weusten[1], N. van Lelyveld[1], M. Los[6], [1]Dept of Gastroenterology, and [2]Dept of Internal Medicine, St Antonius Hospital, Nieuwegein, [3]Dept of Oncology, Diakonessenhuis, Utrecht, [4]Dept of Oncology, Meander Medical Center, Amersfoort, [5]Dept of Gastroenterology, University Medical Center Utrecht, Utrecht, [6]Dept of Oncology, St Antonius Hospital, Nieuwegein, The Netherlands

10.50 Koffiepauze, expositie

Vervolgprogramma met voordrachten Sectie Gastrointestinale Oncologie vindt plaats in de **Parkzaal**

State of the Art lecture **Auditorium**

11.30 **EUS: van diagnostiek naar interventie**
Dr. F. Vleggaar, MDL-arts, UMC Utrecht

Radiologie symposium **Auditorium**

Voorzitters: J.J. Keller en F. Vleggaar

12.00 PET voor stadiëren tractus digestivus tumoren?
Dr. E.F.I. Comans, nucleair geneeskundige, MC Haaglanden, Den Haag

12.20 Pancreaskopcarcinoom of auto-immuun pancreatitis?
Dr. M. van Leeuwen, radioloog, Universitair Medisch Centrum Utrecht

12.40 CT-colonografie: voor de dagelijkse praktijk of alleen bij incomplete colonoscopie?
Prof. dr. J. Stoker, radioloog, Academisch Medisch Centrum, Amsterdam

13.00 Einde symposium, lunch in de expositiehal.

Poster rounds DEGH meeting *(including breakfast buffet)* **Zaal 19**

09.00 – 10.00

Chairs: D.M.A.E. Jonkers and A.A. te Velde

1. BMP4 signaling is involved in epithelial-mesenchymal transition in Barrett's esophagus and esophageal adenocarcinoma through induction of SNAIL2

C. Kestens[1], P.D. Siersema[1], J.W.P.M. van Baal[1], [1]Dept. of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherlands

2. Portal release of the bile salt homeostatic factor FGF19 by the human gut

K.V.K. Koelfat1, F.G. Schaap1, J.G. Bloemen1, P.L.M. Jansen1, C.H.C. Dejong1, S.W.M. Olde Damink1, 1Department of Surgery, Maastricht University Medical Center and NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University, Maastricht, the Netherlands

3. Inhibition of BMP2 and BMP4 by a novel llama-derived nanobody sustains intestinal stem cells in organoid cultures

S. Calpe[1], A. Correia[1], M. El Khattabi[4], C.Zimberlin[3], J.P. Medema[3], C.T.Verrips[4], K.K. Krishnadath[1,2] ,[1]Center for Experimental & Molecular Medicine; [2]Department of Gastroenterology & Hepatology; [3]Laboratory for Experimental Oncology and Radiobiology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands. [4]QVQ BV, Utrecht, The Netherlands*

4. Dissecting crosstalk between hepatitis e virus infection and the 4e-bp1 translational regulator

X. Zhou[1], L. Xu[1] , W. Wang[1], K. Watashi[2], Y. Wang[1], D. Sprengers[1], H.L.A. Janssen[1, 3], P.E. de Ruiter[4], L.J.W. van der Laan[4], J. Neyts[5], H.J. Metselaar[1], N. Kamar[6,7,8], M.P. Peppelenbosch[1], and Q. Pan[1] ,[1]Department of Gastroenterology and Hepatology, Erasmus MC-University Medical Center and Postgraduate School Molecular Medicine, Rotterdam, Netherlands. [2]Department of Virology II, National Institute of Infectious Diseases, 1-23-1 Toyama, Shinjuku-ku, 162-8640 Tokyo, Japan. [3]Division of Gastroenterology, University Health Network, Toronto, Canada. [4]Department of Surgery, Erasmus MC-University Medical Center and Postgraduate School Molecular Medicine, Rotterdam, Netherlands. [5]Department of Microbiology and Immunology, Rega Institute for Medical Research, KU Leuven, Leuven, Belgium, [6]Department of Nephrology and Organ Transplantation, CHU Rangueil, France, [7]INSERM U1043, IFR–BMT, CHU Purpan, Toulouse, France, [8]Université Paul Sabatier, Toulouse, France*

5. Barrett's esophagus cell of origin does not derive from cytokeratin 5 expressing squamous cells in mice

D. Straub[1,2]; N. Buttar[3]; P. Fockens[1], K.K. Krishnadath[1,2], [1]Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, Netherlands. [2]Center for Experimental and Molecular Medicine (CEMM), Amsterdam, Netherlands. [3]Barrett Esophagus Unit, Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, MN, USA.

6. Relating genetic variants in IBD to aberrant cytokine profiles: a focus on TNFSF15

N.W. Duijvis[1], F.H. van Dooren[1], D. Oudejans[1], S.C. Wolfkamp[2], S. Keskin[1], E.W. Vogels[1], P. Henneman[3], P.C. Stokkers[4], G. D'Haens[2], W. de Jonge[1], A.A. te Velde[1], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, The Netherlands. [2]Dept. of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [3]Department of Clinical Genetics, Academic Medical Center, Amsterdam, The Netherlands. [4]Dept. of Gastroenterology and Hepatology, Sint Lucas Andreas Ziekenhuis, Amsterdam, the Netherlands

7. Toll-like receptor 2 enhanced lysosomal activity and endocytosis in a Barrett's esophagus cell line

R.E. Verbeek[1], P.D. Siersema[1], F.P. Vleggaar[1], F.J. ten Kate[2], G. Posthuma[3], R.F. Souza[4], J. de Haan[1], J.W.P.M. van Baal[1], [1]Dept. of Gastroenterology and Hepatology, [2]Dept. of Pathology, [3]Dept. of Cell Biology, Center for Electron Microscopy, University Medical Center Utrecht, Utrecht the Netherlands, [4]Dept. of Medicine, University of Texas Southwestern Medical Center, VA North Texas Health Care System, Dallas, Texas, USA

8. IFN-free therapy for chronic HCV: transcriptomics and NK cell analyses

M. Spaan[1], G. van Oord[1] , K. Kreefft[1], J. Hou[1], B.E. Hansen[1], H.L.A. Janssen[1,2], R.J. de Knegt[1], A. Boonstra[1], [1]Department of Gastroenterology and Hepatology, [2]Department of Gastroenterology and Hepatology, University Health Network, Toronto Western Hospital, Canada

9. Human plasma toxicity in differentiated HepaRG progenitor cells the context of the bioartificial liver

M. van Wenum[#], R.A.F.M. Chamuleau[#], E.J. Hendriks[*], T.M. van Gulik[*], R. Hoekstra[*#], [*]Experimental Surgery, [#]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, the Netherlands*

10. Establishment of genetically stable canine liver organoids for translational studies

Schotanus[1], Spee[1], Nantasanti[1], Kruitwagen[1], Huch[2], Vries[2], Clevers[2], Penning[1], Rothuizen[1], [1]Department of Clinical Sciences of Companion Animals, Utrecht University, Utrecht, the Netherlands. [2]Hubrecht Institution, Utrecht, the Netherlands

11. Simple coculture system shows mutualism between anaerobic faecalibacteria and epithelial Caco-2 cells

Sadaghian Sadabad M[1, 2], Tanweer Khan M., Blokzijl T.[3], Paglia G.[4,5], Dijkstra G.[2], Harmsen H.J.M[1*] and Faber KN[2*]. Departments of [1]Medical Microbiology, [2]Gastroenterology and Hepatology, [3]Laboratory Medicine, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. [4]Istituto Zooprofilattico Sperimentale di Puglia e Basilicata, Foggia, Italy. [5]Center for Systems Biology University of Iceland Reykjavik, Iceland. [*]These authors contributed equally to this study.*

12. Mitochondrial Bio-genesis in the context of the AMC-Bio-Artificial Liver

'Adam A.A.A., [2]Jongejan A., [2]Moerland P.D., [3]M.van Wenum, [3]Van Gulik T.M., â´R. Houtkooper, â´R. Wanders, Oude Elferink RP, 'Chamuleau R.A.F.M., ' [3]Hoekstra R., 'Tytgat Institute for Liver and Intestinal Research, [2]Bioinformatics Laboratory, Department of Clinical Epidemiology, Biostatistics and Bioinformatics, [3]Surgical Laboratory Academic Medical Center, University of Amsterdam, the Netherlands, â´AMC department of genetic and metabolic diseases

13. Expression of the short-chain fatty acid receptors GPR41 and GPR43 throughout the human ileum and colon

C.M. van der Beek[1,2], K. Lenaerts[1,2], M. van Avesaat[1,3], F.J. Troost[1,3], A.A.M. Masclee[1,3], C.H.C. Dejong[1,2], [1]Top Institute Food and Nutrition, Wageningen, the Netherlands, [2]Department of Surgery, and [3]Department of Internal Medicine, Division of Gastroenterology-Hepatology; NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, The Netherlands

Poster rounds DEGH meeting — Zaal 20

10.00 – 11.00

Chairs: D.M.A.E. Jonkers en A.A. te Velde

1. Modeling rotavirus infection and antiviral therapy using primary intestinal organoids

Y. Yin[1], M. Bijvelds[1], K. Knipping[2], Y. Wang[1], J. de Jonge[3], N. Tuysuz[4], D. ten Berge[4], D. Sprengers[1], L.J.W. van der Laan[3], H.J. Metselaar[1], H. de Jonge[1], M.P. Peppelenbosch[1], Q. Pan[1], [1]Department of Gastroenterology and Hepatology, Erasmus MC-University Medical Center, Rotterdam. [2]Nutricia Research Utrecht. [3]Department of Surgery, Erasmus MC-University Medical Center, Rotterdam. [4]Department of Cell Biology, Erasmus MC Stem Cell Institute, Erasmus MC-University Medical Center, Rotterdam

2. Interaction of BDCA3$^+$ dendritic cells with HBsAg specifically inhibits IFN-lambda production

E. van der Aa[1], P.J. Biesta[1], F.A. Ayhan[1], A. van den Bosch[1], N. van Montfoort[1], A.M. Woltman[1], [1]Erasmus MC University Medical Center

3. Tumor antigen expression in hepatocellular carcinoma in a low-endemic western area

K. Sideras[1], S. Bots[1], K. Biermann[2], D. Sprengers , W.G. Polak[3], J.N.M. Ijzerman[3], R.A. de Man[1], Q. Pan[1], S. Sleijfer[4], M.J. Bruno[1], J. Kwekkeboom[1], [1]Erasmus Medisch Centrum, afdeling Maag, Darm, en Leverziekten [2]Erasmus Medisch Centrum, afdeling Pathologie [3]Erasmus Medisch Centrum, afdeling Heelkunde Algemeen [4]Erasmus Medisch Centrum, afdeling Interne Oncologie

4. The actual usage and quality of experimental colitis models in preclinical efficacy testing

S.B. Zeeff[1], C. Kunne[1], A.A. te Velde[1], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam

5. Stool proteomics reveals novel candidate biomarkers for colorectal cancer screening

A.C. Hiemstra[1], S. Piersma[2], T.V. Pham[2], G. Oudgenoeg[2], G.L. Scheffer[1], S. Mongera[1], M.A. Komor[1], J. Terhaar Sive Droste[3], F.A. Oort[3], S.T. van Turenhout[3] , I. Ben Larbi[3], C.J.J. Mulder[3], B. Carvalho[1], R.J.A. Fijneman[1], C.R. Jimenez[2], G.A. Meijer[1], [1]Department of Pathology, [2]Medical Oncology, and [3]Gastro-enterology and Hepatology, VU University Medical Center, Amsterdam, The Netherlands

6. Next generation sequencing of circulating miRNAs: towards predictive biomarkers for celiac disease

I.L. Tan[1], R. Almeida[2], J. Di Tommaso[1], S. Vriezinga[3], Y. Li[1], R.K. Weersma[4], C. Wijmenga[1], M.L. Mearin[3], S. Withoff[1] on behalf of the PreventCD project group, [1]Department of Genetics, University of Groningen and University Medical Center Groningen, [2]Department of Genetics, Human Molecular Genetics Laboratory, Federal University of Paraná, Curitiba, Paraná, Brazil, [3]Department of Pediatric Gastroenterology, Leiden University and Leiden University Medical Center, [4]Department of Gastroenterology and Hepatology, University of Groningen and University Medical Center Groningen

7. Adult stem cell transplantation in a canine model for Wilsons disease

Spee B.[1], Schotanus B.A.[1], Kruitwagen H.S.[1], Geijsen N.[1,2], Penning L.C.[1], Rothuizen J.[1,] [1]Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands, [2]Hubrecht Institute and University Medical Center (UMC) Utrecht, Utrecht, The Netherlands

8. Selective Janus Kinase 1 inhibitor targets monocytes and tissue macrophages during DSS colitis

De Vries L.C.S.[1,2], Duarte J.M.[1], Hilbers F.W.M.[1], De Winther M.[4], Moerland P.D.[5], Woodrow M.D.[3], Sims M.J.[3], Ludbrook V.J.[3], D'Haens G.R.A.M.[2], De Jonge W.J.[1,2] ,[1]Tytgat Institute for Liver and Intestinal Research, AMC, Amsterdam, Netherlands, [2]Department of Gastroenterology and Hepatology, AMC, Amsterdam, Netherlands, [3]Kinase DPU, GlaxoSmithKline, Stevenage, United Kingdom, [4]Department of Medical Biochemistry, AMC, Amsterdam, Netherlands, [5]Department of Clinical Epidemiology, Biostatistics and Bioinformatics, AMC, Amsterdam, The Netherlands

9. Self-limited and acute to chronic HCV infections in at risk individuals result in phenotypically distinct NK cell compartments

R.A. de Groen[1], G. van Oord[1], Zwier M.A. Groothuismink[1] , H.L.A. Janssen[1,2], J. Schinkel[3], and A. Boonstra[1],[1]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, The Netherlands. [2]Liver Clinic University Health Network, Division of Gastroenterology, University of Toronto, Canada. [3]Department of Medical Microbiology, AMC, Amsterdam, The Netherlands

10. Histone deacetylases in inflammatory mucosa distinguish Crohn's disease from ulcerative colitis

J. de Bruyn[1] [2], R. Wichers[3], T. Radstake[3], J. Broen[3], G. D'Haens[1],[1]Academic Medical Center Amsterdam, Department of Gastroenterology and Hepatology, [2]Academic Medical Center Amsterdam, Tytgat Institute for Liver and Intestinal Research, [3]University Medical Center Utrecht / Wilhelmina Children's Hospital, Department of Rheumatology & Clinical Immunology

11. PKC / AP-1 signaling drives transcription of interferon-stimulated genes and exerts potent and broad antiviral activity

W. Wang[1], W. Yijin[1], X. Zhou[1], Y. Yin[1], L. Xu[1], D. Sprengers[1], H.J. Mason[1], Y. Debing[2], J. Neyts[2], M.P. Peppelenbosch[1], and Q. Pan[1,] [1]Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center and Post Graduate School in Molecular Medicine, Rotterdam, Netherlands, [2]Department of Microbiology and Immunology, Rega Institute for Medical Research, Katholieke Universiteit Leuven, Leuven, Belgium.*

12. Impact of Vasopressin AVP1a Receptor Gene Polymorphisms on mortality and renal failure in patients with acute decompensation of chronic liver disease

J.J. Schaapman[1], J.C. Kerbert[1], J.J. van der Reijden[1], A.A. Navarro[2], M. Pavesi[2], B. van Hoek[1], V. Arroyo[3], M. Bernardi[4], G. Soriano[5], M. Catalina[6], P. Aguilar[7], H.W. Verspaget[1], M.J. Coenraad[1], [1]Gastroenterology-Hepatology, Leiden University Medical Center, Leiden, Netherlands, [2]Data Management Centre, CLIFconsortium, [3]Gastroenterology-Hepatology, University of Barcelona, Barcelona, Spain, [4]Gastroenterology-Hepatology, University of Bologna, Bologna, Italy, [5]Gastroenterology, Hospital de la Santa Creu i Sant Pau, Barcelona, [6] Gastroenterology Hepatology, Hospital Gregorio Maranon, Madrid, [7]Gastroenterology- Hepatology, Hospital Reina Sofia, Cordoba, Spain*

13. De novo nucleotide biosynthesis pathway tightly regulates hepatitis e virus infection

Y. Wang, W. Wang, X. Zhou, D. Sprengers, H.J. Metselaar, M.P. Peppelenbosch, and Q. Pan, Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center and Post Graduate School in Molecular Medicine, Rotterdam, Netherlands.

11.00 Koffiepauze expositie

DEGH oral presentations — Baroniezaal

Voorzitters: G. Bouma en S.W.C. van Mil

Voordrachten in het Engels, spreektijd 8 minuten, discussietijd 4 minuten

11.30 Colorectal tumor prevention by progestins is critically dependent on postmenopausal hormone status (p.157)

M.C.B. Wielenga[1], J. Heijmans[1], M. Schukking[1], B. Meijer[1], P.S. Montenegro-Miranda[1], P.B. Hoyer[2], J.M. Amos-Landgraf[3,4], W.F. Dove[3,4], G.R. van den Brink[1], [1]Tytgat institute for Liver and Intestinal Research and Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, the Netherlands, [2]Department of Physiology, University of Arizona, Tucson, USA, [3]McArdle Laboratory for Cancer Research, Department of Oncology, University of Wisconsin–Madison, Madison, USA, [4]Laboratory of Genetics, University of Wisconsin–Madison, Madison, USA

11.42 Multi Layered columnar epithelium (MLCE) induced by bile at the squamo-columnar junction in mice originates from squamous and columnar cells (p.158)

D. Straub[1,2,] K. Parikh[1,2]; P. Fockens[1], K.K. Krishnadath[1,2], [1]Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, Netherlands. [2]Center for Experimental and Molecular Medicine (CEMM), Amsterdam, Netherlands.

11.54 Lipid phosphatase SHIP2 functions as oncogene in colorectal cancer by regulating PKB activation (p.159)

E. Hoekstra[1] , A.M. Das[2] , M. Willemsen[1] , C.J. van der Woude[1] , T.L.M. ten Hagen[2] , M.P. Peppelenbosch[1], G.M. Fuhler[1] ,Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands[1] Department of Surgery, Erasmus MC, University Medical Center Rotterdam, The Netherlands.[2]

12.06 miR-511-3p, embedded in the macrophage mannose receptor gene, contributes to experimental colitis (p.160)

S.E.M. Heinsbroek[i€± §] , M. Leonardo Squadrito[2] , R. Schilderink[i€±], F.W. Hilbers[i€±], M. Hofmann[i€±], A. Helmke[i€±], L. Boon[4], M.E. Wildenberg[i€±], J.J.T.H Roelofs[3], C.Y. Ponsioen[i€±], C.P. Peters[i€±] , A.A. te Velde[i€±], S. Gordon[5], M. De Palma[2], W.J. de Jonge[i€±], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, University of Amsterdam, AMC, Amsterdam, The Netherlands. [2] The Swiss Institute for Experimental Cancer Research (ISREC), École Polytechnique Fédérale de Lausanne (EPFL), Switzerland. [3]Department of Pathology, Academic Medical Center, University of Amsterdam, AMC, Amsterdam, The Netherlands. [4]Bioceros, Utrecht, The Netherlands. [5]Sir William Dunn School of Pathology, University of Oxford, Oxford, UK. [§]Corresponding author.

12.18 Homozygous disruption of the HNF1α-binding site in the UGT1A1 proximal promoter region results in Crigler-Najjar syndrome (p.161)

R. van Dijk[1], I. Mayayo Peralta[1], S. Aronson[1], R. Oude Elferink[1], A. Kattentidt[2], U.H.W. Beuers[1] and P. Bosma[1], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands. [2]Department of Clinical Genetics, Erasmus MC, Rotterdam, The Netherlands

12.30 Normal mucus composition is essential in colonic anastomotic healing in mice (p.162)

J.W.A.M. Bosmans[1,2], A.C.H.M. Jongen[1,2], G.M.H. Birchenough[3], M.J.J. Gijbels[4], E.E.L. Nyström[3], J.P.M. Derikx[1,2], N.D. Bouvy[1,2], G.C. Hansson[3], [1]Department of Surgery, Maastricht University Medical Center, Maastricht, the Netherlands. [2]NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University, Maastricht, the Netherlands. [3]Department of Medical Biochemistry, The Sahlgrenska Academy, University of Gothenburg, [4]Department of Pathology, Maastricht University Medical Centre+ Maastricht, Netherlands

12.42 Mesalazine and cigarette smoke inhibit neutrophil extracellular trap formation in vitro (p.163)

M.C. Buis[1], N. Sinnema[2], T. Blokzijl[1], K.N. Faber[1], J. Westra[2], G. Dijkstra[1], [1]Department of Gastroenterology and Hepatology, University of Groningen, University Medical Center, Groningen, The Netherlands. [2]Department of Rheumatology and Clinical Immunology, University of Groningen, University Medical Center, Groningen, The Netherlands.

12.54 Lunchpauze

DEGH oral presentations — Baroniezaal

Voorzitters: H. Blokzijl en R. Shiri-Sverdlov

14.00 Inflammation in liver and gut
Dr. J. Blokzijl, MDL-arts, Universitair Medisch Centrum Groningen en Dr. R.S. Shiri-Sverdlov, Universiteit Maastricht

Voordrachten in het Engels, spreektijd 8 minuten, discussietijd 4 minuten

14.50 Intestinal goblet cell and mucus alterations in obesity (p.164)
N. van Best[1], F. Segers[1], F.J. Verdam[1], C. de Jonge[1], K. Lenaerts[1], J.W. Greve[1], W.A. Buurman[1], S.S. Rensen[1],[1]Department of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

15.02 Delayed bile acid uptake with metabolic consequences in Na^+ -taurocholate cotransporting polypeptide knockout mice (p.165)
D. Slijepcevic[1], J.M. Donkers[1], C. Kaufman[2,3], C.G.K. Wichers[4], E.H. Gilglioni[1], F.A. Lempp[2], S. Duijst[1], D.R. de Waart[1], R.P.J. Oude Elferink[1], W. Mier[3], B. Stieger[5], U. Beuers[1], S. Urban[2,6] and K.F.J. van de Graaf[1], [1]Tytgat Institute for Liver and Intestinal Research & Department of Gastroenterology & Hepatology, AMC, Amsterdam, the Netherlands, [2]Department of Infectious Diseases, Molecular Virology, University Hospital Heidelberg, Germany, [3]Department of Nuclear Medicine, University Hospital Heidelberg, Germany, [4]Department of Molecular Cancer Research, Section Metabolic Diseases, University Medical Center Utrecht, the Netherlands, [5]Department of Clinical Pharmacology and Toxicology, University Hospital Zurich, Switzerland, [6]German Center for Infection Research, Heidelberg University, Germany

15.14 Clinical description and genetic analyses of a large cohort of 3402 PSC patients (p.166)
R. Alberts[1], E.M.G. de Vries[2], C.Y. Ponsioen[2], R.K. Weersma[1] on behalf of the International PSC Study Group, [1]Dept. of Gastroenterology and Hepatology, University of Groningen and University Medical Centre Groningen, Groningen, [2]Dept. of Gastroenterology and Hepatology, Amsterdam Medical Centre, Amsterdam, The Netherlands

15.26 Einde programma

Vrije voordrachten Ned. Vereniging voor Gastroenterologie — Parkzaal

Voorzitters: A.D. Koch en J.Ph. Kuijvenhoven

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

09.30 Evaluation of the first results of the Dutch colorectal cancer (CRC) screening program in a general teaching hospital (p.167)

L. van Meijel[1], R.P.R Adang[1], [1]VieCuri MC, Venlo, The Netherlands

09.40 Offering colonoscopy to participants with a negative FIT and a first degree relative with CRC increases the detection of advanced neoplasia in a screening program (p.168)

F.G.J. Kallenberg[1], J.L.A. Vleugels[1], T.R. de Wijkerslooth[1], I. Stegeman[1], M.E. van Leerdam[2], P.M.M. Bossuyt[3], E.J. Kuipers[2], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, [2]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, [3]Dept of Epidemiology and Biostatistics, Academic Medical Center, University of Amsterdam, The Netherlands

09.50 A family history questionnaire sent to patients undergoing outpatient colonoscopy enhances genetic counseling for hereditary colorectal cancer (p.169)

K. Kessels[1,2], J.D. Eisinger[1], T.G. Letteboer[3], G.J.A. Offerhaus[4], P.D. Siersema[1], L.M.G. Moons[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Flevohospital, Almere, [3]Dept of Clinical Genetics, University Medical Center Utrecht, Utrecht, [4]Dept of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

10.00 Randomized comparison of surveillance intervals in familial colorectal cancer: the Dutch FAmilial ColorecTal cancer Surveillance study (the FACTS study) group (p.170)

S.D. Hennink[1], A.E. van der Meulen-de Jong[1*], R. Wolterbeek[2], A.S.L.P. Crobach[3], M.C.J.M. Becx[4], L.F.S.J. Crobach[5], M. van Haastert[6], W.R. ten Hove[5], J.H. Kleibeuker[7], M.A.C. Meijssen[8], F.M. Nagengast[9], M.C.M. Rijk[10], J.M.J.I. Salemans[11], A. Stronkhorst[12], H.A.R.E. Tuynman[13], J. Vecht[8], M.L. Verhulst[11], W.H. de Vos tot Nederveen Cappel[8], H. Walinga[14], O.K. Weinhardt[15], B.D. Westerveld[8], A.M.C. Witte[5], H.J. Wolters[6], R.A. Veenendaal[1], H. Morreau[3], H.F.A. Vasen[1] *Both authors contributed equally tot this work, [1]Dept of Gastroenterology and Hepatology, [2]Dept of Medical Statistics and Bioinformatics, and [3]Dept of Pathology, Leiden University Medical Center, Leiden, [4]Dept of Gastroenterology, St. Antonius Hospital, Nieuwegein, [5]Dept of Gastroenterology, Diaconessenhuis, Leiden, [6]Dept of Gastroenterology, Martini Hospital, Groningen, [7]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [8]Dept of Gastroenterology, Isala Clinics, Zwolle, [9]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [10]Dept of Gastroenterology, Amphia Hospital, Breda, [11]Dept of Gastroenterology, Máxima Medical Center, Eindhoven, [12]Dept of Gastroenterology, Catharina Hospital, Eindhoven, [13]Dept of Gastroenterology, Medical Center Alkmaar, Alkmaar, [14]Dept of Gastroenterology, Reinier de Graaf Gasthuis, Delft, [15]Dept of Gastroenterology, Scheper Hospital, Emmen, The Netherlands*

Vrijdag 20 maart 2015

10.10 Cost-effectiveness of routine screening for Lynch syndrome in colorectal cancer patients up to 70 years of age (p.171)

A. Goverde[1,2], C.H.M. Leenen[1*], E.W. de Bekker-Grob[3], A. Wagner[2], M.G.F. van Lier[1], M.C.W. Spaander[1], M.J. Bruno[1], C.M. Tops[6], A.M.W. van den Ouweland[2], H.J. Dubbink[4], E.J. Kuipers[1,5], W.N.M. Dinjens[4], M.E. van Leerdam[1,7], E.W. Steyerberg[3], On behalf of the LIMO study group, [*]Both authors contributed equally to this work, [1]Dept of Gastroenterology and Hepatology, [2]Dept of Clinical Genetics, [3]Dept of Public Health, [4]Dept of Pathology, and [5]Dept of Internal Medicine, Erasmus MC, University Medical Center, Rotterdam, [6]Dept of Clinical Genetics, Leiden University Medical Center, Leiden, [7]Dept of Gastroenterology and Hepatology, Antoni van Leeuwenhoek Hospital, Netherlands Cancer Institute, Amsterdam, The Netherlands*

10.20 Small-bowel surveillance in patients with Peutz-Jeghers syndrome: comparing magnetic resonance enteroclysis and double balloon enteroscopy (p.172)

A. Goverde[1,2], A. Wagner[2], S.E. Korsse[1], M.E. van Leerdam[1,6], N. Krak[3], J. Stoker[4], H. van Buuren[1], R.M.W. Hofstra[2], M.J. Bruno[1], P. Dewint[1,7], E. Dekker[5], M.C.W. Spaander[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Clinical Genetics, and [3]Dept of Radiology, Erasmus MC, University Medical Center, Rotterdam, [4]Dept of Radiology, and [5]Dept of Gastroenterology and Hepatology, Amsterdam Medical Center, Amsterdam, [6]Dept of Gastroenterology and Hepatology, Antoni van Leeuwenhoek Hospital, Netherlands Cancer Institute, Amsterdam, [7]Dept of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam, The Netherlands

10.30 Frequent use of antibiotics and colorectal cancer risk – results of a nested case-control study (p.173)

V.K. Dik[1], M.G.H. Van Oijen[1,2], H.M. Smeets[3,4], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, [3]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, [4]Achmea Health Insurance, Amersfoort, The Netherlands

10.40 Are we missing serrated polyposis syndrome patients? (p.174)

Y.J. van Herwaarden[1], P. Dura[1], S. Pape[1], F.M. Nagengast[1], T.M. Bisseling[1], I.D. Nagtegaal[2], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands

10.50 Training on detection and resection of nonpolypoid colorectal neoplasms reduces the postcolonoscopy colorectal cancer (p.175)

R.J.J.M. Marx[1], C.M.C. le Clercq[1], R.M.M. Bogie[1], B. Winkens[2], J.W. Kruimel[1], J. Conchillo[1], R.J.J. de Ridder[1], T. Kaltenbach[3], R. Soetikno[3], A.A.M. Masclee[1], S. Sanduleanu[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, and [2]Dept of Methodology and Statistics, Maastricht University Medical Center, Maastricht, The Netherlands, [3]VA Healthcare System, Palo Alto, Stanford School of Medicine, United States of America

11.00 Koffiepauze

Vrije voordrachten Sectie Gastrointestinale Oncologie — Parkzaal

Voorzitters: M. Bigirwamungu en R.W.M. Schrauwen

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

11.30 Statin use after diagnosis improves survival in colon cancer patients (p.176)

**P.W. Voorneveld[1], *M.S. Reimers[2], E. Bastiaannet[2,3], R.J. Jacobs[1], R. van Eijk[4], M.M.J. Zanders[5], R.M.C. Herings[6], M.P.P. van Herk-Sukel[6], L.L. Kodach[1], T. van Wezel[4] , P.J.K. Kuppen[2], H. Morreau[4], C.J.H. van de Velde[2], **J.C.H. Hardwick[1], **G.J. Liefers[2,1] Gastroenterology & Hepatology, Leiden University Medical Center, [2]Surgery, Leiden University Medical Center, [3]Gerontology & Geriatrics, Leiden University Medical Center, [4]Pathology, Leiden University Medical Center, Netherlands, [5] Research, Comprehensive Cancer Centre the Netherlands, [6]PHARMO Institute for Drug Outcomes Research, The Netherlands, * § These authors contributed equally.*

11.40 The efficiency and efficacy of a multidisciplinary team meeting (p.177)

Y.L. Basta[1,2], O.L. Baur[3], S. van Dieren[2], J.H. Klinkenbijl[4], P. Fockens[1], K.M. Tytgat[1], On behalf of GIOCA team, [1]Dept of Gastroenterology, and [2]Dept of Surgery, Academic Medical Center, Amsterdam, [3]Student of Medicine, Academic Medical Center, Amsterdam, [4]Dept of Surgery, Gelre Hospitals, Apeldoorn, The Netherlands

11.50 Higher prevalence of cystic lesions of the pancreas in first degree relatives of familial pancreatic cancer cases than in carriers of pancreatic cancer-prone gene mutations (p.178)

I.C.A.W. Konings[1], F. Harinck[1], J.W. Poley[1], C.M. Aalfs[2], A. van Rens[3], N.C. Krak[4], A. Wagner[5], C.Y. Nio[6], R. Sijmons[7], H. van Dullemen[8], F.P. Vleggaar[9], M.G.E.M. Ausems[10], P. Fockens[11], J.E. van Hooft[11], M.J. Bruno[1], On behalf of the Dutch research group on pancreatic cancer surveillance in high-risk individuals, [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, [2]Dept of Clinical Genetics, Academic Medical Center, Amsterdam, [3]Family Cancer Clinic, The Netherlands Cancer Institute, Amsterdam, [4] Dept of Radiology, Erasmus MC, University Medical Center, Rotterdam, [5]Dept of Clinical Genetics, Erasmus MC, University Medical Center, Rotterdam, [6]Dept of Radiology, Academic Medical Center, Amsterdam, [7]Dept of Clinical Genetics, University Medical Center Groningen, Groningen, [8]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [10]Dept of Clinical Genetics, University Medical Center Utrecht, Utrecht, [11]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

12.00 Endoscopic ultrasound based surveillance of non-functioning pancreatic neuroendocrine tumors in multiple endocrine neoplasia type 1 syndrome; a retrospective cohort study to assess growth-rate (p.179)

W.F.W. Kappelle[1], G.D. Valk[2], M. Leenders[1], P.D. Siersema[1], F.P. Vleggaar[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Internal Medicine, University Medical Center Utrecht, Utrecht, The Netherlands

Vrijdag 20 maart 2015

12.10 Hospital of diagnosis for pancreatic cancer influences surgery rate and survival in a nationwide analysis: a plea for further centralization (p.180)

M.J.A.M. Bakens[1,2], Y.R.B.M. van Gestel[2], M. Bongers[1], M.G.H. Besselink[3], C.H.C. Dejong[4], V.E.P.P. Lemmens[2], I.H.J.T. de Hingh[1], On behalf of the Dutch Pancreatic Cancer Group (DPCG), [1]Dept of Surgery, Catharina Hospital, Eindhoven, [2]Netherlands Cancer Registry, Comprehensive Cancer Organisation Netherlands, Eindhoven, [3]Dept of Surgery, Academic Medical Center, Amsterdam, [4]Dept of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

12.20 Clonal diversity based on single-cell analysis predicts progression in Barrett's esophagus (p.181)

M.R. Timmer[1,2], P. Martinez[3], C.T. Lau[1,2], P. Fockens[1], J.J.G.H.M. Bergman[1], C.C. Maley[4], T.A. Graham[3], K.K. Krishnadath[1,2], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [2]Center for Experimental and Molecular Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Centre for Tumour Biology, Barts Cancer Institute, London, United Kingdom, [4]Center for Evolution and Cancer, University of California, San Francisco, United States of America

12.30 High prevalence of Barrett's esophagus and histological inflammatory changes in patients after esophageal atresia repair (p.182)

F.W.T. Vergouwe[1,2], H. IJsselstijn[2], K. Biermann[3], R.M. Wijnen[2], M.J. Bruno[1], M.C. Spaander[1], [1]Dept of Gastroenterology and Hepatology, and [3]Dept of Pathology, Erasmus MC, University Medical Center, Rotterdam, [2]Dept of Pediatric Surgery, Erasmus MC, University Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands

12.40 T1b esophageal adenocarcinoma: retrospective cohort study on patient management and risk of metastatic disease (p.183)

D.W. Schölvinck[1,2], H.T. Künzli[1,2], S.L. Meijer[3], C.A. Seldenrijk[4], J.J.G.H.M. Bergman[2], B.L.A.M. Weusten[1,2], [1]Dept of Gastroenterology and Hepatology, and [4]Dept of Pathology, St. Antonius Hospital, Nieuwegein, [2]Dept of Gastroenterology and Hepatology, and [3]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands

12.50 SOX2 and P53 protein expression predicts response to preoperative chemoradiotherapy in patients with esophageal adenocarcinoma (p.184)

S. van Olphen[1,2], K. Biermann[2], B.P.L. Wijnhoven[3], M.C.W. Spaander[1], A. van der Gaast[4], J.B. van Lanschot[3], M.J. Bruno[1], L.H.J. Looijenga[2*], *Both authors contributed equally to the work, [1]Dept of Gastroenterology and Hepatology, [2]Dept of Pathology, [3]Dept of Surgery, and [4]Dept of Medical Oncology, Erasmus University Medical Center, Rotterdam, The Netherlands*

13.00 Lunchbuffet in de expositiehal

Vrije voordrachten Nederlandse Vereniging voor Gastroenterologie — Parkzaal

Voorzitters: C.H.C. Dejong en B.W.M. Spanier

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

14.00 Inleiding op het programma

14.10 The impact of organ failure on mortality in necrotizing pancreatitis (p.185)

O.J. Bakker[1], N.J. Schepers[2,3*], M.G. Besselink[4], U. Ahmed Ali[1], T.L. Bollen[5], H.G. Gooszen[6], H.C. van Santvoort[4], M.J. Bruno[2], For the Dutch Pancreatitis Study Group, *Both authors contributed equally to this work, [1]Dept of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, [3]Dutch Pancreatitis Study Group, St. Antonius Hospital, Nieuwegein, [4]Dept of Surgery, Academic Medical Center, Amsterdam, [5]Dept of Radiology, St. Antonius Hospital, Nieuwegein, [6]Dept of Operation Rooms and Evidence Based Surgery, Radboud University, Nijmegen Medical Center, Nijmegen, The Netherlands*

14.20 Outcome in patients with presumed groove pancreatitis: long-term follow-up from a single center (p.186)

S.J. Lekkerkerker[1], C.Y. Nio[2], Y. Issa[3], P. Fockens[1], O.R.C. Busch[3], T.M. van Gulik[3], E.A.J. Rauws[1], M.A. Boermeester[3], J.E. van Hooft[1], M.G.H. Besselink[3], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Radiology, and [3]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

14.30 Validation of a 9-microRNA panel in pancreatic cyst fluid for the risk stratification of pancreatic cysts in a prospective cohort (p.187)

W.K. Utomo[1], L.H. Looijenga[2], M.J. Bruno[1], M.P. Peppelenbosch[1], H. Braat[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Pathology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

14.40 Malignant progression during long-term follow-up of pancreatic cysts: how often do we change treatment strategy? (p.188)

S.J. Lekkerkerker[1], P. Fockens[1], M.G.H Besselink[2], E.A.J. Rauws[1], J.E. van Hooft[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

14.50 Are the current diagnostic criteria for acute cholangitis (TG13) applicable in patients with acute biliary pancreatitis? (p.189)

N.J. Schepers[1,2], O.J. Bakker[3], U. Ahmed Ali[3], E.J.M. van Geenen[4], H.C. van Santvoort[5], M.G. Besselink[5], M.J. Bruno[1*], For the Dutch Pancreatitis Study Group, *Co-senior authorship, [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [2]Dutch Pancreatitis Study Group, St. Antonius Hospital, Nieuwegein, [3]Dept of Surgery, University Medical Center Utrecht, Utrecht, [4]Dept of Gastroenterology and Hepatology, Radboud University, Nijmegen Medical Center, Nijmegen, [5]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands*

Vrijdag 20 maart 2015

15.00 Patient-reported outcomes of uncomplicated symptomatic cholecystolithiasis patients following cholecystectomy: A prospective multi-center cohort study (p.190)

M.P. Lamberts[1,2,3], B.L. Den Oudsten[4], J.J.G.M. Gerritsen[5], A.J. Roukema[6], G.P. Westert[1], J.P.H. Drenth[2], C.J.H.M. van Laarhoven[3], [1]Scientific Institute for Quality of Healthcare (IQ healthcare), Radboud University Medical Center, Nijmegen, [2]Dept of Gastroenterology and Hepatology, and [3]Dept of Surgery, Radboud University Medical Center, Nijmegen, [4]Dept of Medical and Clinical Psychology, CoRPS, Tilburg University, Tilburg, [5]Dept of Surgery, Medisch Spectrum Twente, Enschede, [6]Dept of Surgery, St. Elisabeth Hospital, Tilburg, The Netherlands

15.10 Nomogram to predict recurrent disease after curative pancreatic resection for patients with grade 1 or 2 non-functional neuroendocrine tumor (p.191)

A.P.J. Jilesen[1], C.H.J. van Eijck[2], F.J. van Kemenade[3], S. van Eeden[4], J.Verheij[4], S. van Dieren[5], D.J. Gouma[1], E.J.M. Nieveen van Dijkum[1], [1]Dept of Surgery, [4]Dept of Pathology, and [5]Dept of Methodology and Statistic CRU, Academic Medical Center, Amsterdam, [2]Dept of Surgery, and [3]Dept of Pathology, Erasmus Medical Center, Rotterdam, The Netherlands

15.20 Diagnostic workup for small subepithelial upper gastrointestinal tumors is inadequate in guiding management (p.192)

J.R. ten Hove[1], N. van Lelyveld[2], F.P. Vleggaar[1], L.M.G. Moons[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology, St. Antonius Hospital, Utrecht, The Netherlands

15.30 Einde programma

Vrije voordrachten Sectie NESPEN — Zaal 80

Voorzitters: C.F. Jonkers en M.A.E. de van der Schueren

Voordrachten in het Nederlands, spreektijd 7 minuten, discussietijd 3 minuten

09.00 Nutrition before, during, and after surgery increases the arginine/ADMA ratio and relates to improved myocardial glucose metabolism: a randomized controlled trial (p.193)

M. Visser[1,2,3], M. Davids[4], H.J. Verberne[5], W.E.M. Kok[6], R. Tepaske[7], R. Cocchieri[2], E.M. Kemper[8], T. Teerlink[4], M.A. Jonker[9], W. Wisselink[1], B.A.J.M. de Mol[2], P.A.M. van Leeuwen[1], [1]Dept of Surgery, VU University Medical Center, Amsterdam, [2]Dept of Cardio-thoracic Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, [3]Research Unit, Gelderse Vallei Hospital, Ede, [4]Dept of Clinical Chemistry, VU University Medical Center, Amsterdam, [5]Dept of Nuclear Medicine, [6]Dept of Cardiology, and [8]Dept of Pharmacy, Academic Medical Center, University of Amsterdam, Amsterdam, [7]Intensive Care Unit, Academic Medical Center, University of Amsterdam, Amsterdam, [9]Dept of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

09.10 Patients with a positive SNAQ score stay 1.4 days longer in hospital (p194)

H.M. Kruizenga[1,2], F. Neelemaat[1], C.Bijl[1], A. Thijs[1,3], P. Weijs[1], [1]Dept of Nutrition and Dietetics, VU University Medical Center, Amsterdam, [2]Dutch Malnutrition Steering Group, Amsterdam, [3]Dept of Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands

09.20 The prebiotic inulin enhances fat oxidation in overweight males (p.195)

C.M. van der Beek1,2, E.E. Canfora1,3, E.E. Blaak1,3, C.H.C. Dejong1,2, K. Lenaerts1,2, 1Top Institute Food and Nutrition, Wageningen, 2Dept of Surgery, and 3Dept of Human Biology, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, The Netherlands

09.30 The impact of different diagnostic criteria on the prevalence of sarcopenia in healthy elderly individuals and geriatric outpatients (p.196)

E.M. Reijnierse[1], M.C. Trappenburg[1,2], M.J. Leter[1], G.J. Blauw[3], S. Sipilä[4], E. Sillanpää[4], M.V. Narici[5], J.Y. Hogrel[6], G. Butler-Browne[6], J.S. McPhee[7], H. Gapeyeva[8], M. Pääsuke[8], M.A.E. de van der Schueren[9,10], C.G.M. Meskers[11], A.B. Maier[1,2], [1]Dept of Internal Medicine, Section of Gerontology and Geriatrics, VU University Medical Center, Amsterdam, The Netherlands, [2]Dept of Internal Medicine, Amstelland Hospital, Amstelveen, The Netherlands, [3]Dept of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, The Netherlands - Dept of Geriatrics, Bronovo Hospital, The Hague, The Netherlands, [4]Gerontology Research Center and Dept of Health Sciences, University of Jyväskylä, Jyväskylä, Finland, [5]Division of Medical Sciences and Graduate Entry Medicine, MRC-ARUK Centre of Excellence for Musculoskeletal Ageing Research, University of Nottingham, Royal Derby Hospital Centre, Birmingham-Nottingham, UK, [6]UPMC UM 76, INSERM U974, CNRS 7215, Institut de Myologie, Paris, France, [7]School of Healthcare Science, John Dalton Building, Manchester Metropolitan University, Manchester, UK, [8]Institute of Exercise Biology and Physiotherapy, University of Tartu, Centre of Behavioral and Health Sciences, University of Tartu, Tartu, Estonia, [9]Dept of Internal Medicine, Section Nutrition and Dietetics, VU University Medical Center, Amsterdam, The Netherlands, [10]Dept of Nutrition, Sports and Health, Faculty of Health and Social Studies, HAN University of Applied Sciences, Nijmegen, The Netherlands, [11]Dept of Rehabilitation Medicine, VU University Medical Center, Amsterdam, The Netherlands.

Vrijdag 20 maart 2015

09.40 Incidence of non-alcoholic fatty liver disease in a large population cohort in the north of The Netherlands: a lifelines cohort analysis (p.197)

E.H. van den Berg[1], M. Amini[2*], R.P.F. Dullaart[3], K.N. Faber[1], A. Timmer[4], The LifeLines Cohort Study[5], B.Z. Alizadeh[1,2*], H. Blokzijl[1*], *These authors contributed equally, [1]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [2]Dept of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [3]Dept of Internal Medicine (Endocrinology), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [4]European Medical School Oldenburg-Groningen, Oldenburg, Germany, [5]The LifeLines Cohort Study, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands*

09.50 Percutaneous transhepatic feeding tube placement: a single-center experience in 37 patients (p.198)

A. Gerritsen[1], J. Damstra[1], K.P. van Lienden[2], O.M. van Delden[2], O.R.C. Busch[1], T.M. van Gulik[1], M.A. Boermeester[1], J.S. Laméris[2], M.G.H. Besselink[1], [1]Dept of Surgery, and [2]Dept of Radiology, Academic Medical Center, Amsterdam, The Netherlands

10.00 The association of nutritional status with brain atrophy and cerebrovascular lesions on MRI in a cohort of geriatric outpatients (p.199)

M.A.E. de van der Schueren[1], S. Lonterman-Monasch[2], M.A. Chung[1,5], W.M. van der Flier[3], A.B. Maier[4], M. Muller[5], [1]Dept of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, [2]Dept of Internal Medicine, Haga Hospital, The Hague, [3]Alzheimer Center, Dept of Neurology, Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, [4]Dept of Gerontology, Internal Medicine, VU University Medical Center, Amsterdam, [5]Dept of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, The Netherlands

10.10 Undernutrition in nursing home rehabilitation patients (p.200)

J.I. van Zwienen-Pot[1,2], M. Kuipers[3], M.F.A. Grimmerink[4], M.Visser[1,5], D.Z.B. van Asselt[1,6], H.M Kruizenga[1,7], [1]Dutch Malnutrition Steering Group, Amsterdam, [2]Zorgpartners Midden-Holland, Gouda, [3]Heliomare, Wijk aan Zee, [4]Amstelring, Amsterdam, [6]Dept of Health Sciences, Faculty of Earth and Life Sciences, VU University, Amsterdam, [7]Geriatric Medicine, Medical Centre Leeuwarden, [5]Dept of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands

10.20 Koffiepauze

symposium NESPEN **Zaal 80**

Symposium darmfalen

Voorzitters: C.F. Jonkers en M.A.E. de van der Schueren

11.00 TPV & Lijnen: keuze van lijnen voor centraal veneuze toegang
Prof. dr. J.A. Reekers, radioloog AMC, Amsterdam

11.30 TPV& lever complicaties
Dr. G. Wanten, MDL-arts, Radboudumc, Nijmegen

12.00 Kosten en complicaties van dunnedarmtransplantatie
Prof. dr. G. Dijkstra, MDL-arts, UMC Groningen

12.30 Lunch en NESPEN bestuursvergadering

symposium NESPEN **Zaal 80**

Symposium diëtetiek en onderzoek
thema: voeding en bewegen

Voorzitters: M.A.E. de van der Schueren en G. Wanten

13.00 Inleiding
Dr. M.A.E. de van der Schueren, senior nutrition scientist, VUmc en HAN

13.10 Voeding en bewegen
Prof. L.J.C. van Loon, Ph.D. Department of Human Movement Sciences MUMC

13.50 Discussie

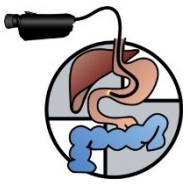
symposium NESPEN - presentaties **Zaal 80**

14.00	**Presentaties eigen onderzoek**
14.00	Controle neusmaagsonde met de ranjatest *Mw. M. Klos, Voedingsverpleegkundige, Gelre Ziekenhuis, Apeldoorn*
14.10	Early high protein intake is associated with low mortality and energy overfeeding with high mortality in non-septic mechanically ventilated critically ill patients *Dr. ir. P. Weijs, lector gewichtsmanagement, VU medisch centrum, Amsterdam*
14.20	Predictive equations for resting energy expenditure (REE) in adult inpatients and outpatients: a validation study *Mw. J. Klaver, afd. voedingswetenschappen VUmc, Amsterdam*
14.30	Validatie van de Meet en Weet lijst een eenvoudig instrument om de eiwitinname in te schatten *Mevr. J. Langius, Hoofddocent Voeding & Diëtiek,* *Haagse Hogeschool /VUmc*
14.40	Lichaamssamenstelling van volwassenen met een energiestofwisselingsziekte. *Mevr. H. Zweers, afd. diëtetiek, Radboudumc, Nijmegen*
14.50	**Proefschriftprijs** Uitreiking van proefschriftprijs en presentatie door winnaar
15.00	Afsluiting symposium

Programma V&VN MDL **Beneluxzaal**

Beroepsvereniging van zorgprofessionals

Maag Darm Lever



Voorzitter: T. Korpershoek

09.45 Ledenvergadering

10.15 opening door de voorzitter

10.15 Endoscopische behandeling van complicaties na poliepectomie
Dr. B.A.J. Bastiaansen, MDL-arts, AMC, Amsterdam

10.45 Ins en outs van PEG, PEJ en PRG
Drs. F. Voogd, MDL-arts in opleiding en
Mw. C.H.C. van den Elzen, enteraal-verpleegkundige,
Radboudumc, Nijmegen

11.15 Geel bij terugkeer uit de tropen
Dr. B.J. Veldt, MDL-arts, Reinier de Graaf Gasthuis, Delft

11.45 Ontwikkelingen in Hypertherme Intraperitoneale Chemotherapie (HIPEC)
Dr. S.W. Nienhuijs, chirurg, Catharina Ziekenhuis, Eindhoven

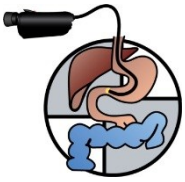
12.15 Irreversibele elektroporatie: een nieuwe vorm van beeldgestuurde tumorablatie. Werkingsmechanisme, indicaties en lopende studies
Dr. M.R. Meijerink, interventieradioloog, VUmc, Amsterdam

12.45 Lunchbuffet in de expositiehal

Vrijdag 20 maart 2015

Middagprogramma Endoscopieverpleegkundigen — Beneluxzaal

Beroepsvereniging van zorgprofessionals
Maag Darm Lever



Voorzitter: W. Kok

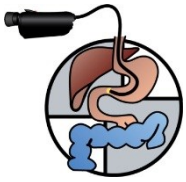
13.50 Erfelijke en/of familiaire darmkanker
Drs. F. Kallenberg, arts-onderzoeker MDL, AMC, Amsterdam

14.20 Endoscopische submucosale dissectie (ESD)
Dr. B.W. van der Spek, MDL-arts, Medisch Centrum Alkmaar

14.50 Digitale Voorlichting voor coloscopie, een alternatief?
Drs. G. Veldhuijzen, MDL-arts in opleiding, Jeroen Bosch Ziekenhuis, Den Bosch

Middagprogramma Lever-/IBD verpleegkundigen — Zaal 52

Beroepsvereniging van zorgprofessionals
Maag Darm Lever



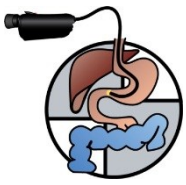
Voorzitter: Hanneke Huijskamp / Angelie de Heer

13.50 E-nose, ontwikkeling in IBD-diagnostiek
Drs. T.G.J. de Meij, kinder-MDL-arts, VUmc, Amsterdam

14.10 IBD-chirurgie en de rol van de 3e lijn
Prof. dr. L.P.S. Stassen, gastrointestinaal chirurg, Maastricht UMC

Middagprogramma Lever-/IBD verpleegkundigen (vervolg) **Zaal 52**

v&vn
Beroepsvereniging van zorgprofessionals
Maag Darm Lever



14.35 Levertransplantatie: van verwijzing tot follow-up

Indicaties voor levertransplantatie, beste verwijsmoment naar transplantatiecentrum en wachtlijstprocedure
Mw. M. Bijmolen, verpleegkundig specialist, UMC Groningen

Post-operatieve- en langetermijncomplicaties na levertransplantatie
Dr. T.C.M.A. Schreuder, MDL-arts, hepatoloog UMC Groningen

15.45 Einde programma

ABSTRACTS

Comparison of Disease Phenotype in 35,128 European and 4,686 non-European IBD patients in the International IBD Genetic Consortium cohorts

R.K. Weersma[1], C.W. Lees[2], S. Ng[3] on behalf of the International IBD Genetics Consortium, [1]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [2]GI Unit, Western General Hospital, Edinburgh, United Kingdom, [3]Institute of Digestive Disease, State Key Laboratory of Digestive Diseases, Medicine and Therapeutics, Chinese University of Hong Kong, China

IBD is relatively common in the West and is increasing in non-Western countries. Comparative data on clinical phenotype of IBD between European and non-European populations are scarce. We have recently characterised the genetic architecture of IBD in European and non-European populations through the International IBD Genetics Consortium (IIBDGC) cohorts. We now describe the detailed distribution of clinical sub-phenotypes across these populations. Detailed sub-phenotpye data were collected on standardised proforma after retrospective case-note review by trained physicians or assistants at each site. Patient demographics and sub-phenotypes were compared between patients of European (n=35,128) versus non-European descent (East Asian, Indian, Iranian; n=4,868). IBD cases had a lower prevalence of a family history of IBD (5.6% vs.28.3%; p=4.78X10-85) in non-European than Europeans. Crohn's disease(CD): (19,290 European CD, 1,991 non-European CD), Whilst the age at diagnosis of CD was similar across populations there was a striking male predominance (67.1% vs.45.1%; p=7.09X10-78) in non-Europeans. In CD, there were more active smokers in Europeans than non-Europeans. CD location was broadly similar. While stricturing (43% vs.27.6%; p=2.73X10-33) and perianal diseases (42.1% vs.27.8%; p=5.35X10-33) were more prevalent in non-Europeans than Europeans, surgical rates forCD were numerically lower in non-Europeans (48.1% vs.52.8%; p=5.42X10-4). Ulcerative colitis (UC): There were very few non-European ex-smokers with UC compared with European patients (1.9% vs.28.7%). Extensive colitis (34.2% vs.48.8%; p=1.52X10-34) and colectomy for UC (4.1% vs.18.5%; p=1.22X10-69) were also less common in non-Europeans. In multi-variable analysis, independent factors for colectomy in UC were extensive colitis (OR 10.35; 95% CI, 7.85-13.64), European origin (OR 4.71; 95% CI, 3.72-5.96) and ex-smoking (OR 1.2; 95% CI, 1.08-1.36).
Conclusions: In the largest dataset comparing IBD sub-phenotype in European and non-European patients, there are several striking demographic differences in non-Europeans (male predominance in CD; less ex-smokers developing UC) which may yield clues to the role of environmental factors in disease etiology. Major disease sub-phenotypes (location, behavior and surgery) are broadly similar. CD phenotype appears to be as severe, if not more severe, in Asia than in the West. This may relate to delayed diagnosis or late presentation or real differences due to underlying genetic and microbial factors.

Epidemiology and characteristics of inflammatory bowel disease in a large population-based cohort in the Netherlands.

E.J. de Groof[1,2], N.G.M. Rossen[1], B.D. van Rhijn[1], E.P.M. Karregat[1], K. Boonstra[1], I. Sadal[1], P.J. Kingma[3], A.H.J. Naber[3], J.H.M. van den Brande[3], R.C. Mallant-Hent[4], M.W. Mundt[4], G. D'Haens[1], C.Y. Ponsioen[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dept of Surgery, Academic Medical Center, Amsterdam, [3]Dept of Gastroenterology and Hepatology, Tergooi Hospitals, Hilversum and Blaricum, [4]Dept of Gastroenterology and Hepatology, Flevohospital, Almere, The Netherlands

Results from population based studies in inflammatory bowel disease (IBD) will reveal information on disease phenotype and may facilitate adequate treatment stratification. Aim of this study was to update prevalence and incidence rates of IBD in a population-based cohort covering 319,976 inhabitants. In addition, use of medical therapy and surgical procedures were assessed. IBD patients living in the adherence area receiving medical care at three regional (non-academic) hospitals between 1-1-2004 and 1-1-2010 were identified. Three independent hospital databases were used for case-finding. Cochrane-Armitage trend test was used to test change in prevalence over time. Montreal classification was used to report on IBD behavior and location. Data on medical and surgical treatment were obtained from medical records. Case-finding identified 2,466 possible IBD patients. In total, 1,461 IBD patients were included (40.7% male). 761 (52.1%) patients had ulcerative colitis (UC), 579 (39.6%) Crohn's disease (CD) and 121 (8.3%) IBD-unspecified (IBD-U). Point prevalence of IBD was 432.1 (CI 409.7-454.5) per 100,000 inhabitants on 1-1-2010 (UC: 225.6, CD 171.8, IBD-U 34.7). Prevalence increased significantly over time from 1-1-2004 to 1-1-2010 (χ^2=49.4, p<0.0001). Mean annual incidence between 2004 and 2009 for IBD was 29.6 (CI 23.6-35.5) per 100,000 inhabitants per year (35.0 for UC, 20.2 for CD and 2.2 for IBD-U). Two peaks in the mean annual incidence rate were observed in UC patients in age categories 40-49 and 70-79 years. In CD, an incidence peak was observed in young adolescent patients. In UC, left-sided colitis was most commonly observed (46.1%), whereas 23.7% had proctitis and 30.2% pancolitis. In the majority of CD patients ileocolonic involvement (L3)(36.3%) was observed. 30.4% had ileitis without colitis (L1), 32.2% had colitis (L2) and 1.1% had upper GI involvement. In CD patients, 53.9% had nonstricturing, nonpenetrating behavior (B1). Stricturing, nonpenetrating behaviour (B2) was found in 21.4% of patients and penetrating in 24.7% (B3). A history of steroid use was significantly more common in CD compared to UC patients (81.5% vs 62.9%, p<0.0001). Proctocolectomy was performed in 4.1% of UC patients after a median follow-up of 8.0 years (IQR 5.0-16.0). In CD patients an ileocecal resection was performed in 12.4%. Point prevalence of IBD was 432.1 per 100,000 inhabitants and increased significantly over the study period. Mean incidence of IBD was 29.6 per 100,000 inhabitants per year. Whereas the incidence of CD was highest in lower age groups, two peaks in the incidence of UC were observed. Steroid use was significantly more common in CD patients.

Disease course, phenotype, and medication use in elderly-onset Crohn's disease patients - A Dutch population-based IBD cohort study

S.F.G. Jeuring[1,2], T.R.A. van den Heuvel[1,2], M.P. Zeegers[3,4], W.H. Hameeteman[1], M.J.L. Romberg-Camps[5], L.E. Oostenbrug[6], A.A.M. Masclee[1,2], D.M.A.E. Jonkers[1,2], M.J. Pierik[1,2], [1]Division of Gastroenterology and Hepatology, Maastricht University Medical Center+, Maastricht, The Netherlands [2] School for Nutrition, Toxicology and Metabolism (NUTRIM), Maastricht University Medical Center, Maastricht, The Netherlands, [3]Dept of Complex Genetics, Cluster of genetics and Cell Biology, Maastricht University Medical Center, Maastricht, The Netherlands, [4]Dept of Epidemiology and Public Health, University of Birmingham, Birmingham, United Kingdom, [5]Dept of Internal Medicine and Gastroenterology, Orbis Medical Center, Sittard-Geleen, The Netherlands, [6]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center, Heerlen, The Netherlands

Population ageing is a demographic phenomenon seen in many Western countries. This may result in an increased prevalence of elderly-onset Crohn's disease (CD) patients in our outpatient clinics. For optimal patient information and treatment, insight in the disease course of elderly-onset CD is mandatory. However, data are scarce and often derived from small, selected populations. Therefore, we aimed to study the disease course of elderly-onset CD compared to adult-onset CD in our population-based cohort.
Since 1991, incident IBD cases in our area are included in our population-based cohort, with over 93% completeness. For this study, two patient groups were defined, based on the age at diagnosis: adult-onset (AO) CD (i.e. <60 years of age at diagnosis) and elderly-onset (EO) CD (i.e. ≥60 years of age at diagnosis). Disease behaviour was classified according to the Montreal classification as B1 (non-stricturing, non-penerating), B2 (stricturing), or B3 (penetrating). The disease course of CD was compared between groups for progression to B2 or B3 phenotype, need for immunomodulators or biologicals, hospitalisation and surgery. Data were analysed with a Kaplan-Meier survival curve, and hazard ratios (HR) were calculated using a Cox regression model. In total, 136 EO and 1026 AO CD patients were included. Mean follow-up was 6.4 (SD 4.9) and 9.0 (SD 5.8) years, respectively. At diagnosis, B1 phenotype was most common in both groups (79.4% and 77.2%) and no difference was found in behaviour distribution (p=0.49). More EO patients than AO patients underwent surgery at diagnosis (14.7% vs. 5.9%, HR 2.49; 95%CI 1.40-4.43). During follow-up, the risk of progression from B1 to B2 or B3 phenotype (47.8% vs. 49.7%, HR 0.92; 95%CI 0.68-1.26), hospitalisation (71.4% vs. 73.1%, HR 0.99; 0.77-1.29) and two or more hospitalisations (36.5% vs. 39.1%, HR 0.87; 95%CI 0.56-1.35) did not differ between groups, nor did the risk of surgery during follow-up (33.1% vs. 37.3%, HR 0.91; 95%CI 0.58-1.43). EO patients were less often treated with immunomodulators (61.8% vs. 77.1%, HR 0.71; 95%CI 0.54-0.95) and biological agents (25.1% vs. 55.2%, HR 0.59; 95%CI 0.37-0.93).
Conclusion: In this population-based IBD cohort, disease presentation was different in elderly-onset CD patients as more surgery was performed at diagnosis. Although elderly-onset CD patients less often used immunomodulators and biologicals, rates of disease progression, hospitalisation and surgery during disease course were similar to adult-onset CD.

Increased cancer risk in Dutch Crohn's disease patients: results from a population based cohort

D.S.J. Wintjens[1], T.R.A. van den Heuvel[1], S.F.G. Jeuring[1], W.H. Hameeteman[1], L.E. Oostenbrug[2], M.J.L. Romberg-Camps[3], A.A.M. Masclee[1], M.P. Zeegers[4,5], D.M.A.E. Jonkers[1], M.J. Pierik[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Center, The Netherlands, [2]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Atrium Medical Center, The Netherlands, [3]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Orbis Medical Center, The Netherlands, [4]Dept of Complex Genetics, Cluster of Genetics and Cell Biology, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, The Netherlands, [5]Dept of Epidemiology and Public Health, University of Birmingham, Birmingham, United Kingdom

Both chronic inflammation and use of immunosuppressive agents can increase the risk of malignancies. Whether (extra) intestinal cancers occur more frequently in Crohn's disease (CD) remains controversial, partly because population based studies on cancer risk are scarce. We studied the cancer risk of CD patients in a Dutch population based cohort. Secondly, we aimed to confirm the previously reported increase of skin and hematologic cancer risk in immunosuppression users. All CD patients, diagnosed in our region between 1991 and 2011, were followed until 2013 and cross-linked with the Dutch Cancer Registry. Observed cancers and age-, sex- and calendar year based expected cancers from the background population were used to calculate standardized incidence ratios (SIR) for overall cancer risk, common cancers (i.e. colorectal- (CRC), upper gastro-intestinal-, lung-, breast- and prostate cancer) and possible immunosuppression related cancers (i.e. overall hematologic and skin cancer, basal cell cancer (BCC), squamous cell cancer (SCC) and melanoma). Confidence intervals were determined by Byar's approximation. Subanalyses were performed for patients without immune-suppression, those ever on thiopurines (>12 months use, without anti-TNF) and ever on anti-TNF (>12 months, regardless of thiopurines). In the last two groups, only patient years after medication start were included in analysis. In total, 1162 CD patients (37% male) contributed to 10705 person years at risk. Mean age at diagnosis and mean disease duration were 37.7 (SD 15.9) and 9.3 (SD 5.9) years, respectively. Overall, CD patients had a 33% increased risk (SIR 1.33; 0.95%CI 1.02-1.71) of developing cancer compared to the general population. CRC risk was not significantly increased (1.95; 0.97-3.48). Overall skin cancer (1.55; 1.06-2.19), SCC (3.83; 1.83-7.04) and hematologic cancer (2.41; 1.04-4.76) risks were increased, while breast cancer risk (0.11; 0.00-0.64) was decreased. In the subanalysis, patients ever on thiopurines had a significantly increased risk to develop SCC (7.12; 1.44-20.92).
Conclusion: In our population based cohort, the overall cancer risk for CD patients was higher compared to the general population. This finding can be attributed to an increased risk for hematologic and skin cancer, which was most pronounced for SCC in longterm thiopurine users. The risk of gastro-intestinal and common extra-intestinal cancers was not increased and the risk of breast cancer was even strongly decreased. The above findings under the increased cancer risk of immunosuppression use in IBD patients and point to the relevance of regular screening, especially for dermatological cancers.

Baseline characteristics and datamodel from a nationwide standardized Inflammatory Bowel Disease collection by all University Medical Centers in the Netherlands: the IBD Parelsnoer Institute

L.M. Spekhorst[1,2], F. Imhann[1,2*], A.A. van Bodegraven[3], N.K.H. de Boer[3], G. Bouma[3], E.A Festen[1,2], H.H. Fidder[4], G.R.A.M. D'Haens[5], F. Hoentjen[6], D.W.Hommes[7], D.J. de Jong[6], M. Lowenberg[5], A.E. van der Meulen[7], B. Oldenburg[4], M.J. Pierik[8], P.C. Stokkers[9], C.J. van der Woude[10], G. Dijkstra[1^], R.K. Weersma[1^], *Both authors contributed equally to this work, ^Shared last author, Parelsnoer Institute[#] , On behalf of the Dutch Initiative on Crohn and Colitis (ICC), [1]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, [2]Dept of Genetics University of Groningen and University Medical Center Groningen, [3]Dept of Gastroenterology and Hepatology, VU University Medical Center, [4]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, [5]Dept of Gastroenterology and Hepatology, Academic Medical Center, [6]Dept of Gastroenterology and Hepatology, University Medical Center St. Radboud, [7]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, [8]Dept of Gastroenterology and Hepatology, University Medical Center Maastricht, [9]Dept of Gastroenterology and Hepatology, St Lucas Andreas Ziekenhuis, Amsterdam, [10]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, The Netherlands*

Inflammatory Bowel Disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory diseases of the gut, with clinical heterogeneous presentations, thought to be a result of environmental, microbial and/or genetic factors. To study this it is essential to analyze these factors in large cohorts of extensively phenotyped patients with standardized collection of biomaterials. The Dutch government supported Parelsnoer Institute was founded to collect this data and biomaterials from all eight University Medical Centers (UMCs) in the Netherlands. In order to collect uniform data, the UMCs created the IBD Pearl Information Model (PIM). Upon informed consent this PIM and a standard laboratory set, DNA, serum and a stool sample were collected at baseline.
Currently 3394 patients (2118 CD, 1190 UC, 59% female) are included. Mean age at inclusion was 43,6 years, mean age at diagnosis 29,6 years, 93% is Caucasian, and 27% of the patients have a positive family history for IBD. At base 31% of the IBD patients were smoking (40% of the CD patients and 16% of UC patients) and 12% had a history of appendectomy (15% CD patients, 6% UC patients). CD disease localization according to the Montreal classification was 23% ileal; 31% colonic; 46% ileocolonic, 8% upper GI and 27% Perianal. For UC disease localization at base was 8% proctitis, 36% left sided and 56% pancolitis. Extra-intestinal manifestations are present in 29% of the patients consisting of eye involvement 4%, arthritis 6%, skin manifestation 10%, and arthropathy 15%. Modified Harvey Bradshaw score at base showed that 71% of the CD patients were in remission, 15% mild disease, 13% moderate disease and 1% severe disease. For UC the Modified SCCAI score showed that 78% were in remission and 22% had active disease. During the disease course 71% of CD and 56% of UC patients used immunomodulation and 48% (CD) and 19% (UC) a biological. Surgery was performed in 32% of the IBD patients; 31% underwent an ileocoecal resection in CD and 15% a colectomy in UC. Stoma and pouch was present in 12% and 4% respectively.
Conclusions: We provide a nationwide standardized framework for the collection of IBD data and biomaterials. Our framework already contains more than 3394 IBD patients. In this nationwide UMC based cohort we found a higher percentage of positive family history and lower surgery rates than in literature. Percentage of biological use is high in this tertiary referral cohort. Our framework allows us to integrate clinical phenotypes with multi-omics data in order to unravel and redefine IBD, predict the disease course and personalize treatment.

Smoking is associated with extra-intestinal manifestations in inflammatory bowel disease

M. Severs[1], S.J.H. van Erp[13], G. Dijkstra[3], M.E. van der Valk[1], M.J. Mangen[2], M. Leenders[1], A.A. van Bodegraven[4], H.H. Fidder[1], D.J. de Jong[5], M. Pierik[6], C.J. van der Woude[7], M.J. RombergCamps[8], C.H. Clemens[9], J.M. Jansen[10], N. Mahmmod[11], P.C. van de Meeberg[12], C.Y. Ponsioen[14], C.J. Bolwerk[15], J.R. Vermeijden[16], P.D. Siersema[1], A.E. van der Meulen-de Jong[13], B. Oldenburg[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Julius Centre for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, [3]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [4]Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, [5]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [6]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [7]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [8]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [9]Dept of Gastroenterology and Hepatology, Diaconessenhuis, Leiden, [10]Dept of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, [11]Dept of Gastroenterology and Hepatology, Antonius Hospital, Nieuwegein, [12]Dept of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, [13]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [14]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [15]Dept of Gastroenterology and Hepatology, Reinier de Graaf Groep, Delft, [16]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, The Netherlands

Smoking appears to influence the disease activity in inflammatory bowel disease (IBD). We aimed to study the association between smoking and extra- intestinal manifestations (EIMs) in IBD. The association between smoking and EIMs such as joint complaints, chronic skin disorders and eye complaints was investigated in three Dutch cohorts. The COIN-study is a large prospective cohort study with data collected by questionnaires about demographics, disease course and associated cost items. In a second, Northern cohort, questionnaires on cigarette smoke exposure and disease behaviour in IBD patients were collected. The JOINT- study is a prospective longitudinal study focused on IBD patients with and without back pain and peripheral joint complaints. A putative dose-response relationship between smoking and EIMs, and the association between smoking and specific phenotypes of arthropathies was explored. In the COIN- study, 3,030 patients (1,558 Crohn's disease (CD), 1,054 ulcerative colitis (UC) and 418 IBD-unspecified) were enrolled; 16.0% were current smokers. In the Northern cohort, 780 IBD patients (420 CD, 298 UC, 62 IBD-unspecified) were included; 23.6% were current smokers. In the JOINT- study, 255 patients (186 CD, 69 UC) were enrolled; 23.5% were current smokers. EIMs were significantly more prevalent in the smoking IBD population (COIN- study: 39.1% vs. 29.8%, p <0.001 and Northern cohort: 42.8% vs. 31.2%, p <0.001). This association was more pronounced in CD than in UC. Joint complaints were the most prevalent EIM in both CD and UC. Of all EIMs, smoking appeared to have the most significant association with joint complaints (COIN- study: CD 30.7% vs. 22.1%, p <0.001, UC 25.3% vs. 18.5%, p =0.11 and Northern cohort: CD 46.4% vs. 40.4%, p =0.26, UC 31.0% vs. 23.0%, p =0.34). Likewise, in the JOINT- study, smoking was more prevalent in IBD patients with artropathies (30.3% s. 13%, p =0.001). A dose-response relationship is suggested by the fact that EIMs were more prevalent in heavy smoking patients compared to low exposure smokers (56.0% vs. 37.1%, p =0.10). Smoking was not associated with a specific phenotype of spondylarthropathy.
Conclusions:The results of three cohort studies confirm a positive association between smoking and extra-intestinal manifesttations in IBD. This association appears to be subject to a dose-response effect.

Identification of genetic and clinical risk factors for hidradenitis suppurativa in inflammatory bowel disease

L.M. Spekhorst[1,2], I.C. Janse[3], M. Koldijk[3], A. Vich Vila[2], R.K. Weersma[1], G. Dijkstra[1], B. Horváth[3], [1]Dept of Gastroenterology, [2]Dept of Genetics and [3]Dept of Dermatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

Patients with inflammatory bowel disease (IBD) often have distinct skin manifestations. Hidradenitis suppurativa (HS), is a disabling chronic skin disease characterized by painful cutaneous abscesses and sinus tracts in the body folds that has recently been associated with IBD. The objective of this study was to study the prevalence and risk factors for HS in IBD. A for HS validated questionnaire was sent to 1,969 IBD patients from a University Medical Centre. Verification of diagnosis HS was checked in patient records, confirming the diagnosis by a surgeon, dermatologist or gastroenterologist, or by phone by a dermatologist. Logistic regression analysis was performed in order to obtain a predicting model for HS in IBD patients. Genetic association analysis was performed in 352 patients using genotype data from the Immunochip which is a custom-made genotyping array including ~200.000 genetic variants with dense coverage of immune related genes. From all 1,260 patients who returned the questionnaire, 50.3% was diagnosed with Crohn's disease (CD) and 49.7% with ulcerative colitis (UC). The prevalence of HS in our IBD cohort was significantly higher than in the general population (10 % vs 1-2%). Female gender was the best independent predictor for having HS (OR = 4.282), followed by IBD type (CD, OR = 2.761). Cigarette smoking, high BMI and young age were independent predictors for HS as well. Within cases allelic association analysis was performed for 59 cases (IBD pts with HS) and 293 controls (IBD pts without HS). Although the current study lacks power to detect genetic association signals at genome wide significance level, we observed two promising new associations in genomic regions harbouring ELOVL7 (rsnumber 10057395 p = 7.15x10-5, OR = 0.4) and in the intergenic region between SULT1B1 and SULT1E1 (rsnumber 2014777 p = 7.48x10-5, OR = 2.3).

Conclusions: This large cohort study confirms the association between IBD and HS with a high prevalence of 10.6%. Female gender, cigarette smoking, high BMI and young age are important risk factors for developing HS in IBD patients. Furthermore, there is suggestive genetic evidence for a protective association with ELOVL7 and risk association with SULT1B1 and SULT1E1. SULT1E1 encodes for an estrogen sulfo-transferase enzyme, which is expressed in abdominal subcutaneous adipose tissue and associated with the expression of inflammatory cytokines as TNF-α and suppressor of cytokine signalling 3 (SOCS3). It's established that TNF-α plays an important role in the pathogenesis of both diseases. More research is needed to confirm this possible candidate gene for HS in IBD.

Drug repositioning in inflammatory bowel disease by using genetic information

V. Collij[1], E.A.M. Festen[1], R. Alberts[1], R.K. Weersma[1], [1]University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal tract and medical therapy for IBD is not yet optimal. At this moment 233 genetic risk loci have been identified for IBD. Although these findings have significantly advanced our insight into the biology of IBD, there has been little progress in translating this knowledge towards clinical care or drug development. In fact, there is very little literature on using genetic information for drug identification at all. In this study we aim to use the knowledge on the genetic background of IBD to identify new drug targets for IBD and identify biologicals or small molecules targeting these genes. We first assessed plausible candidate genes within each of the known IBD risk loci by using multiple gene prioritization strategies (GRAIL, DAPPLE, eQTL and cSNP analyses), identifying 362 candidate genes. We then downloaded Drugbank, the largest publicly available database containing drugs and their protein targets. Using R we developed a tool linking putative IBD genetic drug targets directly to drugs. We studied direct protein-protein interactions (PPIs) to gain insight in the networks in which the proteins encoded by IBD risk genes function (DAVID, KEGG). Finally, we did an advanced literature search based on these results to select the most promising new drugs for IBD based on the evidence from phase I/II/III randomized controlled trials (RCTs) or animal studies (PubMed, Clinical-trials.gov). First we validated our method by showing that eight known IBD drugs target IBD risk genes. For example mesalazines and anti-TNFs are linked to IBD risk genes, either directly or through one PPI. Secondly, we identified 44 drugs targeting IBD candidate genes, which have already been investigated in IBD, either through RCTs or through animal studies. Examples are vitamin D analogues and thalidomide. We also identified 28 drugs targeting IBD risk genes, which are already used or investigated in other inflammatory disorders. Two examples are Muromonab, investigated in multiple sclerosis and Alefacept, used for treatment in psoriasis. These drugs could possibly be repositioned for treatment of IBD. Finally, we identified 27 experimental or investigational drugs whose mechanism looks promising for IBD; for example INCB3284, an anti-CCR2, and SGN-30, an anti-CD30.
Conclusions: In this study we showed that genes associated with IBD are targeted by approved therapies for IBD and we identified drugs that can possibly be repositioned or further developed for the treatment of IBD. These findings could lead to better treatment for IBD patients, using already existing drugs.

Genetic polymorphisms in IBD determine response to treatment

V.J.A.A. Nuij[1], M.P. Peppelenbosch[1], C.J. van der Woude[1], G.M. Fuhler[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

Background: The role of single nucleotide polymorphisms (SNPs) associated with inflammatory bowel disease (IBD) is gaining interest. We previously observed that patients (pts) carrying an NCF4 risk allele are more exposed to prednisone and are highly steroid dependent, indicating divergent use of treatment in different genetic risk groups. Treatment strategies in IBD are aimed towards a personalized approach in the future. We wondered whether other IBD-associated SNPs are able to predict response to treatment as well. Methods: Data on response to treatments were retrieved for all IBD pts from whom DNA was available in our center. SNP status of IRGM (rs13361189), NOD2 (rs2066844, rs2066845, rs2066847), XBP1 (rs35873774), LRRK2 (rs11175593), IL23R (rs11465804), CCR6 (rs2301436) and STAT3 (rs744166) were determined (KBiosciences, UK). Correlations were calculated using logistic regression analysis using odds ratio's (OR) and confidence intervals (CI). Results: Of the 583 pts (46% men) 71% suffered from Crohn's disease, 27% from Ulcerative colitis and 2% from IBD-unclassified. Associations between IBD related SNP and response to treatment included an increased use of Adalimumab (ADA) ($p<0.0001$ OR3.2 CI 1.7-5.7) and a decreased use of cyclosporine ($p=0.003$ OR0.3 CI 0.2-0.7) in pts carrying the ATG16L1 SNP. Pts carrying the XBP1 SNP had an increased risk of non-response to Infliximab (IFX) ($p=0.02$ OR3.7 CI 1.3-10.9) and ADA ($p=0.02$ OR4.5 CI 1.2-16.3) and an increased use of Methotrexate (MTX) ($p=0.005$ OR2.3 CI 1.3-4.1).STAT3 risk allele carriers had an increased risk at side effects (SE) ($p=0.006$ OR2.2 CI 1.3-3.9) but a decrease in none-response on IFX ($p=0.02$ OR0.4 CI 0.2-0.8). IRGM SNP carriers showed less IFX non-response ($p=0.045$ OR2.4 CI 1.02-5.7). Pts carrying one of the SNPS in the NOD2 gene, had an increased risk for Budenoside use ($p=0.02$ OR1.8 CI 1.1-3.0). IL23R SNP carriers were more likely to experience non response to prednisone ($p=0.02$ OR4.2 CI 1.3-13.8) and carriers of the LLRK2 SNP used more 6-Mercaptopurine (6MP) ($p=0.02$ OR2.5 CI 1.2-5.5). Pts carrying the CCR6 SNP showed a decrease of SE in prednisone ($p=0.003$ OR0.5 CI 0.3-0.8) and 5-ASA ($p=0.03$ OR0.5 CI 0.3-0.9) and an increased risk for MTX SE ($p=0.03$ OR2.7 CI 1.1- 6.8).

Conclusion: Genetic polymorphisms in known IBD-associated genes correlate with response to treatment towards the higher end of the treatment pyramid. This suggests that the genetic make-up of IBD patients may help physicians decide on personalized treatment strategies. Further investigation will need to elucidate the implications of these findings and asses the significance of pts genetic profile on differences in disease severity, disease phenotype and/or disease duration.

Disease specific differences in intestinal microbiota between pediatric-IBD and healthy control

E.F.J. de Groot[1], N.K.H. de Boer[1], M.A. Benninga[3], A.E. Budding[4], A.A. van Bodegraven[5], P. Savelkoul[4], T.G.J. de Meij[2], [1]Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, [2]Dept of Pediatric Gastroenterology, VU University Medical Center, Amsterdam, [3]Dept of Pediatric Gastroenterology, Academic Medical Center, Amsterdam, [4]Dept of Medical Microbiology and infection control, VU University Medical Center, Amsterdam, [5]Dept of Gastroenterology and Hepatology, ORBIS Medical Center, Sittard, The Netherlands

Introduction: In the etiology of inflammatory bowel disease (IBD), comprising Crohn's disease (CD) en ulcerative colitis (UC), intestinal microbiota seems to play a crucial role. However, data is limited and conflicting. Here we studied intestinal microbiota in a large cohort of children during onset of IBD and followed-up until achieving remission. We compared results to healthy controls. Methods: Children suspected for IBD were included. All patients were recruited from 2 tertiary centers in Amsterdam, The Netherlands. Fecal samples were collected, prior to bowel cleansing (t0) and at week 1, 3, 6 and 18 after initiation of therapy. All patients were treated according to standard care guidelines. CD patients received thiopurines and were offered 6 weeks exclusive enteral nutrition (EEN) and in case of reluctance, unresponsiveness or intolerance, cortico-steroids were prescribed instead. UC patients received aminosalycilates, dependent on disease severity, combined with corticosteroids, and also as maintenance (mono)-therapy. Healthy controls collected samples at similar intervals. Disease activity was assessed by Global-Physician-Assessment (GPA) score, fecal calprotectin and CRP. Fecal samples were analyzed by IS-pro, a clinically applicable PCR-based microbiome profiling technique. Results: Fecal samples of 101 newly diagnosed IBD-patients (median 14 years) and healthy controls (median 8 years) were collected. All patients were in clinical remission at t6. Preliminary results showed distinct differences in microbiota for CD (n=60), UC (n=41) and controls (n=61). For the phylum Firmicutes diversity and total abundance were significantly higher in UC compared to controls at t0 (resp. p0.003, p0.001). Total abundance in CU increased even further at t6 (p0.039). For the phylum Bacteroidetes total abundance was lower in both UC and CD compared to controls at t0 (resp. p0.003, p0.07). Furthermore one of the core microbiota in controls, Alistipes putredinis, had a lower abundance or was totally absent in almost all IBD patients. For the phylum Proteobacteria diversity was higher in CD compared to controls at t0 (p0.041) with a higher total abundance (p0.001). In CD, microbiota changed towards normal when patients went into remission, while this effect was not seen in UC.
Conclusion: Microbiota-analysis demonstrated clear disease specific differences in composition between pediatric-IBD and controls. Furthermore one of the core microbiota in controls, Alistipes putredinis, had a lower abundance or was totally absent in almost all IBD patients. Shifting towards normal control microbiota was only seen for CD patients.

Incidence and severity of pre-pouch Ileitis: a distinct disease entity or a manifestation of refractory pouchitis?

S. Sahami[1,2], M.A. Samaan[3], D.C. de Jong[1], S.M. Morgan[3], G.R. van den Brink[1], M. Lowenberg[1], C.I. Ponsioen[1], C.J. Buskens[2], P.J. Tanis[2], A. de Buck van Overstraeten[4], A. D'Hoore[4], W.A. Bemelman[2], G.R. D'Haens[1], [1]Dept of Gastroenterology, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands, [3]Dept of Gastroenterology, University College Hospital London, London, United Kingdom, [4]Dept of Surgery, University Hospital Leuven, Leuven, Belgium

Pre-pouch ileitis (PI) is a complication that can occur after proctocolectomy and ileal pouch-anal anastomosis (IPAA) for ulcerative colitis (UC). It is characterized by inflammation of pre-pouch ileum in the afferent limb of the pouch. At endoscopy, PI can mimic Crohn's disease, however, current evidence suggests PI is a distinct disease entity. The development of PI has been noted to be associated with the presence of primary sclerosing cholangitis (PSC) in previous studies. Our aims were to assess the prevalence of PI as well as to identify predictive factors and investigate the medications needed for its management. Data on 546 patients who underwent IPAA for UC was retrospectively collected from three tertiary inflammatory bowel disease (IBD) referral centers. Data was collected from sites in the Netherlands, Belgium and England. PI was considered present if there was endoscopic, as well as histological inflammation in the afferent limb. Wherever possible, Crohn's disease was excluded as the underlying diagnosis by assessing the histology of colectomy resection specimens. PI was present in 33/546 (6%) UC patients, all of these had concurrent pouchitis. 144 (26%) patients had pouchitis without PI. 369 (68%) patients did not have any inflammatory pouch problems. Of the 33 patients with PI: 6 (18%) did not require treatment, 9 (27%) responded to antibiotics and 18 (54%) required escalation in therapy, to include steroids/immunomodulators or anti-TNF agents. Rates of requiring potent immunosuppressive treatment were higher amongst patients with PI than those with pouchitis alone. Patients who went on to develop PI were significantly younger at the time of their UC diagnosis. PSC was significantly more common in patients with PI than those with pouchitis alone. PI is a much less common and more treatment refractory condition than pouchitis alone. Pouchoscopy should be considered in any patient with symptoms of pouchitis. This should include careful endoscopic evaluation of the afferent pouch limb as well as biopsies of the pre-pouch ileum. Once a diagnosis of PI is made, clinicians should commence immunomodulatory therapy early in the disease course and consider escalating to an anti-TNF if this proves ineffective.

MLDS VOORDRACHT: Faecal Microbiota Transplantation in ulcerative colitis: a randomised controlled trial

N. Rossen[1], S. Fuentes[2], M. van der Spek[1], J. Tijssen[3], J. Hartman[2], Ann Duflou[1], L. Mathus- Vliegen[1], W. de Vos [2,4], E. Zoetendal[2], G. D'Haens[1], C. Ponsioen[1]. [1]Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam. [2]Department of Cardiology, Academic Medical Centre, Amsterdam, The Netherlands. [3]Laboratory of Microbiology, Wageningen University, the Netherlands. [4]Departments of Bacteriology & Immunology and Veterinary Biosciences, University of Helsinki, Finland

Background & aims: An aberrant microbiota has been implicated in the pathophysiology of ulcerative colitis (UC) and several case series reported favorable effects of faecal microbiota transplantation (FMT). We aimed to assess the efficacy FMT in active UC patients in a randomized parallel group study. Methods: Patients with mild-moderate UC (Simple Clinical Colitis Activity Index [SCCAI] score of 4-11 and a Mayo endoscopic score of ≥1) were randomly assigned (1:1) to FMT derived from faeces from a healthy donor: FMT-D or their own faeces used as a placebo: FMT-P. FMT was administered via a naso-duodenal tube at week 0 and 3. Patients, physicians and endoscopists were blinded, with exception of the nurse who performed randomisation and prepared the faeces filtered with normal saline. The composite primary endpoint was clinical remission (SCCAI score ≤2) and endoscopic response (≥1 point decrement on the Mayo endoscopic score) at week 12. Main secondary endpoints were microbiota composition in faecal samples and safety. Results: Of 50 patients who were screened, 48 were randomised (23 to FMT-D and 25 to FMT-P. In the ITT analysis, seven out of 23 patients (30.4%) in the donor arm versus five out of 25 patients in the placebo arm (20.0%) achieved the primary endpoint, P= .51. In the per protocol analysis 37 patients completed endoscopic follow-up; seven out of 17 patients in the donor arm (41.2%) versus five out of 20 (25.0%) in the placebo arm achieved the primary endpoint, P= .29. The majority of patients experienced mild adverse events with spontaneous recovery. Serious adverse events occurred in four patients and were considered not related to FMT. The trial was terminated after 50 inclusions due to futility. Redundancy analysis showed that at 12 weeks faecal microbiota of responders in the FMT-D group overlapped with healthy donors, which was associated with occurrence of Clostridium cluster XIVa. This was not seen in responders from the FMT-P group.
Conclusions: FMT with faeces of a healthy donor did not result in statistically higher clinical and endoscopic remission rates as compared to placebo in moderately active unselected UC patients. However, both FMT(donor) and FMT(placebo) are associated with signature changes in responders. Future studies should focus on mode of administration, matching of donors for selected patients, as well as the observed shifts in microbiota composition in responders. ClinicalTrials.gov number NCT01650038.

Non-trough IFX concentrations reliably predict trough levels and accelerate dose-adjustment in Crohn's disease

D.R. Hoekman[1], M. Lowenberg[1], R.A. Mathot[2], G.R. D'Haens[1], [1]Dept of Gastro-enterology and Hepatology, and [2]Dept of Hospital Pharmacy, Academic Medical Center, Amsterdam, The Netherlands

Introduction: Therapeutic drug monitoring (TDM) of infliximab (IFX) is an effective strategy to treat secondary loss of response to IFX in patients with Crohn's disease (CD). Furthermore, it is hypothesized that TDM of IFX may prevent the loss of response to IFX. Current TDM algorithms are exclusively based on IFX trough levels (TLs). There is however a significant delay between TL blood draw and the availability of the result. As a result dose adjustment usually can only be done at the following infusion 8 weeks later. Therefore, it would be of great value if TDM of IFX can be performed using IFX serum concentrations at intermediate time points. The aim of this study was to investigate the relationship between intermediate IFX levels (at week 4 and 6 of the dosing interval) and IFX TLs in CD patients receiving IFX maintenance treatment.Methods: In this ongoing, prospective, observational study, patients with CD in clinical remission based on a Harvey-Bradshaw index of ≤4 are included. All patients are receiving standard IFX maintenance treatment (5mg/kg every 8 weeks). Prior to two consecutive infusions and 28 days (week 4) and 42 days (week 6) after the first infusion, serum IFX concentration, CRP and albumin are determined. IFX concentration is analyzed using an ELISA assay (Sanquin Diagnostics, Amsterdam, the Netherlands). The relation between non-trough IFX concentrations and IFX TL is investigated using linear regression analysis. Pharma-cokinetic modelling will be performed using nonlinear mixed effects modeling.Results: Thus far, 20 patients have been included (11 male, median age 45 years (IQR 38-55)). The median duration of IFX treatment was 63 months (IQR 13-99). Median IFX concentrations at week 4, week 6 and trough are 16 µg/ml (IQR 14-20), 7 µg/ml (IQR 5.8-11) and 2.6 µg/ml (IQR 1.7-6.0), respectively. Preliminary linear regression analysis shows an excellent correlation between IFX concentration at 4 and 6 weeks after infusion and IFX TL 8 weeks after infusion (β=0.46; r=0.95; $p<0.001$ and β=0.60; r=0.96; $p<0.001$, respectively). IFX concentrations of ≥15 µg/ml and ≥7.5 µg/ml at week 4 and 6, respectively, appear to predict IFX concentrations of ≥3 µg/ml at trough.
Conclusion: IFX concentrations 4 and 6 weeks after infusion show a strong correlation with IFX concentration at trough. Determination of non-trough IFX levels can facilitate earlier concentration-guided dose adjustments in Crohn's disease.

Antibodies to infliximab, body weight and low serum albumin levels increase clearance of infliximab, a population pharmacokinetic study in 324 IBD patients

J.F. Brandse[1], D.R. Mould[2], Y.K. Ashruf[1], O.S. Smeekes[1], M. Löwenberg[1], C.Y. Ponsioen[1], G.R. van den Brink[1], G.R. D'Haens[1], [1]Dept of Gastroenterology, The Netherlands, [2]Projections Research Inc., Phoenixville, United States of America

Factors suggested to influence the pharmacokinetics (PK) of infliximab (IFX) in patients with inflammatory bowel disease (IBD) have mainly been derived from clinical trials or computer modelling, clinical data are scarce. Therefore we aimed to study the real-life PK of IFX in a large historical cohort of IBD patients and to identify patient, disease and treatment characteristics that influence serum concentrations and clearance of IFX. In this cross-sectional study all measurements (November 2004 - August 2014) of IFX serum concentrations in IBD patients collected in a tertiary referral center were identified. Medical charts of these patients were reviewed for patient, disease and treatment characteristics. IFX serum concentrations and antibodies to IFX (ATI) had been measured using an ELISA and antigen binding test (radioimmunoassay, Sanquin Laboratories). PK was analysed by nonlinear mixed-effects modelling and described using a 2-compartiment PK model. All influential covariates were combined into a full model. A total of 734 distinct IFX concentrations measurements were included, comprising data from 324 IBD patients (mean 2.27 measurements). Disease extent was scored based on the Montreal classification for 252 Crohn's disease patients (L1:53/252, L2:79/252, L3: 120/252) and 72 ulcerative colitis patients (E1: 6/72, E2: 26/72, E3:40/72). 318/324(98%) of patients were anti-TNF naïve at start of IFX. Mean dose of IFX was 5.49 mg/kg (SD 1.39). ATI were detected in 100/324 (31%) patients. Mean (inter individual variability) values for clearance, central and peripheral volume of distribution were 0.34 L/day (74%), 12.8 L (98%) and 15.1 L (153%). Disease extent did not affect PK. Body weight and anti-IFX antibodies were identified as independent covariates ($P<0.001$) increasing clearance (mean (SE)) by 2.76 (14.1) fold and 6.04 (10.3) fold respectively, whereas serum albumin had a -0.69 (22.2) fold inverse impact on clearance. Because serum CRP values tended to change rapidly after initiation of treatment, and use of concomitant immunomodulators was often intermittent, these factors could not be evaluated as independent covariates although the administration of continuous concomitant immunomodulators was associated with a decrease in clearance.

Conclusions: Antibodies to infliximab, body weight and low serum albumin levels increase clearance of infliximab.

Elevated 6-methylmercaptopurine metabolites assessed shortly after thiopurine therapy initiation are associated with hepatotoxicity in inflammatory bowel disease patients

D.R. Wong[1], M.J.H. Coenen[2], L.J.J. Derijks[3], C.J. van Marrewijk[2], S.H. Vermeulen[2,4], A.L.M. Verbeek[4], B. Franke[2,6], H-J. Guchelaar[7], D.J. de Jong[8], L.G.J.B. Engels[9], P.M. Hooymans[1], On behalf of the TOPIC study group, [1]Dept of Clinical Pharmacy and Toxicology, Orbis Medical Center, Sittard-Geleen, [2]Dept of Human Genetics, Radboud University Medical Center, Nijmegen, [3]Dept of Clinical Pharmacy, Máxima Medical Center, Veldhoven, [4]Dept for Health Evidence, Radboud University Medical Center, Nijmegen, [5]Dept of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute of Pharmaceutical Sciences, Utrecht University, Utrecht, [6]Dept of Psychiatry, Radboud University Medical Center, Nijmegen, [7]Dept of Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, [8]Dept of Gastroenterology, Radboud University Medical Center, Nijmegen, [9]Dept of Gastroenterology, Orbis Medical Center, Sittard-Geleen, The Netherlands

Hepatotoxicity is one of the most common adverse events of azathioprine (AZA) and mercaptopurine (6MP) therapy in inflammatory bowel disease (IBD) patients, which has been related to highly elevated 6-methylmercaptopurine ribonucleotide (6MMPR) metabolite concentrations. The aim of our study was to evaluate the predictive value of 6MMPR metabolite concentrations, assessed one week after thiopurine therapy initiation, for the development of thiopurine-induced hepatotoxicity during the first 20 weeks of treatment. Our study was performed in thiopurine-naïve IBD patients starting thiopurine treatment as part of the Dutch randomised multi-centre TOPIC trial (ClinicalTrials.gov NCT00521950). Blood samples for 6-thioguanine nucleotides (6TGN) and 6MMPR assessment were collected one week after thiopurine therapy initiation (T1). Hepatotoxicity was defined by an elevation from base of alanine aminotransaminase and aspartate aminotransaminase and/or alka phosphatase enzymes, up to at least twice the upper limit of the reference values. We included the first 270 patients of the TOPIC trial.
Forty-seven patients (17%) showed signs of hepatotoxicity during the first 20 weeks of thiopurine treatment. T1 6MMPR metabolite levels were significantly higher in patients who developed potential hepatotoxicity, compared to patients who did not: 3,111 pmol/8x10*8 red blood cells (RBC) (range 300-15,691) versus 1,811 pmol/8x10*8 RBC (range 300-11,230; p<0.001), respectively. 6-MMPR concentrations above the defined T1 threshold of ~3615 pmol/8x10*8 RBC correlated with gastrointestinal complaints (i.e. nausea, vomiting and anorexia; OR=2.4 (95%CI: 1.4-4.3)) and general malaise (OR=2.0 (95%CI: 1.1-3.7). Analysis of patients on stable thiopurine dose (n=174) revealed that at the defined T1 6MMPR threshold, patients with elevated metabolite concentrations were at increased risk of hepatotoxicity: 48% (19/40) of the patients above the threshold developed hepatotoxicity versus 19% (26/134) below the threshold (OR=3.8 (95%CI: 1.8-8.0); p<0.001). A predictive algorithm was developed based on the relevant determinants age, gender, BMI and the 6MMPR threshold to assess the risk of hepatotoxicity in patients starting thiopurine therapy (AUC 0.83 (95% CI: 0.75-0.91)).
In conclusion, assessment of the 6MMPR concentration one week after initiation identifies IBD patients at risk for thiopurine-induced hepatotoxicity, gastrointestinal complaints and general malaise, allowing to optimise therapy in the early stage of thiopurine treatment.

Azathioprine and 6-mercaptopurine are equally effective in thiopurine naïve IBD patients

M.M.T.J. Broekman[1], M.J. Coenen[8], B. Franke[7,8], L.J. Derijks[2], S.H. Vermeulen[3,8], D.R. Wong[4], O.H. Klungel[5], A.L. Verbeek[3], P. Hooymans[4], H. Scheffer[8], H.J. Guchelaar[6], C.J. van Marrewijk[8], D.J. de Jong[1], [1]Dept of Gastroenterology, Radboud University Medical Center, Nijmegen, [2]Dept of Clinical Pharmacy, Máxima Medical Center, Veldhoven, [3]Dept for Health Evidence, Radboud University Medical Center, Nijmegen, [4]Dept of Clinical Pharmacy and Toxicology, Orbis Medical Center, Sittard-Geleen, [5]Dept of Pharmacoepidemiology and Pharmacotherapy, Utrecht University, Utrecht, [6]Dept of Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, [7]Dept of Psychiatry, Radboud University Medical Center, Nijmegen, [8]Dept of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands

6-Mercaptopurine (6-MP) and its pro-drug azathioprine (AZA) are frequently prescribed for the treatment of inflammatory bowel diseases (IBD), however studies comparing both agents are scarce. Our aim was to compare the incidence of side effects and efficacy of AZA and 6-MP in thiopurine naïve patients.We analyzed data from the TOPIC-study ("Thiopurine response Optimization by Pharmacogenetic testing in Inflammatory bowel disease Clinics" (ClinicalTrials.gov: NCT00521950)). In this multicentre trial, 768 thiopurine naïve IBD patients were randomized for thiopurine dosing based on thiopurine S-methyltransferase (TPMT) genotype versus standard thiopurine dosing. In this study physicians were free in their choice for AZA or 6-MP. Patients were followed for 20 weeks and treatment response was assessed with Harvey-Bradshaw index in Crohn's disease (CD) and the partial Mayo score in Ulcerative colitis (UC). Gastro-intestinal side effects were defined as the occurrence of nausea, vomiting or decrease of appetite. Hepatic side effects were defined as an increase above two times the upper limit of normal (ULN) of either ALT, AST, GGT or AP, with no other explanation. Thiopurine induced pancreatitis was defined as amylase or lipase above two times the ULN with clinical symptoms or radiological findings suggestive for pancreatitis. Differences were assessed using chi-squared and Mann-Whitney U-tests. AZA was prescribed in 495 (64.5%) patients (mean dose: 2.05 mg/kg) and 6-MP in 273 (35.5%) patients (mean dose: 1.14 mg/kg). The majority of patients had CD (n=464) compared to UC (n=297) and undetermined colitis (n=4). AZA was prematurely withdrawn in 42.4% and 6-MP in 44.0% of the patients (P=0.4). The incidence of gastro-intestinal side effects was similar in both groups; 47.2% (AZA) vs. 50.5% (6-MP); P=0.38). In total, 26 (3.4%) patients developed pancreatitis that was attributed to thiopurine use, 18 (3.7%) AZA and 8 (2.9%) 6-MP (P=0.59). Hepatotoxicity was reported in 99 (20%) patients with AZA and 71 patients (26.0%) taking 6-MP (P=0.06). 6-Thioguanine nucleotide levels measured at week 8 were significantly higher in 6-MP users (314 pmol/10e8 vs. 276 pmol/10e8 per red blood cell) (P=0.03). Treatment response was known for 273 patients with CD and 132 with UC and showed no significant differences (P=0.79 and P=0.46) between AZA and 6-MP.
Conclusion: This clinical trial suggests that AZA and 6-MP are similar in terms of efficacy, and safety as initial thiopurine in the treatment of IBD

Short term prevalence of nodular regenerative hyperplasia of the liver in IBD patients treated with allopurinol-thiopurine combination therapy

M.L. Seinen[1], D.P. van Asseldonk[1], N.K. de Boer[1], G. Bouma[1], C.J. Mulder[1], E. Bloemena[2], A.A. van Bodegraven[1,3], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Pathology, VU University Medical Center, Amsterdam, [3]Dept of Internal Medicine, Gastroenterology, and Geriatrics, Orbis Medical Center, Sittard-Geleen, The Netherlands

Background: Tioguanine has been associated with nodular regenerative hyperplasia (NRH) of the liver. Combination therapy of allopurinol and adapted dose conventional thiopurine leads to a pharmacokinetic profile partly comparable with that of tioguanine ((high 6-thioguanine nucleotides (6-TGN) and low 6-methylmercaptopurine (6-MMPR) concentrations)). Therefore, combination therapy of allopurinol and conventional thiopurines may induce NRH of the liver in a comparative way. We assessed short term prevalence of NRH in IBD-patients treated with allopurinol-thiopurine combination therapy. Methods: This was an observational, single-centre cross-sectional study. All adult IBD-patients who were treated at least one year with allopurinol-thiopurine combination therapy were eligible. Subjects were identified at the Outpatients' clinic and they were consecutively invited to participate. All patients underwent a liver biopsy, and venous blood was drawn to measure haematological and hepatic parameters, including thrombocyte count and alka phosphatase, but also to determine thiopurine metabolite concentrations. Histopathology was assessed by an experienced hepatopathologist. Results: Eighteen IBD-patients, of which thirteen were diagnosed with Crohn's disease were included. The median age at inclusion was 36 year (IQR 25-42). Combination therapy was initiated in nine patients as a result of elevated transaminase activities during thiopurine monotherapy. The median duration of combination therapy at inclusion was 24 months (IQR 20-28). The median 6-TGN and 6-MMPR level was 685 pmolx10^8 RBC (IQR 498-940) and 305 pmolx10^8 RBC (IQR 198-608). In none of the patients NRH was observed; sinusoidal dilatation was observed in four patients. No trombocytopenia was observed.
Conclusion: Short term prevalence of NRH in IBD-patients who were treated with a combination of allopurinol and low dose conventional thiopurine, was low, as in none of the included eighteen patients NRH was observed.

Development of a patient reported disease activity score to screen for mucosal inflammation in inflammatory bowel disease.

M.J. de Jong[1], J.H.R.J. Degens[1], T.R.A. van den Heuvel[1], M. Romberg-Camps[2], B. Winkens[3], T. Markus[4], A.A.M. Masclee[1], A. van Tubergen[5], D.M.A.E. Jonkers[1], M.J. Pierik[1], [1]Dept of Gastroenterology, Maastricht University Medical Center, Maastricht, [2]Dept of Gastroenterology, Orbis Medical Center, Maastricht, [3]Dept of Methodology and Statistics, Maastricht University, Maastricht, [4]CCUVN, Woerden, [5]Dept of Reumatology, Maastricht University Medical Center, Maastricht, The Netherlands

Integrated care and patient empowerment improve the outcome of chronic diseases. Telemedicine programmes are of interest for Inflammatory Bowel Diseases (IBD), but should include adequate monitoring of mucosal inflammation to prevent longterm complications. Different clinical activity questionnaires have been developed for systematic follow-up of disease activity in Crohn's disease (CD) and ulcerative colitis (UC). However, none has been validated against endoscopy, which is the golden standard for assessing mucosal inflammation. Recently published validated clinical activity scores include laboratory parameters and are therefore not suitable for telemedicine programs. The objective of this study was to develop the first patient reported disease activity score for IBD patients to predict endoscopic disease activity, which can be used in telemedicine programmes. Twenty-three questions regarding disease activity in IBD were selected based on literature review and expert opinion. Consecutive patients undergoing a colonoscopy for clinical evaluation between March 2013 and April 2014 were invited to fill out this 23 item questionnaire 24 hours before endoscopy (i.e. prior to bowel cleansing). Mucosal inflammation was assessed during endoscopy with the simplified endoscopic activity score for CD (SES – CD) and the Mayo endoscopic subscore (MES) for UC. Questions were reduced to a total of 6 for CD and 5 for UC, based on individual correlation coefficients with endoscopic inflammation and expert opinion. Then, logistic regression was used to find the best fitting model. ROC curves were used to find the optimal cut-off value in terms of sensitivity and specificity. Ninety-eight CD patients (41.8% male, mean ± SD age 44.7 ± 14.2 years, 55.1% active disease) and 80 UC patients (58.8% male, mean ± SD age 52.2 ± 15.3 years, 63.8% active disease) were included. The multivariable logistic regression model for CD with a sensitivity of 90.4% (specificity 40.9%) included questions on blood loss, mucus, number of stools, urgency, fatigue and IBD symptoms in general. The multivariable logistic regression model for UC with a sensitivity of 88.3% (specificity 65.5%) contained items on blood loss, number of stools, urgency, abdominal pain and IBD symptoms in general.

Conclusions: We developed a patient reported disease activity score with a high sensitivity for detecting endoscopic disease activity in IBD patients. Such a tool is warranted in telemedicine programmes for screening patients who need further assessment of disease activity with biochemical markers and/or endoscopy. At present we are validating the score in an independent patient cohort.

Long-term disease outcome of Crohn's disease in the biological era – Results from a Dutch population-based IBD cohort

S.F.G. Jeuring[1,2], T.R.A. van den Heuvel[1,2], M.P. Zeegers[3,4], W.H. Hameeteman[1], M.J.L. Romberg-Camps[5], L.E. Oostenbrug[6], S.O. Breukink[7], L.P.S. Stassen[7], A.A.M. Masclee[1,2], D.M.A.E. Jonkers[1,2], M.J. Pierik[1,2], [1]Division of Gastroenterology-Hepatology, Maastricht University Medical Center, Maastricht, The Netherlands, [2]School for Nutrition, Toxicology and Metabolism (NUTRIM), Maastricht University Medical Center, Maastricht, The Netherlands, [3]Dept of Complex Genetics, Cluster of genetics and Cell Biology, Maastricht University Medical Center, Maastricht, The Netherlands, [4]Dept of Epidemiology and Public Health, University of Birmingham, Birmingham, United Kingdom, [5]Dept of Internal Medicine and Gastroenterology, Orbis Medical Center, Sittard-Geleen, The Netherlands, [6]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center, Heerlen, The Netherlands, [7]Dept of General Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

In the course of Crohn's disease (CD), patients are at risk for developing strictures or fistulas and many require surgery for these conditions or for refractory inflammatory disease. In the last decades, treatment modalities in CD have changed with the introduction of biological agents and an increased and earlier use of immunomodulators. Its effect on disease outcome is yet unknown, mostly due to lack of data before and after biological availability from the same source population. Therefore, we aimed to compare long-term disease outcome of CD patients diagnosed in the pre- biological era to CD patients diagnosed in the biological era in a population-based cohort. Since 1991, incident IBD cases in our area are included in our population-based cohort, with over 93% completeness. All CD patients were divided in two time cohorts. The pre-biological cohort comprised patients diagnosed between 1991 and 1998, followed until 1999 (registration of biological therapy for CD). The biological cohort comprised patients diagnosed between 1999 and July 2011, followed until 2014. Disease behaviour was classified at diagnosis and during follow-up according to the Montreal classification as B1 (non-stricturing, non-penetrating), B2 (stricturing), or B3 (penetrating). Disease outcome, in terms of progression to B2 or B3 phenotype, hospitalisation risk and surgery risk, was analysed with a Kaplan-Meier survival curve. Hazard ratios (HR) were calculated using a Cox regression model, corrected for confounders. In total, 342 patients in the pre-biological and 820 patients in the biological era were included, with a mean follow-up of 4.0 (SD 2.5) and 6.4 (SD 3.6) years, respectively. At diagnosis, patients in the biological era less often presented with B2 or B3 phenotype (12.8% vs. 22.0%, HR 0.52; 95%CI 0.38-0.73), and were less often hospitalised (21.1% vs. 36.8%, HR 0.45; 95%CI 0.34-0.60) and operated (3.8% vs. 14.4%, HR 0.23; 95%CI 0.15-0.38). During disease course, disease progression to B2 or B3 phenotype was similar between eras (28.3% vs. 29.7%; HR 0.95; 95%CI 0.70-1.29). Patients in the biological era had a 2.2-fold lower risk of surgery during follow-up (24.0% vs. 40.0%; HR 0.46; 95%CI 0.34-0.63), in particular for inflammatory disease (5.9% vs. 11.7% HR 0.41; 95%CI 0.25-0.68). We also observed a lower hospitalisation risk during follow-up in the biological era (34.4% vs. 51.4%, HR 0.65; 95%CI 0.49-0.87).

Conclusion: In an era of biological availability and more frequent use of immune-suppressive treatment in CD, risk of surgery for inflammatory disease decreased 2.2-fold, while the risk of progression to stricturing or penetrating disease remained unchanged.

Lower long-term colectomy rates with IFX than with CsA treatment in moderate to severe UC

N.W. Duijvis[1], A. ten Hove[1], C. Ponsioen[2], G.R. van den Brink[1,2], A. te Velde[1], G.R.A.M. D'Haens[2], M. Löwenberg[2], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

Background: Cyclosporine A (CsA) and infliximab (IFX) are similarly effective in preventing short-term colectomy in patients with moderate to severe ulcerative colitis (UC), but long-term outcomes are lacking. The aim of this study was to compare long-term efficacy of CsA and IFX in moderate to severe UC by analyzing colectomy rates as the outcome parameter for treatment success. Methods: We retrospectively studied a cohort of patients who had received treatment with CsA or IFX between January 2000 and May 2014 at the Academic Medical Centre in Amsterdam for moderate to severe UC. The primary end point was time to colectomy. Variables such as gender, age, Mayo endoscopic subscore at start of treatment, extent of the disease and concomitant treatments were studied as relevant variables affecting outcome. Results: 182 patients were studied (CsA group, n=43; IFX group, n=139). Follow-up of at least 6 months was available for all patients. Patient characteristics (age, gender, disease duration, disease extent and severity) were comparable between the two groups, with the exception that the mean follow-up was significantly longer in CsA treated patients (IFX 61.5 months + 36.8 vs. CsA 124.7 months + 41.5), and steroid use was significantly higher in CsA treated patients (CsA 73% vs. IFX 40%). Colectomy-free survival at different end points was significantly higher in the IFX group as compared to CsA treated patients:at 1 month 98% vs 74%, at 6 months 84% vs 56%, and at 12 months 80% vs 49% (all P<0.0005). Finally, at three years, colectomy-free survival was 67% vs 45% (IFX vs CsA, P<0.015, Kaplan Meier Log Rank P<0.0005). CsA treated patients were at increased risk of undergoing colectomy (HR 2.61, P<0.001). When adding all significant covariates into a multivariate Cox regression model, therapy with CsA or IFX barely loses its significance (HR 1.84, P=0.084). Independent predictors for colectomy were male sex (p=0.018; HR=1.97), younger age (p=0.036; HR 0.98) and endoscopic disease severity (p=0.001; HR 2.50).
Conclusion: IFX treatment is associated with lower colectomy rates compared to CsA in patients with moderate to severe UC.

Healthcare expenditures for inflammatory bowel disease peak in patients with a short disease duration

M. Severs[1], M.E. van der Valk[1], M.J. Mangen[2], M. Leenders[1], G. Dijkstra[3], A.A. van Bodegraven[4], H.H. Fidder[1], D.J. de Jong[5], M. Pierik[6], C.J. van der Woude[7], M.J. Romberg-Camps[8], C.H. Clemens[9], J.M. Jansen[10], N. Mahmmod[11], P.C. van de Meeberg[12], A.E. van der Meulen-de Jong[13], C.Y. Ponsioen[14], C.J. Bolwerk[15], J.R. Vermeijden[16], P.D. Siersema[1], B. Oldenburg[1], COIN study group - Dutch Initiative on Crohn and Colitis, [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Julius Centre for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, [3]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [4]Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, [5]Dept of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Center, Nijmegen, [6]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [7]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [8]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [9]Dept of Gastroenterology and Hepatology, Diaconessenhuis, Leiden, [10]Dep of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, [11]Dept of Gastroenterology and Hepatology, Antonius Hospital, Nieuwegein, [12]Dept of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, [13]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [14]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [15]Dept of Gastroenterology and Hepatology, Reinier de Graaf Groep, Delft, [16]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, The Netherlands

Purpose: We aimed to study whether disease duration influences the healthcare costs in inflammatory bowel disease (IBD) patients in a large cohort. Methods: A large number of IBD patients from academic and non-academic hospitals were prospectively followed for two years (the COIN- study). At baseline, the disease duration of all patients was calculated. Used healthcare resources, disease activity and quality of life were assessed using three-monthly questionnaires. Healthcare resources were multiplied by their unit prices to obtain costs. These parameters were cross-sectionally compared between patients with a short (0-1 yr), median (1-5 yrs), long (5-10 years) and extended (10-20 yrs and >20 years) disease duration at baseline. Results: A total of 3,030 patients (1,558 Crohn's disease (CD), 1,054 ulcerative colitis (UC) and 418 IBD-unspecified) were enrolled in the study. Fifty-six patients had a disease duration of 0-1 years, 502 of 1-5 years, 569 of 5-10 years, 899 of 10-20 years and 998 of over 20 years. The proportion of patients with active disease gradually decreased over time, being 30.4% in IBD patients with a short disease duration, and 13.2% in those with an extended (>20 yrs) disease duration (CD: from 36.0% to11.8%; UC: from 21.1% to 16.5%). The total IBD healthcare costs peaked at 1-5 years of disease duration, which was mainly due to a high number of TNF-α inhibitor users (CD: 30.7% vs. 17.7% after 20 years; UC: 5.7% vs. 3.4% after 20 years). In patients with a longer disease duration, total healthcare costs were lower than in the first years after diagnosis. In CD, healthcare costs after the first year following the diagnosis shifted from hospitalizations to medication costs (TNF-α-inhibitors). Hereafter, medication costs remained the major driver of total healthcare costs. In UC, total healthcare costs decreased over time, but increased again in patients with a disease duration of 20yrs or more, due to an increase of hospitalizations. The quality of life was lowest in patient shortly after diagnosis of IBD and increased gradually in both CD and UC patients with a longer disease duration (median IBD- questionnaire: CD from 175 to 179; UC from 179 to 190).
Conclusions: The healthcare costs of IBD peak in patients with a short disease duration. The quality of life is higher in patients with a longer disease duration.

Evolution of IBD-related costs over two years of follow up: increase of anti-TNF α therapy related costs with a dec of hospitalization costs

M.E. van der Valk[1], M.J.J. Mangen[1], M. van der Have[1], M. Severs[1], G. Dijkstra[2], A.A. van Bodegraven[3,4], H.H. Fidder[2], D.J. de Jong[5], M. Pierik[7], C.J. van der Woude[8], M. Romberg-Camps[4], C.H.M. Clemens[6], J.M. Jansen[15], P.C. van de Meeberg[9], M. Mahmmod[10], A.E. van der Meulen - de Jong[11], C.Y. Ponsioen[12], C. Bolwerk[13], J.R. Vermeijden[14], P.D. Siersema[1], M. Leenders[1], B. Oldenburg[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [3]Dept of Gastroenterology and Hepatology, VU Medical Center, Amsterdam, [4]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [5]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [6]Dept of Gastroenterology and Hepatology, Diaconessenhuis, Leiden, [7]Dept of Gastroenterology and Hepatology, Maastricht, University Medical Center, Maastricht, [8]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, [9]Dept of Gastroenterology and Hepatology, Slingeland Hospital, Doetinchem, [10]Dept of Gastroenterology and Hepatology, Antonius Hospital, Nieuwegein, [11]Dept of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, [12]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [13]Dept of Gastroenterology and Hepatology, Reinier de Graaf Group, Delft, [14]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [15]Dept of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

With the introduction and increasing use of anti-TNF α therapy in IBD a shift of costs has been observed with medication costs replacing hospitalization and surgery as the greatest source of healthcare expenditure. We explored the impact of the use of anti-TNF α therapy on IBD-related costs from a societal perspective over two years of follow-up. A total of 1,307 Crohn's disease (CD) patients and 915 ulcerative colitis (UC) patients was prospectively followed for two years by three-monthly web-based questionnaires (the COIN study). Changes of healthcare costs, productivity costs and out-of-pocket costs over time were assessed using mixed model analysis. Multivariable logistic regression analysis was used to examine the impact of base demographics and clinical characteristics on increase of costs over time. A total of 737 CD patients (40% males, mean age 48 years (SD 13 years)) and 566 UC patients (53% males, mean age 50 yaers (SD 13 years)) were followed for two years. Total costs were stable over two years of follow-up, with annual total costs of € 8,317 in CD and € 4,114 in UC. Although healthcare costs did not change over time, the proportion of anti-TNFa therapy-related costs increased over two years from 64% to 72% in CD ($p<0.01$) and from 31% to 39% in UC ($p < 0.01$). In contrast, the proportion of hospitalization costs decreased from 19% to 13% in CD ($p<0.01$), and 22% to 15% in UC ($p < 0.01$). Penetrating disease course was associated with increase of healthcare costs (adjusted odds ratio (adj. OR) 1.95 (95% CI 1.02-3.37) in CD. In UC only age < 40 years was associated with an increase of healthcare costs (adj. OR 4.72 (95% CI 1.61-13.86).
Conclusions: Total IBD-related costs do not change over time. However, the proportion of anti-TNF α related healthcare costs increased over two years of follow-up, at the expense of hospitalization costs. Factors associated with increased healthcare costs were penetrating disease course in CD and age < 40 in UC.

Fertility in IBD women is comparable to fertility in non-IBD controls

A. de Lima[1], M. van Amelsfort[1], E.A.P. Steegers[2], C.J. van der Woude[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Obstetrics and Gynecology, Erasmus University Medical Center, Rotterdam, The Netherlands

Background: As inflammatory bowel diseases (IBD) often arises in young people, questions about fertility and reproduction are common. Prior studies on infertility in IBD women are scarce and conflicting. The aim of this study was to compare subfertility between IBD women and non-IBD controls. Furthermore, we investigated the effect of several IBD associated factors on fertility. Methods: All consecutive IBD women with a pregnancy wish from 2008-2014 were prospectively followed a specialized preconception outpatient clinic. Data on patient characteristics, disease and obstetric/gynecologic history, paternal health, time to conception and pregnancy outcomes were recorded. The control group consisted of a random age-, and ethnicity-, matched sample from a large non-diseased birth cohort (Generation R) from the same geographical region. Primary aim was to compare subfertility rates between IBD women and non-IBD controls. Subfertility was defined as the inability to conceive within 12 months of unprotected intercourse and/or the need for fertility treatment to conceive. Secondary aim was to identify risk factors for subfertility in IBD women. Results: A total of 333 cases in 227 IBD women (236 CD (70.9%), 87 UC (26.1%), 10 IBDU (3.0%)) and 804 non-diseased controls were included. Mean maternal age was 30.5 yrs (SD=4.4 yrs). There were no differences between the IBD and the control group in maternal and paternal BMI (p=0.55 and p=0.53, respectively) and smoking status (p=0.14 and p=0.06, respectively). Median time to conception was 2.4 months (IQR: 0.9-7.2) in the IBD group versus 3.0 months (IQR: 2.0-7.0) (p=0.001) in the control group. IBD was not significantly associated with subfertility when compared to controls (aOR: 1.39 (95% CI: 0.99-1.94, adjusted for maternal age, BMI, education and paternal smoking). IBD women more often underwent fertility treatment than controls (21 (10.1%) vs 30 (3.7%), p=0.001). Reasons for fertility treatment in the IBD group were of gynecologic or andrologic cause in 18 cases (85.7%). Diagnosis, previous bowel surgery, perianal disease activity, IBD medication type and the number of disease flares in the past year were not associated with subfertility in IBD women.

Conclusion: This study shows IBD is not associated with increased time to conception or subfertility. Fertility treatment was more common in IBD women, but this was not associated with IBD. Type of IBD, previous bowel surgery, perianal disease, IBD medication and disease activity were not associated with subfertility in IBD women.

Long term outcome of children born to IBD mothers Preliminary result from a multicenter retrospective study in the Netherlands

S.L. Kanis[1], A. de Lima[1], Z. Zelinkova[1], G. Dijkstra[2], R.L. West[3], R.J. Ouwendijk[4], N.K.H. de Boer[5], A.E. van der Meulen[6], M.J. Pierik[7], L.E. Oostenbrug[8], M. Romberg-Camps[9], G.L. Bodelier[10], B. Oldenburg[11], F. Hoentjen[12], R. Beukers[13], J.M. Jansen[14], C.J. van der Woude[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University, Erasmus Medical Center, Rotterdam, [2]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, [3]Dept of Gastroenterology and Hepatology, Sint Franciscus Gasthuis, Rotterdam, [4]Dept of Gastroenterology and Hepatology, Ikazia Hospital, Rotterdam, [5]Dept of Gastroenterology and Hepatology, Free University, Free University Medical Center, Amsterdam, [6]Dept of Gastroenterology and Hepatology, Leiden University, Leiden University Medical Center, Leiden, [7]Dept of Gastroenterology and Hepatology, Maastricht University, Maastricht University Medical Center, Maastricht, [8]Dept of Gastroenterology and Hepatology, Atrium Medical Center, Heerlen, [9]Dept of Gastroenterology and Hepatology, Orbis Medical Center, Sittard, [10]Dept of Gastroenterology and Hepatology, Amphia Hospital, Breda, [11]Dept of Gastroenterology and Hepatology, Utrecht University, University Medical Center Utrecht, Utrecht, [12]Dept of Gastroenterology and Hepatology, Radboud University, Radboud Medical Center, Nijmegen, [13]Dept of Gastroenterology and Hepatology, Albert Schweitzer Hospital, Dordrecht, [14]Dept of Gastroenterology and Hepatology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

Background: The long term outcome of children born to mothers with inflammatory bowel disease(IBD) are relatively unexplored. The aim of this study is to analyze the health status of children who were born to mothers with IBD. Methods: All women diagnosed with IBD prior to their pregnancy that gave birth between 1999 and 2011 were invited. After informed consent from both parents, the general practitioner (GP) was contacted for the following child outcomes: growth, number of infections for which antibiotics were needed, allergies and allergic reactions to vaccinations. Low birth weight was stated as <2500g, preterm birth as gestational age <37 weeks. The EUROCAT guide was used to classify congenital abnormalities. Results: In total 935 invitations (in 2 rounds) were sent to women with IBD from 8 Dutch hospitals. The response was 46.8%(438). Until November 2014 362 children from 239 IBD mothers (257(71.0%) CD,93(25.7%)UC and 12(3.3%)IBDU) were included. Median child age at follow up was 6 years (IQR 4-11). In utero 118(32.6%) children were not exposed to any IBD drug, 97(26.8%) to only mesalazine, 79(21.8%) to thiopurine, 38(10.5%) to anti- TNF, 20(5.5%) to both anti-TNF and thiopurine and for 10(2.8%) children drug exposure was unknown. There was no difference in anti- TNF exposed and the non- anti TNF exposed children considering; median gestational age (39 weeks(IQR38-40)), pre- term births (67(18.5%)), overall birth weight (3268 gram(IQR 2893-3638)), low birth weight (40(11 %)) and major congenital abnormalities (8(2.2 %)).Five(1.5%) children showed a primary or secondary growth deficiency. None of these children were exposed to anti- TNF. Apart from one extended rash after vaccination there were no reports of severe vaccination reactions. Overall 88 children had allergies. These allergies were more common in the non- anti TNF exposed children (36.9%)compared to the anti- TNF exposed children (15.7%)(p=0.03). Median number of infections was 1(IQR 0-3). There was no difference in infections rate between anti- TNF exposed children compared to non- anti TNF exposed children. Furthermore, there was no increased infection rate in thiopurine exposed children or children exposed to both anti-TNF and thiopurine.

Conclusion: In this long term follow-up study in children born to IBD mothers we show no major adverse events, an overall normal growth and development as compared to the Dutch population. Apart from a lower incidence of allergies no difference was observed between in utero anti-TNF exposed and non-exposed children.

Persistent low-grade dysplasia in Barrett's esophagus identifies patients at higher risk for esophageal adenocarcinoma: a Dutch nationwide cohort study

C. Kestens[1], G.J.A. Offerhaus[2], J.W.P.M. van Baal[1], P.D. Siersema[1], [1]Dept of Gastro-enterology and Hepatology, and [2]Dept of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

Background: Confirmation of low-grade dysplasia (LGD) in Barrett's esophagus (BE) by an expert pathologist has been suggested to increase the risk of progression to esophageal adenocarcinoma (EAC). However, even after a confirmed LGD diagnosis, in 28-39% of patients, non-dysplastic (ND) BE is found in follow-up biopsies. To avoid unnecessary risks and costs associated with ablative treatment, further risk stratification of patients with confirmed LGD is therefore required. Aim: To determine whether persistence of LGD in BE could be used for risk stratification in identifying the subgroup of patients actually benefiting from ablative treatment. Methods: Patients with a first diagnosis of LGD in BE were selected between 2005-2010 using PALGA, a registry of histopathology diagnoses in the Netherlands. Exclusion criteria were a diagnosis of high-grade dysplasia (HGD)/EAC prior to or simultaneously with the initial LGD diagnosis, or within 1 year after LGD diagnosis, a diagnosis of indefinite for dysplasia and patients with a follow-up less than 1 year. Persistent LGD was defined as LGD at the index and the first follow-up endoscopy. Results: A total of 1582 LGD patients were identified, of whom 161(10%) had confirmed and 1351(85%) unconfirmed LGD at the index endoscopy. Patients were followed-up for a median of 4.2 years (IQR 2.76-5.96). The overall incidence rate of developing HGD/EAC and EAC in patients with LGD at the index endoscopy was 2.10(95% CI 1.78-2.46) and 1.19(95% CI 0.96-1.48) per 100 person years, respectively. In the subgroup of patients with confirmed LGD, the incidence rate significantly increased to 5.18(95% CI 4.32-8.10) and 2.51(95% CI 1.46-3.99) per 100 person years, respectively. Of patients with a confirmed LGD diagnosis, 51% (n=82) regressed to ND and 30% (n=49) had persistent LGD. For patients with confirmed and persistent LGD (median follow-up 3.72 years, IQR 1.78-5.38), the incidence rate of developing HGD/EAC and EAC was 7.65(95% CI 4.45-12.34) and 2.04 (95% CI 0.65-4.92) per 100 person years, respectively. The incidence rate for patients with ND at follow-up endoscopy after initial confirmed LGD was significantly lower, 2.32(95% CI 1.08-4.40) and 1.45(95% CI 0.53-3.21) for HGD/EAC and EAC, respectively. Patients with 2 consecutive endoscopies showing ND BE (29%, n=46) after a confirmed LGD diagnosis developed no HGD/EAC during follow-up.
Conclusion: In this large population-based cohort of patients with LGD in BE, confirmed and persistent LGD identifies patients at a higher risk for the development of HGD/EAC. Ablative treatment should therefore be considered in patients with a combination of confirmed and persistent LGD in BE.

Detection of lesions in dysplastic Barrett's esophagus: are expert endoscopists doing a better job than community endoscopists?

D.W. Schölvinck[1,2], K. van der Meulen[1], J.J.G.H.M. Bergman[2], B.L.A.M. Weusten[1,2], [1]Dept of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

Radiofrequency ablation is the treatment of choice for eradication of flat dysplastic Barrett's esophagus (BE). All visible lesions in dysplastic BE, however, should be resected first to prevent ablation of invasive cancer. Recognition of lesions is challenging, and most guidelines advocate that these patients should be treated in expert centers. Data supporting this recommendation, however, is lacking. The aim was to compare the detection of neoplastic lesions (high grade dysplasia [HGD] and early adenocarcinoma [EAC]) in BE by endoscopists from community and expert centers. Patients were included when referred between Jan 2008 and Dec2013 with a diagnosis of HGD or EAC, confirmed by expert pathologist, to two Dutch Barrett expert centers. All referral letters, endoscopy and pathology reports were reviewed for the description of BE, presence of lesions, and histopathological analysis of target and random biopsies. Primary outcome parameter was the endoscopic detection rate of histopathologically proven HGD or EAC lesions in community and expert centers. 200 patients were referred from 37 community hospitals with a median time between community and expert endoscopy of 56 (IQR 34–90) days. Of these, 125 (62%) were referred with visible lesion, the other 75 (38%) with HGD/EAC in random biopsies only. All 125 lesions reported by the referring centers were also recognised by the expert endoscopists. Twelve of the 125 (9.6%) patients had an advanced carcinoma and were referred for surgery. In the remaining 113 patients potentially eligible for endoscopic therapy (ET), pathology showed HGD in 19 (15%), EAC-T1a in 67 (54%), and EAC-T1b in 24 (19%) patients. In 3 (2.4%) the initial confirmed diagnosis of HGD/EAC could not be repeated. In the 75 patients referred for HGD/EAC in random biopsies only, a visible abnormality was found in 68 (91%) patients in the expert centers. At expert endoscopy, 4 (6%) had an advanced carcinoma not eligible for ET. In potential ET patients, EMR pathology of the visible abnormality showed HGD in 8 (12%), EAC-T1a in 37 (54%), and EAC-T1b in 11 (16%) patients. In 8 patients (12%) EMR pathology showed either LGD or ND. In the 7 patients with no visible lesion in either center, worst pathology in random biopsies was HGD in 3 and LGD in 4 patients. Approximately one-third of patients with a diagnosis of HGD or EAC was referred without a visible lesion, while in expert centers a visible abnormality was found in 91% of these patients. Of this group, 60/75 (80%) had relevant disease (visible HGD, EAC or advanced carcinoma) that would preclude RFA as sole treatment. These data support the value of expert centers for the treatment of BE.

First results on visualization of esophageal adenocarcinoma with VEGF-guided near-infrared fluorescent endoscopy

E. Hartmans[1], P.B. Garcia-Allende[2], F.T.M. Peters[1], J.J.J. Tjalma[1], H. de Jong[3], M. Linssen[4], M. Koller[5], A. Jorritsma-Smit[4], R. Bijlsma[1], J.H. Kleibeuker[1], G.M. van Dam[5], V. Ntziachristos[2], W.B. Nagengast[1], [1]Dept of Gastroenterology and Hepatology, [4]Dept of Clinical Pharmacy and Pharmacology, and [5]Dept of Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [2]Chair for Biological Imaging & Institute for Biological and Medical Imaging, Technical University of Munich and Helmholtz Center Munich, Munich, Germany, [3]Dept of Pathology, University of Utrecht, University Medical Center Utrecht, Utrecht, The Netherlands

Esophageal adenocarinoma (EAC) is a pressing clinical problem, as it has one of the fastest rising cancer incidence rates worldwide. Barrett Esophagus (BE), a metaplastic change of the normal epithelial lining, is a known precursor for the formation of adenocarcinoma of the esophagus. Intestinal metaplasia (IM) can progress gradually into low grade dysplasia (LGD), high grade dysplasia (HGD) and eventually invasive cancer. Although BE surveillance is routinely performed, the currently applied random-based biopsy approach is found to be controversial and often considered insufficient. Despite improvements in early EAC diagnostics due to implementation of narrow-band imaging (NBI) and high-definition (HD) endoscopy, detection of focal dysplastic and neoplastic lesions remains challenging. By incorporating molecular imaging, an emerging imaging modality that visualizes and identifies lesions by labeling cell specific proteins or cell products, a valuable supplementary technique in surveillance endoscopy might arise. We performed a pilot intervention study to investigate the use of vascular endothelial growth factor (VEGF) targeted molecular guided endoscopy in early EAC. Thus far five patients with established dysplasia and/or superficial adenocarcinoma (pT1) scheduled for endoscopic mucosal resection (EMR) are included. Two days prior to the EMR a microdose (4.5 mg) of fluorescently labeled anti-VEGF monoclonal antibody (bevacizumab-IRDye800CW) was intravenously administered. During the procedure, fluorescent signals were visualized with a sensitive near-infrared (NIR) camera system coupled to a custom made fiber-bundle, developed to fit through the working channel of a routine endoscope. To objectify and (semi)quantify the fluorescent signals ex vivo, fixed tissue slices and embedded tissue slides originating from the resected esophageal specimen were evaluated using multiplex advanced pathology imaging (MAPI). VEGF-targeted optical endoscopy demonstrated real-time identification of four early EAC lesions. One flat EAC lesion was undetectable during VEGF-targeted optical endoscopy. Notably, this lesion was also highly difficult to distinguish with routine NBI and white-light endoscopy. Ex vivo analyses revealed a detectable difference between normal epithelial lining and BE segments compared to carcinoma. In conclusions, we are the first to demonstrate that VEGF-targeted NIR endoscopy is able to detect early esophageal cancer lesions, illustrating the potential of molecular imaging during endoscopy. Though, challenges remain as the sensitivity needs to be improved to fulfill its role in future BE surveillance strategies.

Quantitative analysis of Volumetric Laser Endomicroscopy of histologically correlated images potentially identifies early neoplasia in Barrett's esophagus

A. Swager[1], D.M. de Bruin[2], D.J. Faber[2], B.L. Weusten[1], S.L. Meijer[3], J.J. Bergman[1], T.G. van Leeuwen[2], W.L. Curvers[4], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Biomedical Engineering and Physics, and [3]Dept of Pathology, Academic Medical Center, Amsterdam, [4]Dept of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, The Netherlands

Background: Early neoplastic lesions in Barrett's esophagus (BE) are difficult to detect with white-light endoscopy. Volumetric laser endomicroscopy (VLE) is an optical coherence tomography (OCT)-based imaging technique that provides large circumferential sub-surface maps of the superficial esophageal wall layers at low-power microscopy resolution. VLE data can be quantified by measuring the attenuation coefficient (μ_{VLE}), the decay of detected backscattered light versus depth. μ_{VLE} has the potential of providing quantitative optical diagnosis of interrogated mucosa because it relates to the organization of tissue. Aim: To investigate the feasibility of μ_{VLE} for identification of early neoplasia in BE. Methods: Endoscopic resection (ER) specimens from BE patients with and without neoplasia were scanned ex-vivo with VLE. Histopathology slides from the specimens were correlated one-to-one with VLE scans based on in-vivo and ex-vivo placed markers. Quantification of VLE signal attenuation (μ_{VLE}) was performed on areas of interest (AoIs) from VLE scans that were matched with histology in order to differentiate dysplastic BE from non-dysplastic (ND)BE mucosa. Results: In this study, 42 endoscopic resection (ER) specimens from 23 patients yielded 65 histology-VLE matches containing 70 AoIs consisting of 37 NDBE and 33 dysplastic BE AoIs (HGD n=15, EAC n=18). Median μ_{VLE} values (mm^{-1}) of the different mucosa types were compared: NDBE 1.24 (0.40-1.73 IQR) and dysplastic BE 1.99 (0.89-2.81 IQR). A statistically significant difference was observed between these groups ($p = 0.002$).
Conclusion: Quantitative VLE by means of μ_{VLE} may differentiate early neoplastic BE from NDBE. Further research is necessary to validate μ_{VLE} for diagnosis of early neoplasia in BE.

Exploring diagnostic and therapeutic implications of endoscopic mucosal resection in EUS-staged T2 esophageal adenocarcinoma

A.W. Gotink[1] , M.C.W. Spaander[1] , P. Didden[1] , B.P.L. Wijnhoven[2] , M.J. Bruno[1] and A.D. Koch[1] ,[1] Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam [2] Department of Surgery, Erasmus MC, University Medical Center Rotterdam

Most esophageal cancers are assessed by endoscopic ultrasound (EUS). EUS is accurate in staging cT3-4 tumors and locoregional lymph node metastases but the accuracy is lower when it comes to differentiating cT1 from cT2 tumors with a tendency to 'overstage'. Endoscopic mucosal resection (EMR) allows for a histological diagnosis and staging and is emerging as a treatment option for early esophageal adenocarcinoma (EAC). Because of the possible overstaged cT2 tumors, in recent years we have adopted the policy to be suspicious of cT2 tumors with a low threshold tendency to endoscopic reassessment. The aim of this study is to evaluate the final histological diagnosis in patients with a clinical T2 EAC as determined by EUS and also to assess the value of endoscopic reassessment followed by EMR if deemed possible. Patients with cT2 EAC were identified from 2 institutional databases: a surgical cohort of patients who underwent esophagectomy between January 1990 and October 2014, and a gastro-enterological cohort between January 2007 and April 2014. Main outcome measures were pathological T-stage after esophagectomy without preoperative therapy, and the outcome regarding pathological (p)T-stage of patients that underwent endoscopic reassessment with or without subsequent EMR. A total of 178 patients with T2-staged EAC by EUS were identified. 110 Patients underwent esophagectomy without neo-adjuvant therapy for a cT2-tumor. In 45 patients (41%) the pT-stage was less than T2. In 26 (57 %), of these patients the resection specimen showed tumor characteristics that fulfill current criteria for endoscopic resection. In 10 prospectively identified patients with cT2 EAC, endoscopic resectability was reassessed, and in 9 patients a complete EMR was successfully performed by multiband mucosectomy. Histological evaluation demonstrated a pT1 tumor in all 9 patients and 5 patients were successfully treated with EMR and receive ongoing endoscopic surveillance. 4 Patients were referred for esophagectomy because of submucosal and/or lymphovascular invasion.
Conclusions: This study demonstrates that 41% of cT2 EAC are pT1 tumors after histological examination of the esophagectomy specimen. Curative treatment by EMR is possible in more than half of these patients avoiding the need for esophagectomy. Endoscopic reassessment seems to be justified for all cT2 staged esophageal adenocarcinomas followed by EMR if deemed possible.

Differences in missed adenoma types comparing standard colonoscopy with "behind folds visualizing" techniques – a pooled analysis of three randomized back-to-back tandem colonoscopy studies

E.C. Brand[1], V.K. Dik[1], M.G.H. van Oijen[1,2], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Introduction: Colonoscopy is the gold standard for colorectal adenoma and cancer detection, but significant miss rates have been reported. The Third Eye Retroscope, Full spectrum endoscope (Fuse) and EndoRings were developed to improve visualization behind colonic folds and have all three individually been shown to reduce adenoma miss rates. The aims of this study were to evaluate 1) for which types of adenomas "behind folds visualizing" techniques reduce miss rates and 2) which subgroups of patients benefit most. Methods: Data of three independent multicenter randomized trials were combined: 1) the TERRACE study (NCT01044732); 2) the FUSE study (NCT01549535); and 3) the CLEVER study (NCT01955122). All trials had a back-to-back tandem design with patients undergoing same-day standard colonoscopy followed by Third Eye Retroscope, Fuse or EndoRings colonoscopy or vice versa. We performed a pooled analysis to determine overall polyp and adenoma miss rates, and specific miss rates by localization, size, morphology, histology, and for advanced adenomas. Miss rates in subgroups of patients were determined for gender, age and indication of colonoscopy. Results: A total of 320 patients (57% male, median age: 58 years) underwent standard colonoscopy first, and 330 patients (62% male, median age: 57.5 years) underwent colonoscopy with a "behind folds visualizing" technique first. Adenoma miss rate with a "behind folds visualizing" technique was significantly lower compared to standard colonoscopy for proximally (13% vs. 38% P<0.001) and distally located (15% vs. 35% P<0.001), ≤5mm (17% vs. 38% P<0.001) and 6-9mm (8% vs. 44% P<0.001), sessile (16% vs. 37% P<0.001), flat (9% vs. 52% P=0.014) and tubular (15% vs. 38% P<0.001) adenomas, and for serrated lesions (7% vs. 50% P=0.021). Miss rates for ≥10mm, pedunculated, (tubulo)villous adenomas and for advanced adenomas were not statistically significantly different between both arms. For both sexes, subjects of 50-60 and >60 years, and in screening, surveillance and diagnostic colonoscopies the adenoma miss rate was comparable and significantly lower with "behind folds visualizing" techniques.
Conclusion: This study shows that "behind folds visualizing" techniques reduce the miss rates in all segments of the colon for 1-9 mm adenomas, whereas no significant differences in miss rates were found for ≥10 mm or advanced adenomas. It remains to be determined whether the detection of more <10 mm adenomas with a "behind folds visualizing" technique will indeed reduce CRC mortality on the long term.

Significant risk of post-colonoscopy colorectal cancer due to incomplete adenoma resection: results of a nationwide population-based cohort study

H.J.M. Pullens[1,2], T.D.G. Belderbos[1*], M. Leenders[1], M.E.I. Schipper[3], M.G.H. van Oijen[1,4], P.D. Siersema[1], *Both authors contributed equally tot this work, [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [3]Dept of Pathology, University Medical Center Utrecht, Utrecht, [4]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands*

Background & Aims: Resection of adenomas detected during colonoscopy decreases the risk of subsequent colorectal cancer (CRC). It does however not preclude the occurrence of CRC within a few years after colonoscopy. Many of these post-colonoscopy CRCs (PC-CRCs) are preventable, as they are thought to be due to missed or incompletely resected adenomas. The aims of this study were to assess the overall incidence rate of PC-CRC in patients with one or more adenomas, to determine the risk of PC-CRC due to incomplete adenoma resection, and to identify adenoma characteristics associated with a high risk of PC-CRC due to incomplete adenoma resection. Methods: We performed a population-based cohort study identifying all patients with a first colorectal adenoma between 2000 and 2010 in PALGA, the nationwide Dutch Pathology Registry. Outcomes were the incidence rate of PC-CRC overall and of PC-CRC due to incomplete adenoma resection, defined as the occurrence of CRC between 6 months and 5 years after adenoma removal in the same colon segment. We performed a multivariable cox proportional hazard regression analysis to identify adenoma-related factors associated with both outcomes. Results: During the study period, 119,233 patients were diagnosed with a first adenoma. Mean age was 64.0 years (standard deviation 12.8) and 53.9% were male. We excluded 11,489 patients in whom prevalent CRC was found (CRC before or within 6 months after the first adenoma). Of the remaining 107,744 patients, 1031 (0.96%) developed PC-CRC anywhere in the colon within 5 years (incidence rate 1.9/1000 person years). PC-CRC due to incomplete adenoma resection occurred in 324 of 133,519 adenomas (0.24%). Mean follow up per adenoma was 4.4 years (SD 1.1). The incidence rate of CRC due to incomplete adenoma resection was 0.6 per 1000 years of follow up. High-grade dysplasia (hazard ratio (HR) 2.54, 95% confidence interval (CI) 1.99-3.25), villous (HR 2.63, 95%-CI 1.79-3.87) and tubulovillous histology (OR 1.80, 95%-CI 1.43-2.27) were risk factors for PC-CRC due to incomplete adenoma resection.
Conclusion: In this nationwide cohort, PC-CRC due to incomplete endoscopic resection occurred in one in four hundred adenomas and even more frequently in adenomas with high-grade dysplasia and villous or tubulovillous components. Our results suggest that enhanced surveillance is indicated after removal of adenomas with high-grade dysplasia or villous components.

Endoscopic resection of high-risk T1 colorectal carcinoma prior to surgical resection has no adverse effect on long-term outcomes

A. Overwater[1], M.G.H. van Oijen[1], A. van den Blink[1], B.W.M. Spanier[2], T.C.J. Seerden[3], H.J.M. Pullens[4], W.H. de Vos tot Nederveen Cappel[5], G.J.A. Offerhaus[6], D.J. Bac[7], M. Kerkhof[8], K. Kessels[9], P.D. Siersema[1], M.A.G. Elferink[10], M.M. Lacle[6], L.M.G. Moons[1], Dutch T1 CRC Working Group, [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Rijnstate, Arnhem, [3]Dept of Gastroenterology and Hepatology, Amphia Hospital, Breda, [4]Dept of Gastroenterology and Hepatology, Meander, Medical Center, Amersfoort, [5]Dept of Gastroenterology and Hepatology, Isala, Zwolle, [6]Dept of Pathology, University Medical Center Utrecht, Utrecht, [7]Dept of Gastroenterology and Hepatology, Gelderse Vallei, Ede, [8]Dept of Gastroenterology and Hepatology, Groene Hart Hospital, Gouda, [9]Dept of Gastroenterology and Hepatology, Flevo Hospital, Almere, [10]Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, The Netherlands

Approximately 25% of T1 colorectal carcinomas (CRCs) have no histologic risk factors for lymph node metastasis at base (LNM) and can be treated by endoscopic resection only (low-risk T1 CRC). It is however difficult to reliably distinguish low from high-risk invasive carcinomas during colonoscopy. The aim of the study was to determine whether endoscopic resection of high-risk T1 CRC followed by surgical resection has a negative effect on LNM or recurrence rate compared to primary surgery. Patients with high-risk T1 CRC treated with primary or secondary surgical resection between 2000 and 2012 from 7 hospitals were identified in the Dutch Cancer Registry. Data on recurrence, polyp characteristics, treatment and follow-up were collected from hospital records and endoscopy, radiology and pathology reports. Recurrence was defined as the detection of metastasis or local recurrence during follow-up. A T1 CRC was defined as high-risk in the presence of one or more of the following characteristics: poorly differentiated histology, positive resection margins, submucosal invasion depth of > 1 mm or presence of lymphangio-invasion. Patients were subdivided into group A: primary surgical resection or group B: endoscopic resection with additional surgery. A total of 388 patients were eligible for analysis (group A: n=206; group B: n=182). Median follow-up was comparable between both groups (A: 50 months IQR 22.3-80.2; B: 56 months IQR 22.2-79.8). Overall recurrence was 23/388 (5.9%). This included 3 local and 20 distant recurrences (9 liver, 6 lung, 4 peritoneum, 1 brain). Of the base characteristics, patients treated by primary surgery were more often female and older. Polyps treated by primary surgery were larger in size, more often right-sided and more often had a sessile or flat morphology. Risk analysis was therefore adjusted for the propensity score. No difference was found between primary and secondary surgery for the presence of LNM (9.7% vs. 8.8%; adjusted OR 1.1, 95% CI 0.5-2.5; P=0.796) and development of recurrence (7.3% vs. 4.4%; adjusted HR 1.04, 95% CI 0.3-3.2; P=0.230). Recurrence rates were 15.9/1000 person-years in group A and 9.5/1000 person-years in group B (P=0.233). There was no difference in treatment related mortality and morbidity between group A and B (1.5% vs. 2.2%, P=0.584 and 21.8% vs 29.1%, P=0.105).

Conclusion: Endoscopic resection of high-risk T1 CRCs followed by surgery had no negative effect on patient outcomes (LNM, recurrence rate, morbidity and CRC-related mortality). These findings justify an attempt to remove polyps suggestive of T1 CRC to prevent surgery of low-risk T1 CRC and polyps containing intra-mucosal carcinomas.

Patients with an endoscopic resection of a polyp containing carcinoma in situ or intramucosal carcinoma have a higher risk of postcolonoscopy colorectal cancer

K. Kessels[1,2], M.A.G. Elferink[3], M.G.H. van Oijen[1], G.J.A. Offerhaus[4], M.M. Lacle[4], P.D. Siersema[1], L.M.G. Moons[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Flevo Hospital, Almere, [3]Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, [4]Dept of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

Background: In Western guidelines, carcinoma in situ (CIS) and intramucosal carcinoma (IMC) in resected polyps are classified as high-grade dysplasia to avoid unnecessary surgery. No consensus exists on whether a polyp containing CIS or IMC (CIS/IMC) is a marker of an increased risk for development of a postcolonoscopy colorectal cancer (PCCRC) compared to the observed incidence rate of 170-240/100,000 person years in adenoma follow-up trials. Aim: To determine the incidence and etiology of PCCRC after endoscopic resection of CIS/IMC. Methods: Patients diagnosed with CIS/IMC in the period 1995 to 2005 were selected from the Netherlands Cancer Registry, with data on patient-, tumor- and treatment characteristics of all newly diagnosed malignancies in the Netherlands. Patients with an unknown or surgical resection of CIS/IMC, known hereditary colorectal cancer (CRC) or a diagnosis of CRC within 6 months after resection of CIS/IMC were excluded. Diagnoses and dates of diagnosis of CRC during follow-up (from January 1st 1995 to December 31st 2011) were available. According to the most commonly used algorithms, PCCRCs were attributed to an incomplete resection of CIS/IMC if detected in the same segment within 5 years, to a missed lesion if either detected in another segment within 3 years or if advanced CRC was detected in another segment after 3 to 5 years, or to a new CRC if non-advanced CRC was detected in another segment after 3 to 5 years. Results: A total of 3,508 patients were diagnosed with CIS/IMC in the Netherlands from 1995 to 2005. This concerned 1,979 (56%) patients with an endoscopic resection. In total, 48/1,979 (2,4%) patients were diagnosed with PCCRC within 5-years of follow-up. Incidence of PCCRC was 616/100,000 person years at 3-year follow-up and 568/100,000 person years at 5-year follow-up. No trend in declining incidence of PCCRC over the years was found. Twenty-three of 48 PCCRCs (48%) were classified as missed lesions, 19 (40%) as incomplete resections, and 6 (13%) as new CRCs. All PCCRCs due to an incomplete resection were located in the distal colon and 18/23 (78%) PCCRCs due to a missed lesion were located in the proximal colon.
Conclusion: The incidence of PCCRC after endoscopic resection of CIS/IMC is two- to three-fold higher than reported in adenoma follow-up trials. Approximately 40% of these PCCRCs may be attributed to incomplete endoscopic resections. Particularly when complete resection of CIS/IMC is uncertain (uncertain radical excision at histology, or piecemeal resection), short term follow-up colonoscopy within 6 to 12 months should be considered.

A randomized comparison of degradable esophageal stent versus dilation therapy for patients with recurrent benign esophageal strictures: 6-month results (DESTINY study)

D. Walter[1], M.W. van den Berg[2], M.M. Hirdes[1], F.P. Vleggaar[1], A. Repici[3], E.C. Ferrara[3], P.H. Deprez[4], B.L. Viedma[5], L. Lovat[6], B.L. Weusten[7], R. Bisschops[8], E.E. O'Leary[9], J.E. van Hooft[2], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, The Netherland, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands, [3]Dept of Gastroenterology and Hepatology, IRCCS Humanitas, Milano, Italy, [4]Dept of Gastroenterology and Hepatology, Clinique Universitaire Saint Luc, Bruxelles, Belgium, [5]Dept of Gastroenterology and Hepatology, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain, [6]Dept of Gastroenterology and Hepatology, University College London, London, United Kingdom, [7]Dept of Gastroenterology, St. Antonius Hospital, Nieuwegein, The Netherlands, [8]Dept of Gastroenterology, University Hospitals Leuven, Leuven, The Netherlands, [9]MED Institute, Inc, West Lafayette, IN, United States of America

Endoscopic dilation is the standard treatment for recurrent dysphagia in patients with benign esophageal strictures. While stent placement is thought to prolong dilation of the stricture, reducing recurrences, metal stents are associated with migration or difficult stent removal. A degradable stent might preclude these issues. Our aim was to compare the efficacy and safety of degradable esophageal stent placement to standard dilation therapy in recurrent benign esophageal strictures (RBES). We performed a multicenter, randomized study including patients with RBES with a history of at least one and a maximum of five previous dilations. Patients were randomized to degradable esophageal stent (SX-ELLA, Ella-CS, Czech Republic) placement or standard dilation therapy. Dysphagia scores were recorded daily for one month and monthly thereafter. Quality of life (QoL) was assessed using the EQ-5D and the WHO performance score. Primary outcome was the number of repeat endoscopic dilations for recurrence of dysphagia after 3 and 6 months. Secondary outcomes included safety, time to recurrent dysphagia, and QoL. Thirty-two patients were randomized to stent placement, and 34 patients were randomized to dilation therapy. Base patient demographics and lesion characteristics were similar between the two groups. The most common stricture etiology was anastomotic stenosis (74%). Compared to baseline, dysphagia scores were significantly improved for both groups at 3 and at 6 months ($p<0.001$ for all comparisons). In the first 3 months, significantly fewer dilations were required in the stent group compared to the dilation group (median 0 [range 0-9] vs. 1 [range 0-11], $p<0.001$). There was no difference between the two groups at 6 months (median 1 [range 0-13] vs. 2 [range 0-13], $p=0.40$). Procedure related serious adverse events were reported in 8 patients in both groups (8/32=25% vs 8/34=24%, $p=0.89$). Time to the first episode of recurrent dysphagia requiring intervention was significantly longer in the stent group compared to the dilation group (median 95 vs. 30 days, $p=0.03$). At 6 months, the QoL was significantly higher in the stent group compared to the dilation group (median 80 vs. 70, $p=0.03$). Significantly more patients in the stent group were able to perform normal levels of activity compared to the dilation group (85.2% vs. 54.8%, $p=0.04$).

We conclude that degradable esophageal stent placement seems relatively safe and is more effective in the short-term than continued dilation therapy in patients with RBES, which suggests that degradable stent placement may be considered at an early stage in the treatment algorithm of RBES.

Complement factor C3 aggravates nonalcoholic steatohepatitis in mice

F. Segers[1], N. van Best[1], C. Hodin[1], S.W.M. Olde Damink[1], A. Driessen[2], J.W. Greve[1,3], W.A. Buurman[1], S. Rensen[1,] [1] Department of Surgery, Maastricht University Medical Center, Maastricht, [2]Department of Pathology, Maastricht University Medical Center, Maastricht; [3]Department of Surgery, Atrium Medical Center Parkstad, Heerlen, The Netherlands

The innate immune system plays a major role in the pathogenesis of nonalcoholic steatohepatitis (NASH). Previously, we reported the first data on hepatic complement activation in human NASH. Activated complement factors were shown to accumulate around steatotic hepatocytes, and a strong correlation between complement activation and hepatic inflammation was observed. We now aimed to assess the role of the central complement component C3 in the development of NASH. Wild type (WT) and C3-deficient ($C3^{-/-}$) C57Bl/6J mice were fed a high fat diet (HFD) for 3 months or a methionine-choline-deficient (MCD) diet for 6 weeks to induce mild or severe NASH. The development of steatosis (grade 0-3), inflammation (grade 0-3), and fibrosis (grade 0-2) in the livers of these mice was compared to that observed in chow fed WT and $C3^{-/-}$ mice. Hepatic inflammation was further characterized by flowcytometric analysis of infiltrated leukocytes and by assessing mRNA expression of specific cytokines and chemokines by qPCR. Hepatic steatosis was substantially reduced in $C3^{-/-}$ mice on HFD (0.59±0.09 vs. 1.00±0.23 for WT, $p<0.05$). Surprisingly, lobular inflammation grade was similar in WT and $C3^{-/-}$ mice on MCD (13.45±1.89 vs. 7.08±0.51 for WT, $p<0.01$). Moreover, TNF-α and Mcp-1 expression were lower in $C3^{-/-}$ mice on MCD (4.78±0.61 vs. 6.75±0.76 for WT, $p\leq0.05$; 9.39±1.24 vs. 4.90±1.03 for WT, $p<0.05$). Interestingly, whereas WT mice displayed moderate fibrosis after MCD feeding, hepatic fibrosis was undetectable in $C3^{-/-}$ mice on both HFD and MCD (0.54±0.14 vs. 0.0±0.0, $p<0.01$).
In conclusion, complement factor C3 appears to promote hepatic steatosis, inflammation, and fibrosis, thereby aggravating the development and progression of NASH in mice. This suggests that currently explored inhibitors of the complement system could be attractive therapeutic agents for NASH.

Dose-escalating placebo-controlled study with allogeneic bone marrow-derived mesenchymal stem cells for the treatment of refractory perianal fistulas in Crohn's disease

I. Molendijk[1], B.A. Bonsing[2], H. Roelofs[3], K.C.M.J. Peeters[2], M.N.J.M. Wasser[4], G. Dijkstra[5], C.J. van der Woude[6], R.A. Veenendaal[1], J.J. Zwaginga[3], H.W. Verspaget[1], W.E. Fibbe[3], A.E. van der Meulen-de Jong[1], D.W. Hommes[1,5], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Surgery, [3]Dept of Immunohematology and Blood Transfusion, and [4]Dept of Radiology, Leiden University Medical Center, Leiden, The Netherlands, [5]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [6]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands, [7]Division of Digestive Diseases, University of California, Los Angeles, United States of America

Background: Mesenchymal stromal cells (MSCs) have potential as cellular treatment for perianal Crohn's disease (pCD), because of their ability to regenerate damaged tissue and to regulate immune responses. Patients and methods: In a prospective double blind phase I-II trial 21 CD patients with draining perianal fistulas (total 32 fistulas, max 3 external and max 2 internal openings), but without active luminal disease and not responding to current therapy modalities, were randomized (5:2) to receive either protocolized local injections of 10, 30 or 90x10^6 (cohort 1, 2 or 3) allogeneic bone marrow-derived MSCs (bmMSC) or placebo. Treatment, preceded by endoscopy, MRI and removal of the seton, consisted of curettage and closure of the internal opening of the fistulous tract and standardized local injection of the study drug at the internal opening. Follow-up visits were at 6, 12 and 24 weeks. Primary endpoints were safety and preliminary efficacy of bmMSC treatment. Secondary objectives were a.o. the changes in CRP, disease activity (PDAI), and quality of life scores (sIBDQ and SF-36). A complete healed fistula (CHF) was defined as no discharge upon pressure at physical examination. Results: Local infusion of bmMSC was safe as no serious adverse events were detected. After bmMSC therapy CHF was reached in 60% of the patients at week 6, in 40% at week 12 and in 80% at week 24 in cohort 1, and in 67% (6/9) of the fistulas. In cohort 2, 80% of patients had CHF at all three follow-up visits, and in 86% (6/7) of the fistulas. In cohort 3 this was 20% and 29% (2/7), resp, at any time point. Placebo resulted in CHF in 17% of the patients at week 6 and in 33% at week 12 and 24, for the fistulas this was 22% (2/9) and 33% (3/9) resp. Seton drainage was needed in 2 patients after bmMSC therapy (1 in cohort 1; 1 in cohort 3) and in 1 patient after placebo. Abscess drainage was needed in 1 patient in cohort 2 at 16 weeks after bmMSCs, however, this fistula was completely healed at week 24. PDAI scores at week 0, 12 and 24 coincided perfectly with therapy efficacy: in cohort 1 changing from 4.4 to 3.0 and 2.0, respectively. In cohort 2 from 3.8, 0.8 to 1.3, and in cohort 3 from 5.0, 3.8 to 4.2 as opposed to 5.2, 5.5 and 3.8 in the placebo group. No major differences were observed in other secondary endpoints.

Conclusions: Local administration of allogeneic bmMSC is safe and feasible in patients with refractory pCD. Local treatment with bmMSC showed superior fistula healing compared to placebo with 30x10^6 bmMSC dose having the best response rates, a low dose had good and the highest dose rather poor CHF results.

Induction of ER stress identifies Id2 as a potential esophageal stem cell marker

S.L. Rosekrans[1], B. Baan[1], E.J. Westerlund[1], C.A.J. Puylaert[1], J. Heijmans[1], V. Muncan[1], G.R. van den Brink[1,2], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, the Netherlands, [2]Department of Gastroenterology & Hepatology, Academic Medical Center, Amsterdam, the Netherlands

The esophageal squamous epithelium is a rapidly renewing tissue. To date, no specific markers have been identified that distinguish stem cells from other proliferating cells. We have previously shown that endoplasmic reticulum (ER) stress induces epithelial cell differentiation in the esophageal epithelium, presumably acting directly on the stem cell pool(Gut, 2014). We aimed to identify stem cell genes that mark a hierarchically distinct population of cells in the basal layer of esophageal cells by analysis of a gene signature that is lost upon induction of ER stress.Two independent human esophageal carcinoma cell lines TE7 and OE21 were used to identify potential stem cells genes in esophageal epithelium. ER stress was induced in both cell lines using SubAB, a cytotoxin that depletes the major ER chaperone GRP78. Gene array analysis was performed using Illumina HT12 V3 slides. mRNA was localized by Dig labeled in situ hybridization. Id2-CreERT2- CAG-ZsGreen1 mice were used for lineage tracing experiments. Mice were treated with a single injection of tamoxifen at the dose of 1 mg/mouse. Mice were sacrificed at different time points after recombination:1 day, 3 days, 1 week, 2 weeks, 1 month, 3 months and 6 months. Using RNA micro-arrays, we identified a gene signature of 47 genes that were lost in both individual cell lines upon induction of ER stress. By in situ hybridization we found that expression of 29 genes out of the 47 genes is restricted to the basal layer of the mouse esophagus. Out of which, 9 genes show expression in only a small proportion of the basal cells, potentially marking stem cells. We have selected Id2 for further analyses. Expression profile of ZsGreen in Id2-CreERT2-CAG-ZsGreen1 mice matched the results obtained by in situ hybridization. We used these animals to perform lineage tracing experiments utilizing a dose of tamoxifen that marks single epithelial cells in the basal layer of the esophagus. At day 1 we could detect single labeled cells that formed clones at 1week, that were traceable up to 6 months.
Conclusion: Our in vitro screen combined with in situ hybridization identified nine genes, including Id2, that are specifically expressed in a subset of proliferating epithelial genes in the mouse esophagus. Id2 positive cells were able to create long lived clones up to six months, thereby potentially marking esophageal stem cells.

Genetic variants of recipient PD-1 and donor PD-L1 affect risk of acute rejection after liver transplantation

X-L. Shi[1], S. Mancham[1], B.E. Hansen[1], L.J.W. van der Laan[2], H.J. Metselaar[1], J. Kwekkeboom[1] , [1]Department of Gastroenterology and Hepatology, [2]Department of Surgery, Erasmus MC – University Medical Center, Rotterdam, The Netherlands

Co-inhibitory receptor-ligand interactions fine-tune immune responses by negatively regulating T-cell function, and have been shown to be involved in transplant tolerance in experimental animal studies. Whether they affect transplant rejection in humans is still unclear. The aim of this study is to examine whether single nucleotide polymorphisms (SNPs) in co-inhibitory receptors or their ligands in donors and recipients influence the rate of rejection after liver transplantation (LT). 10 SNPs of PD-1, PD-L1, CD244, and TIM-3 were genotyped in 528 LT recipients and 410 donors. Associations with both early (≤ 6 months after LT) and late (> 6 months after LT) acute rejection were analyzed by a likelihood ratio test. Multivariate analysis of SNPs in combination with patient characteristics were performed using cox regression model. PD-L1 expression on hepatic leukocytes of donors with different genotypes was measured by flow cytometry after in vitro stimulation by IFN-γ. Donor PD-L1 rs1411262 (p=0.008), CD244 rs3766379 (p=0.034) and rs6682654 (p=0.023), were associated with early acute rejection. Meanwhile, recipient PD-1 rs11568821 (p=0.019) and donor PD-L1 rs4143815 (p=0.006) were associated with late acute rejection. After adjusting for base characteristics, donor PD-L1 rs1411262 was the only SNP independently associated with early acute rejection (AA versus AG/GG; HR=3.592; 95% CI=1.775-7.269; P=0.002), while the A allele of recipient PD-1 rs11568821 (AA/AG versus GG HR=2.951; 95% CI=1.269-6.861; P=0.014) and the C allele of donor PD-L1 rs4143815 (CC/CG versus GG; HR=0.236; 95% CI=0.086-0.648; P=0.002) remained to be independent factors associated with late acute rejection. In vitro analysis showed that C allele of PD-L1 rs4143815 is associated with higher PD-L1 expression on donor hepatic $BDCA1^+$ dendritic cells upon IFN-γ stimulation.

To conclude, functional SNPs in donor PD-L1 and recipient PD-1 are associated with the development of acute rejection after liver transplantation. Donor PD-L1 and recipient PD-1 interaction is involved in the regulation of allogeneic immune responses to liver graft in humans.

CMV primary infection is associated with donor-specific T-cell hyporesponsiveness and fewer late acute rejections after liver transplantation

X-L Shi[1,5], E.L.D. de Mare-Bredemeijer[1], Ö. Tapirdamaz[1], B.E. Hansen[1], Rogier van Gent[1], M.J.H. van Campenhout[1], S. Mancham[1], N.H.R. Litjens[2], M.G.H. Betjes[2], A.A. van der Eijk[3], Q. Xia[5], L.J.W. van der Laan[4], J. de Jonge[4], H.J. Metselaar[1], J. Kwekkeboom[1,], [1]Department of Gastroenterology and Hepatology, [2]Department of Internal Medicine, [3]Department of Virology, [4]Department of Surgery, Erasmus MC - University Medical Center, Rotterdam, The Netherlands, [5]Department of Liver Surgery, Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China*

Viral infections, including cytomegalovirus (CMV), abrogate transplantation tolerance in animal models. Whether this also occurs in humans remains elusive. We investigated how CMV affects T cells and rejection episodes after liver transplantation (LT). Phenotype and alloreactivity of peripheral and allograft-infiltrating T cells from LT patients with different CMV status were analyzed by flow cytometry. The association of CMV status with early and late acute rejection was retrospectively analyzed in a cohort of 639 LT patients. CMV positivity was associated with expansion of peripheral effector memory T-cell subsets after LT. Patients with CMV primary infection showed donor-specific $CD8^+$ T-cell hyporesponsiveness. While terminally differentiated effector memory cells comprised the majority of peripheral donor-specific $CD8^+$ T cells in CMV primary infection patients, they were rarely present in liver allografts. Retrospective analysis showed that R^-D^+ serostatus was an independent protective factor for late acute rejection by multivariate Cox regression analysis (hazard ratio=0.17, 95%CI=0.04-0.83, P=0.01). Additionally, CMV primary infection patients showed the highest Vδ1/Vδ2 γδ T-cell ratio, which has been shown to be associated with operational tolerance after LT.
In conclusion, our data suggest that CMV primary infection may promote tolerance to liver allografts, and CMV status should be considered when tapering or withdrawing immunosuppression.

Low soluble CD14 in neonates may prevent immune activation by Hepatitis B surface antigen

N. van Montfoort[1], E. van der Aa[1], A. van den Bosch[1], H. Brouwers[1], H. Javanbakht[2] and A. Woltman[1], [1]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center Rotterdam, The Netherlands, [2]Infectious Diseases Discovery & Translational Area, Roche Innovation Center Basel Switzerland

Upon infection with Hepatitis B virus (HBV), only 10% of infected neonates and 90-95% of adults is able to clear this liver-specific virus by mounting HBV-specific immunity. The mechanism underlying initiation of effective HBV-specific immunity is not well understood and likewise it is not clear why the majority of neonates cannot control the infection. Dendritic cells (DC) play a central role in the regulation of anti-viral immunity. BDCA1+ myeloid DC (mDC), a population of DC that reside in liver and peripheral blood, have been shown to interact with HBV surface antigen (HBsAg) in vivo. The purpose of this study was to examine the interaction of BDCA1+ mDC with HBsAg in vitro, investigate the receptors involved and compare the response between adults and neonates. Exposure of peripheral blood-derived BDCA1+ mDC to HBsAg resulted in strong DC maturation, cytokine production and enhanced capacity to activate antigen-specific CTL. HBsAg-dependent DC maturation was dose-dependent and observed with both recombinant HBsAg and plasma-derived HBsAg, isolated from HBV-infected patients. Since CD14 is important for binding of HBsAg to monocytes, the role of CD14 in HBsAg-mediated DC maturation was studied. By using CD14 neutralizing antibodies, we identified a crucial role for CD14 in HBsAg-mediated maturation of DC, which was independent of CD14 expression on a small sub-population of mDC. HBsAg-mediated DC maturation was completely absent in serum-free cultures, however, could be restored when supplemented with FCS and plasma obtained from healthy adults, that both contain soluble CD14 (sCD14), indicating a potential role for sCD14 in HBsAg-mediated DC maturation. Notably, we showed that sCD14 directly interacts with HBsAg and that sCD14-HBsAg complexes can be detected in the serum of HBV-infected patients, but not healthy controls. Since the amount of sCD14-HBsAg complexes was correlated with the viral load and the concentration of HBsAg in the serum of patients, the clinical significance of sCD14 and sCD14-HBsAg complexes in chronic HBV patients needs to be further examined. Although neonatal mDC were able to respond to HBsAg in the presence of FCS, neonatal cord blood contained significantly less sCD14 than adult plasma, which correlated with significantly reduced HBsAg-mediated mDC maturation.
We conclude that sCD14 is a pattern-recognition receptor for HBsAg. Furthermore, our findings suggest that reduced sCD14 in neonates is associated with a poor initial immune activation after perinatal HBV infection and may explain why perinatal HBV acquisition frequently results in persistent infection.

Long-term therapy-induced viral clearance in chronic HCV does not lead to normalization of the intrahepatic T cell compartment

M. Spaan[1], M.A.A. Claassen[1,2], H.L.A. Janssen[1,3], R.J. de Knegt[1], A. Boonstra[1], [1]Department of Gastroenterology and Hepatology, [2]Department of Internal Medicine, Infectious Diseases Unit, Erasmus MC University Hospital, Rotterdam, The Netherlands. [3]Department of Gastroenterology and Hepatology, University Health Network, Toronto Western Hospital, Canada

Although treatment-induced HCV eradication leads to normalization of ALT levels, we previously showed that 4 weeks after cessation of therapy, T cell infiltrates in the liver were still not normalized. We now investigate the phenotype and activity of intrahepatic and blood T cells in a follow up study in individuals with undetectable HCV RNA for over 4 years following successful antiviral treatment (SVR). Peripheral blood and multiple aspirate biopsies from the liver were collected from chronic HCV patients before and after IFN-based therapy (wk4-follow up, wk24-follow up and year4-follow up). PBMC were stimulated with HCV peptide pools to induce T cell proliferative responses, which were assessed in the presence or absence of neutralizing antibodies to the IL-10 receptor, TGF-beta or after depletion of $CD25^+$ Treg. Liver aspirate biopsies were evaluated by flow cytometry for $CD3^+$ T cells, $CD4^+$ T cells and Treg ($CD4^+CD25^+FoxP3^+$ cells) as well as T cell memory markers. From a cohort of 13 patients that obtained SVR after therapy, 4 individuals agreed with additional sampling of the liver. By flowcytometry, we found that intrahepatic Treg frequencies remained increased not only at 4 weeks after therapy as we previously reported, but also at week 24 (Treg/CD4: 9.4%) and, importantly, even at 4 years after successful completion of therapy (Treg/CD4: 5.7%). In contrast, in healthy liver samples obtained from individuals never exposed to HCV antigens, hardly any Treg were detected. On the basis of expression of CD45RO and CD62L, the majority of Treg in the livers sampled at 4 years after clearance of HCV were identified as central memory Treg (73.2% $CD45RO^+CD62L^-$ cells). In contrast to the liver, the frequency of blood Treg did not differ between individuals during short-term and long-term follow up and those who had never been exposed to HCV. Functionally, however, 2 out of 5 patients displayed potent regulation in PBMC of HCV-specific T cell proliferation by TGF-beta and Treg (maximum increase 4-fold and 8-fold up to 8,000 cpm, respectively) but no regulation by IL-10 was observed. Our findings, gathered by multiple sampling of the liver and peripheral blood, demonstrate that the local immune response does not revert to a resting state comparable to healthy livers after successful HCV eradication, even after 4 years of follow up . The persisting presence of high numbers of Treg with relatively weak suppressive activity, based on their phenotype, suggests ongoing residual regulation of immunopathology.

NK Cell Characteristics in Chronic Hepatitis B Patients are Associated with HBsAg Clearance After Combination Treatment with Peginterferon Alfa-2a And Adefovir

F. Stelma[1,2], A. de Niet[1,2], R.B. Takkenberg[1], L. Jansen[1,2], H.L.A. Janssen[3], M.J. Tempelmans Plat-Sinnige[2], N.A. Kootstra[2], E.M.M. van Leeuwen[2], and H.W. Reesink[1,2,] [1]Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands. [2]Experimental Immunology, Academic Medical Center, Amsterdam, The Netherlands. [3]Department of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands; Toronto Centre for Liver Disease, Toronto Western & General Hospital, University Health Network, Toronto, Canada

The role of natural killer (NK) cells in the clearance of HBsAg is not well understood. Furthermore, it is unknown whether the NK cell phenotype is related to treatment outcome. In a prospective study, 92 (44 HBeAg pos, 48 HBeAg neg) chronic hepatitis B (CHB) patients (HBVDNA>17,000 IU/mL) were treated with peginterferon alfa-2a and adefovir for 48 weeks. PBMCs were collected at baseline, during therapy and follow-up. Response was defined as HBsAg loss at week 72 (functional cure). From this cohort NK cell characteristics of 7 responders (3 HBeAg pos/ 4 HBeAg neg) and 7 matched non-responders were analysed, together with 7 healthy controls (HC). Markers of NK cell activation, proliferation, migration and functionality were measured by flowcytometry. Subsequently, 35/44 base (BL) samples of HBeAg-positive CHB patients were analysed. At BL, the NK cell subset distribution (CD56bright and CD56dim) of CHB patients was comparable to HC. At end of treatment (EoT), the percentage - as well as absolute numbers - of CD56bright NK cells had increased significantly (11.3% at BL to 44.4% at EoT, $p<0.0001$), whereas CD56dim NK cells had decreased. At BL, patients with HBsAg loss had significantly lower expression of chemokine receptor CX3CR1 on CD56bright and inhibitory receptor NKG2A on CD56dim NK cells compared to non-responders (gMFI CX3CR1 149.7 vs. 222.1, $p<0.05$ and NKG2A+ 37.3% vs. 50.9% $p<0.05$). At end of treatment CD56bright TRAIL expression and total NK cell IFNy production was higher in responders compared to non-responders. These differences at BL were not found in BL samples from HBeAg positive patients with HBeAg seroconversion, but without HBsAg loss (CX3CR1 CD56bright $p=0.89$ and NKG2A CD56dim $p=0.85$).
Conclusion: Base expression of inhibitory receptor NKG2A on CD56dim and chemokine receptor CX3CR1 on CD56bright NK cells are significantly different in CHB patients with HBsAg loss upon peginterferon/ADF combination therapy compared to non-responders. At end of treatment, responders have higher TRAIL expression and IFNγ production. These data suggests that NK cells may play a role in the clearance of HBsAg upon peginterferon based therapy.

IgG4+ B-cell receptor clones in peripheral blood distinguish IgG4-associated cholangitis/autoimmune pancreatitis from primary sclerosing cholangitis

L.M. Hubers[1,2], M.E. Doorenspleet[3,4*], E. Culver[5,6], L.J. Maillette de Buy Wenniger[1,2], P.L. Klarenbeek[3,4], S.F. van de Graaf[2], J. Verheij[7], T. van Gulik[8], F. Baas[9], E. Barnes[5,6,10], N. de Vries[3,4], U. Beuers[1,2,] [1]Gastroenterology and Hepatology, [2]Tytgat Institute of Liver and Intestinal Research, [3]Clinical Immunology and Rheumatology, [4]Laboratory of Experimental Immunology, Academic Medical Center, Amsterdam, Netherlands; [5]Translational Gastroenterology Unit, John Radcliffe Hospital, [6]NDM, Oxford University, Oxford, United Kingdom; [7]Pathology, [8]Experimental Surgery, [9]Genome Analysis, Academic Medical Center, Amsterdam, Netherlands, [10]Oxford NIHR Biomedical Research Center, Oxford University, Oxford, United Kingdom; *Contributed equally*

Normal 0 21 false false false NL X-NONE X-NONE Immunoglobulin G4-related disease (IgG4-RD) predominantly affects the biliary tract (IgG4-associated cholangitis, IAC) and pancreas (autoimmune pancreatitis, AIP). Its clinical presentation often mimics primary sclerosing cholangitis (PSC) and/or pancreatobiliary malignancies, and an accurate diagnostic marker is lacking. Recently, we identified dominant IgG4+ B-cell receptor (BCR) clones in blood of 6 patients with active IAC, but not in controls, using next-generation sequencing (NGS). Here, we aimed to validate our findings in larger patient cohorts and to test a novel qPCR protocol in comparison to NGS. 27 patients with IAC/AIP fulfilling HISORt criteria were included in one Dutch (n=17) and one English (n=10) academic hospital. Also, 15 PSC controls were included. The total BCR heavy-chain repertoire was analysed using primers for all V(ariable)-genes and total RNA from peripheral blood. All amplified products encoded CDR3, the region defining a unique clone. The number of identical sequences reflects the size of the BCR clone. In addition, qPCR was performed on 27 IAC/AIP patients and 9 disease controls using forward primers for all IgG subtypes and IgG4 specifically; one generic reverse primer was used within the constant region of the receptor. Differences between the specific IgG4 and total IgG message in peripheral blood were calculated and expressed as differences in CT value. IgG4+ BCR clones were detected in all individuals included. 25/27 of all IAC/AIP patients had IgG4+ BCR clones that were among the 10 most dominant IgG+ BCR clones in blood (median 2nd, range 1-53), whereas the most dominant IgG4+ BCR clone in PSC patients ranked 176th (median, range 73-686, $p<0.0001$). All IgG4+ clones together covered 16,6% of all IgG+ clones, and 19,9% of the IgG+ repertoire (compared to 1,6% and 1,0% resp. in PSC controls). This difference was confirmed using qPCR: in IAC/AIP patients the median ΔCT value was 3,0 (1,0-5,6), compared to 6,9 in PSC patients (range 5,6-10,1, $p<0.0001$). Identification of highly dominant IgG4+ BCR clones by NGS in patients with active IAC/AIP clearly distinguishes IAC/AIP from PSC. Our novel qPCR protocol, in comparison to NGS, could be a simple and inexpensive alternative diagnostic tool. Expansion of patient cohorts (IAC/AIP, PSC, pancreatobiliary malignancies) for test validation is underway.

KIR ligand HLA-C2 is associated with immune activity and response to Peg-interferon and Adefovir in HBeAg-positive chronic hepatitis B patients

L. .Jansen[1,2], F. Stelma[1,2], M.J. Tempelmans Plat-Sinnige[2], R.B. Takkenberg[1], E.M.M. van Leeuwen[2], N.A. Kootstra[2], H.W. Reesink[1,2], [1]Department of Gastroenterology and Hepatology, Academic Medical Center, [2]Department of Experimental Immunology, Academic Medical Center, Amsterdam, The Netherlands

The antiviral activity of NK cells partially depends on the interaction of killer cell immunoglobulin-like receptors (KIR) and their HLA-C ligands. Genetic variations in KIR and HLA-C genes influence the outcome of acute hepatitis C infection and single nucleotide polymorphisms (SNPs) in HLA-C have been implicated in hepatitis B chronicity. However, the role of these variations in relation to treatment outcome in chronic hepatitis B (CHB) patients is unknown. 86 CHB patients (41 HBeAg-positive; 45 HBeAg-negative) who completed 48 weeks of peginterferon alfa-2a and adefovir combination therapy followed by a treatment-free follow-up (week 72) were included. Patient DNA was isolated from PBMC. SNPs located within or near (±500 base pairs) the HLA-C gene (n=12) were genotyped with the Illumina Human Omni1-Quad BeadChip. Genotyping of KIR2DL1, KIR2DL2 and KIR2DL3 was performed by PCR. Combined response at week 72 (HBeAg negativity, HBV-DNA ≤2,000 IU/mL, and ALT normalization) was achieved in 14/41 HBeAg-positive and 17/45 HBeAg-negative patients. One SNP in HLA-C (rs2308557; A allele) was significantly associated with combined response in HBeAg-positive patients after correction for multiple testing (p=0.003), but not in HBeAg-negative patients. This SNP is linked to the presence of an Asparagine or Lysine at position 104 of HLA-C, important for binding specific KIRs (HLA-C group C1 or C2, respectively). The distribution of C1C1, C1C2, C2C2 genotypes in HBeAg-positive patients was 7 (17%), 17 (42%), and 17 (42%), respectively. HBeAg-positive patients with the C2 allele had higher rates of combined response (13/24 vs 1/17, p=0.001), and higher base ALT levels (median ALT 136 vs 50 U/L, p=0.002) than patients with only C1 alleles. The C2 allele is specifically recognized by the KIR2DL1 receptor, which was present in all patients. Presence of HLA-C2/KIR2DL1 predicted response independent of HBV genotype A, HBV-DNA and ALT levels in multivariable analysis (p=0.007). In contrast, the HLA-C1C1/KIR2DL3 combination was more prevalent in HBeAg-positive non-responders than combined responders (15/27 vs 1/14, p=0.003).
Conclusion: Presence of KIR ligand HLA-C2 was strongly associated with combined response in HBeAg-positive patients. These findings support an important role for the interaction of NK cell receptors and their HLA-C ligands in determining the host immune activity and response to interferon-based therapy in chronic hepatitis B patients.

Large-scale Case-Control Study Identifies Relations between the Microbiome and Disease Duration and Activity in Crohn's Disease and Ulcerative Colitis

F. Imhann[1], A. Vich Vila[1], M.J. Bonder[2], L.M. Spekhorst[1], E.A.M. Festen[1], J.A.M. Dekens[2,3], H.M. van Dullemen[1], R. Ter Steege[1], S. van Sommeren[1], E.F. Tigchelaar[2,3], M.C. Cenit[2], L. Franke[2], J. Fu[2], G. Dijkstra[1], C.H. Huttenhower[6], D. Gevers[5], R.J. Xavier[4,5], C. Wijmenga[2,3], A. Zhernakova[2,3], R.K. Weersma[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, The Netherlands, [2]Dept of Genetics, University Medical Center Groningen, Groningen, The Netherlands, [3]Top Institute Food and Nutrition, Wageningen, The Netherlands, [4]Massachusetts General Hospital, Boston, United States of America, [5]Broad Institute of Harvard and MIT, Boston, USA, [6]Harvard School of Public Health, Harvard University, Boston, United States of America

The exact etiology of Crohn's Disease (CD) and Ulcerative Colitis (UC) remains unknown. Prior research into genetic and immunological factors suggests that the inflammation in IBD is triggered by impaired microbial antigen recognition. There is increasing evidence for the importance of the gut microbial composition in disease progression. This largest cross-sectional case-control study to date aims to discover relations between disease status, clinical characteristics and the microbiome in CD and UC. Stool was collected from 356 CD and UC patients and 824 matched healthy participants. Participants were asked to freeze their own stool sample immediately upon collection. Detailed clinical records including disease activity scores, medication use and laboratory parameters such as fecal calprotectin were obtained at the time of sampling. The V4 region of the 16S rRNA-gene was sequenced using established methods. Operational Taxonomic Units (OTU's) were picked using primer selection and QIIME with the Greengenes 13.5 reference database. Differences in microbiome were analysed using the MaAsLin multivariate statistic analysis algorithm. Differences in the microbiome composition between CD patients and healthy participants were identified in 75 taxa ($p < 0,01$, $q < 0,05$). 13 taxonomical families were shown to be less present in CD; including 6 novel identifications and 7 previously described in the literature. The Veillonellaceae and Micrococcaceae families were significantly increased in CD compared to healthy individuals. For UC 8 taxonomical families were significantly more present compared to CD patients.. When IBD is present for a longer time a decrease in Ruminococcaceae and an increase in Proteobacteria is observed. When disease activity increases, defined as an increase in fecal calprotectin, the presence of the combined family Veillonellaceae/Clostridiaceae increases. This project is the most elaborate microbiome case-control study in IBD to date. Collection conditions were uniquely standardized. Distinct microbiome compositions for CD and UC were discovered, where CD patients had a more deviant microbiome than UC patients compared to healthy individuals.

Our results suggest that an increase of Veillonellaceae/Clostridiaceae is related to a more severe disease status. Supporting this finding, Veillonellaceae, previously identified in IBD-studies, is known to modulate the immune response by regulating the cytokines production. The decrease in Ruminococcacea (anaerobes) and the increase in Proteobacteria (facultative anaerobes) over time may be explained by the increase in oxygen radicals caused by epithelial inflammation.

Gut microbiota and lipid metabolism in humans

J. Fu[1,2], M.J. Bonder[1], M.C. Cenit[1], E. Tighchelaar[1], M. Hofker[2], L. Franke[1], C. Wijmenga[1], A. Zhernakova[1], [1]Dept of Genetics, University Medical Center Groningen, University of Groningen, Groningen, [2]Dept of Pediatrics, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Introduction: Lipids are risk factors for many diseases, including obesity, diabetes and cardiovascular disease. Previous studies have shown that lipid levels can be affected by an individual's genetic make-up, and that intestinal microbiota has an effect on metabolic state. In this work we aimed to investigate the combined effect of gut microbiome and host genetics on human lipid metabolites. Methods: After filtering the subjects with antibiotic or lipid-lowering medication, this study included 893 individuals from a population cohort LifeLines Deep. In all samples the blood lipid metabolites (LDL, HDL, triglycerides (TG) and total cholesterol) were measured. 157 SNPs that modify lipid levels were directly genotyped or imputed from genome-wide SNP platforms, and combined in the risk score. Microbiome composition was accessed by 16S rRNA gene sequencing method. We clustered the reads using QIIME and GreenGenes May 2013 as reference. These reads were referred as bacterial operational taxonomic units (OTUs) and the total number of OTU reads per sample was further rarefied to 15,000. We developed the 2-part analysis model to account for both binary (presence/absence) and qualitative (different abundance level) features of OTUs. The variation of lipids explained by genetics risk and gut microbes were estimated using machine-learning technique with 80% random samples as discovery and 20% as validation set. Results: After adjusting for age and gender, we identified 114 OTUs associated with TG; 34 OTU for HDL and 66 for body mass index at false discovery rate < 0.05. Gut microbiota can explain 5.5% triglycerides and 2.9% for HDL. Interestingly, gut microbiota don't seem to contribute the variation in low-density lipoprotein cholesterol (LDL) and total cholesterol level. We also did not observe strong interaction between genetics and gut microbiome in the respect to human lipids.
Conclusion: Gut microbiome can have similar strong effect on human lipid metabolism as human genome (2.9% TG variation explained by genetics but 5.5% explained by gut microbiome). We did not observe strong association between host genome and gut microbiomial composition. Host genome and gut microbiome, together with age and gender, collectively explain 18% variation in TG and 26.4% variation in HDL. These results provided rational for developing microbiome-targeting therapy.

The influence of a short term gluten free diet on the human gut microbiome

M.J. Bonder[1], X. Cai[3*], E.F. Tigchelaar[1,2*], G. Trynka[1,4], M.C. Cenit[1], B. Hrdlickova[1], H. Zhong[3], D. Gevers[4], C. Wijmenga[1,2], Y Wang[3#], A. Zhernakova[1,2#], [1]Dept of Genetics, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [2]TIFN, Wageningen, The Netherlands, [3]BGI-Shenzhen, 518083, China, [4]Broad Institute of MIT and Harvard, Cambridge, MA, United States of America*

Gluten free diet (GFD) is the most common diet worldwide. It is not only an effective treatment for celiac disease, but also commonly followed by individuals with intestinal discomfort. There is an important link between diet and microbiome although how GFD affects the human microbiome is largely unknown. For this reason, we wanted to get more insight into the influence of a short-term GFD on the human microbiome. We studied changes in the gut microbiome in twenty-one healthy volunteers followed a GFD for four weeks. Stool samples were collected at 9 time points: before the start of the diet, then at weekly intervals during the GFD, and after a wash-out period of five weeks again at weekly intervals for four weeks on habitual diet (HD) (1 HD + 4 GFD + 4 HD). Microbiome profiles were determined using 16s rRNA sequencing and subsequently processed for taxonomic analysis using QIIME and GreenGenes as reference as well as imputed functional composition using PiCRUSt and HUMAnN. In addition, the levels of short chain fatty acids (SCFA) in feces were assessed at the same time points as the stool sample collection. The short-term GFD intervention in healthy subjects had a limited overall impact on the microbiome, maintaining the interpersonal diversity observed prior to the start of diet. However, a number of taxon-specific differences were noticed; the most striking shift was seen for the family Veillonellaceae (class Clostridia) that significantly reduced during the intervention ($p=2.81e{-}05, q=0.003$). Additionally, seven other taxa were significantly reduced, two of which are known to play a role in starch metabolism. Differences in pathway activities in relation to diet were more pronounced; twenty-one predicted pathway activity scores showed significant association to the change in diet, with four of the top five pathways related to metabolism. We observed strong correlation of SCFA level with bacterial pathways relevant for SCFA metabolism. In conclusion, even though the gluten free diet period was relatively short, we observed significant differences in the microbiome and gene composition associated to a GFD.

Early postoperative progression to solid foods is safe in Roux-en-Y gastric bypass procedure: a review of 936 patients.

C.M.J. Theunissen[1], J.K. Maring[1], N.J.C. Raeijmaekers[2], I.S. Martijnse[1], B.S. Langenhoff[1], [1]Dept of Surgery and [2]Dept of Nutrition, Elisabeth - TweeSteden Hospital, Tilburg, The Netherlands

While the admission-time decreases with the implementation of various enhanced recovery protocols, many clinics will instruct patients after Roux-en-Y gastric bypass for weight loss to maintain a fluid or minced-food diet for two weeks postoperatively for fear of intestinal leakage. We reasoned that with adequate pre-operative instructions, including adequate chewing of all foods, early progression to solid foods would not increase the risk of (gastro-) enterostomy leakage. In December 2010 a new dietary protocol was implemented for all patients undergoing a Roux-en-Y gastric bypass procedure, allowing for progression to solid foods from 12 hours post-procedure onwards. All patients received preoperative eating instructions and eating-awareness counselling from a qualified dietician and psychologist. A retrospective study was made of 936 patients who underwent a primary or redo laparoscopic Roux-en-Y gastric bypass between January 2011 and June 2014 in our hospital. No 30-day loss to follow-up occurred. All 30 day complications, readmissions and reoperations were noted. We observed no increase in leakage or other complications. Overall 30 day complication rate was 9.4%, with gastro-intestinal leakage occurring in only 0.7%. A low threshold for readmission was maintained due to the short mean admission time of 1.87 days. Readmissions rate was 4.8% -mainly for postoperative pain- and 1.8% of our patients required reoperation within 30 days. Mortality was 0.1%. These results are comparable to results published by other Dutch centres.
Conclusions: We conclude that early progression to solid foods after Roux-en-Y gastric bypass surgery is safe as no increase in complication rate is observed.

Serious Postoperative Complications Affect Early Recurrence After Cytoreductive Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis

G.A. Simkens[1], T.R. van Oudheusden[1], M.D. Luyer[1], S.W. Nienhuijs[1], G.A. Nieuwenhuijzen[1], H.J. Rutten[1], I.H. de Hingh[1], [1]Dept of Surgical Oncology, Catharina Hospital, Eindhoven, [2]Dept of Surgery, St. Antonius Hospital, Nieuwegein, The Netherlands

Background: The prognosis of patients with peritoneally metastasized colorectal cancer has improved significantly with the introduction of cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). Although a macroscopically complete resection is achieved in nearly every patient, recurrence rates are high. This study aims to identify risk factors for early recurrence. Furthermore, we describe a more accurate treatment-related mortality rate than described by conventional parameters. Methods: All patients with colorectal peritoneal carcinomatosis treated with CRS+HIPEC and a minimum follow-up of 12 months in April 2014 were analyzed. Patient data were compared between patients with or without recurrence within 12 months after CRS+HIPEC. Risk factors were determined using logistic regression analysis. Causes of 1-year mortality were carefully analyzed. Results: A complete macroscopic cytoreduction was achieved in 96% of all patients treated with CRS+HIPEC. Forty-six of 133 patients (35%) developed recurrence within 12 months. SAE≥3 after CRS+HIPEC was the only significant risk factor found for early recurrence (OR=2.3; p=0.046). Patients with SAE≥3 showed a reduced survival compared to patients without such complications (22.1 vs. 31.0 months, respectively, p=0.02). The overall treatment-related mortality rate was 3.8% (n=5) and the 30-day mortality was 0.6% (n=1).
Conclusion: Early recurrence after CRS+HIPEC is associated with a significant reduction in overall survival. This study identifies post-operative complications requiring intervention as the only significant risk factor for early recurrence, independent of the extent of peritoneal disease, highlighting the importance of minimizing the risk of post-operative complications. Furthermore, treatment-related mortality was considerably higher than described by the 30-day mortality rate.

Molecular profile of young esophageal adenocarcinoma patients.

A.M.J. van Nistelrooij[1,2], R. Van Marion[1], K. Biermann[1], M.K. Casparie[3], J.J.B. van Lanschot[2], B.P.L. Wijnhoven[2], W.M.N. Dinjens[1], [1]Dept of Pathology and [2]Dept of Surgery, Erasmus MC Cancer Institute, Rotterdam, [3]Stichting PALGA, Utrecht, The Netherlands

Patients diagnosed with esophageal adenocarcinoma (EAC) are typically men with an average age of 68 years. However, recently a group of young aged patients with EAC have been identified. EAC in the young may be a disease distinct from that of the classical EAC patient, with possibly a different etiology. It is unknown which molecular alterations contribute to these early-onset tumors. Therefore the aim of the present study was to compare the DNA alterations profile in the tumors of patients aged ≤40 years with that of patients aged ≥68 years. To identify patients aged ≤40 years and diagnosed with EAC, the PALGA database was searched. Patients aged ≥68 years were collected from the pathology archive and matched with the young based on TNM-stage and tumor differentiation. Of all patients tumor DNA was isolated from the surgically resected specimens and sequenced on the Ion Torrent Personal Genome Machine with the Ion AmpliSeq Cancer Panel. Twenty-eight patients aged ≤40 years were matched with 27 patients aged ≥68 years, and the mean number of mutations between these age groups was not significantly different (p=0.196, independent samples T-test). The most frequently mutated genes were TP53 (73%) and P16 (16%). The genes ATM, RB1, JAK3, and PIK3CA were mutated equally between both age groups. Additional mutations in the patients aged ≤40 years occurred exclusively in the genes: APC, CDH1, CTNNB1, FGFR2, and STK11, while in the patients aged ≥68 years additional mutations were exclusively identified in the genes: ABL1, FBXW7, GNA11, GNAS, KRAS, MET, SMAD4, and VHL. The present data demonstrate that the vast majority of patients diagnosed with EAC in both age groups carried a TP53 mutation. Additional mutations in the young patients occurred mainly in genes classified as cell fate pathways (APC, CHD1, CTNNB1), while additional mutations in older patients occurred essentially in genes involved in cell survival pathways. These data suggest that the development of EAC in young patients underlies a different etiology compared to older patients, and that especially mutations occurring in genes involved in cell fate pathways might initiate early-onset tumors.

SNPs associated with esophageal adenocarcinoma.

A.M.J. van Nistelrooij[1,2], H.A.G.M van der Korput[1], L. Broer[3], R. van Marion[1], M.I. van Berge Henegouwen[4], C.J. van Noesel[5], K. Biermann[1], V.M.C.W. Spaander[6], H.W. Tilanus[2], J.J.B. van Lanschot[2], A. Hofman[7], A.G. Uitterlinden[3,7], B.P.L. Wijnhoven[2], W.N.M. Dinjens[1], [1]Dept of Pathology, [2]Dept of Surgery, [3]Dept of Internal Medicine, [6]Dept of Gastroenterology and Hepatology, and [7]Dept of Epidemiology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, [4]Dept of Surgery, and [5]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands

Recently, the first genome-wide association study (GWAS) on esophageal adeno-carcinoma (EAC) and the premalignant lesion Barrett's esophagus revealed several associated SNPs; rs10419226 (CRTC1), rs11789015 (BARX1), rs2687201 (FOXP1), rs2178146 (FOXF1), rs3111601 (FOXF1), and rs9936833 (FOXF1). The aim of the present study was to validate the association between these six SNPs and the risk of EAC in an independent and large Dutch case-control study.The six identified SNPs were genotyped by a multiplex SNaPshot analysis in 972 EAC patients, who underwent an esophagectomy in two centers in the Netherlands, between January 1994 and December 2013. Allele frequencies were compared to a control group, derived from an ongoing population-based prospective cohort study in the Netherlands (n=6206). Logistic regression analysis and meta-analysis were performed to calculate odds ratio's (OR).Rs10419226 (CRTC1) showed a significantly increased EAC risk for the minor T allele (OR=1.17, p=0.001), and rs11789015 (BARX1) showed a significantly decreased risk for the minor G allele (OR=0.85, p=0.004) in the logistic regression analysis. The meta-analysis of the original GWAS and the current study revealed more accurate effect estimate and improved level of significance for rs10419226 (CRTC1) (OR=1.18, $p=6.66*10^{-10}$) and rs11789015 (BARX1) (OR=0.83, $p=1.13*10^{-8}$). Although the association of the other four SNPs did not reached significance, the direction and effect size was in consistence with the original study.This independent and large Dutch case-control study validated the association of rs10419226 (CRTC1) and rs11789015 (BARX1) with the risk of EAC. These findings suggest a contribution of the patient genetic make-up to the development of EAC and might contribute to gain more insight in the etiology of this cancer.

Diffusion-weighted magnetic resonance imaging (MRI) for the prediction of response to neoadjuvant chemoradiotherapy in esophageal cancer.

P.S.N. van Rossum[1,2], A.L.H.M.W. van Lier[2], M. van Vulpen[2], O. Reerink[2], S.H. Lin[3], R. van Hillegersberg[1], J.P. Ruurda[1], G.J. Meijer[2], I.M. Lips[2], [1]Dept of Surgery, University Medical Center Utrecht, Utrecht, The Netherlands, [2]Dept of Radiotherapy, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Dept of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston (Texas), United States of America

Neoadjuvant chemoradiotherapy (nCRT) for esophageal cancer can induce significant tumor downstaging before surgery, even resulting in a pathologic complete response (pathCR) in 29% of patients. It is speculated that surgery might be safely omitted in this selected group of complete responders. On the other hand, patients with a poor pathologic response may benefit less from nCRT but are exposed to its toxicity. The aim of this study was to explore the value of diffusion-weighted magnetic resonance imaging (DW-MRI) for the prediction of response to nCRT in patients with esophageal cancer.
Between May 2013 and May 2014, 20 patients with newly diagnosed esophageal cancer who were planned to receive nCRT followed by surgery were included. Patients underwent MRI scanning with DW-MRI sequences within 2 weeks before nCRT, after 8-13 fractions, and 3-9 weeks after completion of nCRT (prior to surgery). The median tumor apparent diffusion coefficient (ADC) was determined at the three time points. The predictive potential of initial ADC, and change in ADC (ΔADC) during and after treatment for pathCR and good response was assessed. Good response was defined as pathCR or near-pathCR (tumor regression grade 1 or 2). A pathCR after nCRT was found in 4 of 20 patients (20%), and 8 patients (40%) showed a good response. The ΔADC_{during} was significantly higher in pathCR patients compared to patients without pathCR (in $*10^{-3}$ mm^2/s: 34.6±10.7 [mean±SD] vs. 14.0±13.1; p=0.016), as well as in good responders compared to poor responders (30.5±8.3 vs. 9.5±12.5; p=0.002). Initial tumor ADC and ΔADC_{post} were not significantly related to pathologic response. ROC analysis for ΔADC_{during} resulted in an area under the curve (AUC) of 0.90 for discriminating pathCR from no pathCR at an optimal cut-off value of 28.9% (sensitivity 100%, specificity 75%, accuracy 95%, PPV 94%, and NPV 100%). For discriminating good from poor responders, ΔADC_{during} showed an AUC of 0.92 with an optimal cut-off value of 20.7% (sensitivity 82%, specificity 100%, accuracy 89%, PPV 100%, and NPV 80%).
Conclusions: The treatment-induced change in ADC as determined on DW-MRI during the first 2-3 weeks of nCRT for esophageal cancer allows for accurate early prediction of pathologic response. The high sensitivity and NPV of ΔADC_{during} for predicting residual cancer are particularly promising when considering a patient-tailored wait-and-see approach with omission of surgery. The high specificity and PPV of ΔADC_{during} for predicting poor response seem promising for future considerations regarding modification or discontinuation of nCRT early during treatment.

The influence of sarcopenia and sarcopenic obesity on survival after major liver resection for colorectal liver metastases

F. de Graaff[1,2], S. Mensink[2], M. Brusse-Keizer[3], D.E. Bouman[4], C.H. Slump[2], J.M. Klaase[1], [1]Dept of Surgery, Medisch Spectrum Twente, Enschede, [2]Faculty of Science and Technology, University of Twente, Enschede, [3]Medical School Twente, Medisch Spectrum Twente, Enschede, [4]Dept of Radiology, Medisch Spectrum Twente, Enschede, The Netherlands

Each year, 13,000 patients are diagnosed with colorectal cancer in the Netherlands. Approximately 25% of patients present with synchronous colorectal liver metastases (CRLM) and another 25% will develop liver metastases during follow-up. If possible, surgical resection is the preferred therapy, and approximately two-thirds of liver resections are performed for CRLM. Five year survival rates after resection for CRLM are between 40-50%. Nowadays, sarcopenia (depletion of skeletal muscle mass) is a trending topic. Several studies have shown that sarcopenia is associated with worse overall survival. This study investigated the influence of sarcopenia and sarcopenic obesity (SO) on overall survival after major liver resection (≥3 segments) for CRLM. From our liver database we selected patients who underwent major liver resection for CRLM at our institute between 2008 and early 2014. Skeletal muscle mass was measured in preoperative CT scans as total psoas area (TPA) and total abdominal muscle area (TAMA) at three anatomical levels: (1) slice with both vertebral spines of L3, (2) top and (3) bottom of L4. TAMA and TPA were normalized for patient height (in cm2 m-2). Sarcopenia was defined as skeletal muscle mass below the sex-specific median. SO was defined as sarcopenia combined with BMI > 25 kg m-2. The relation between both sarcopenia and SO and overall survival was analyzed. Ninety patients underwent major liver resection during the study period. Seven patients were excluded due to absent CT scans or absent measurement levels. Another 12 patients were excluded because they did not have CRLM. The final study cohort included 71 patients (50 men (70.4%), median age 65 (36-79) years). The median BMI was 25 kg m-2 (range 16-35 kg m-2). Patients with sarcopenia defined with TAMA at L4 superior, had 5.5 times more chance of dying during follow-up (HR:5.5;95% CI:1.2-24.9). Patients with SO defined with TAMA at L4 superior had an increased risk of dying during follow-up of 3.7 (HR:3.7;95% CI:1.2-11.6). Surgical duration and pringle maneuver were tested as possible confounders, however, sarcopenia and SO measured at L4 superior remained independent predictors of worse overall survival. Sarcopenia and SO measured as TPA at all levels and TAMA other than L4 superior were not significantly related to worse overall survival.

Conclusion: Sarcopenia and SO are independent predictors of worse overall survival after major liver resection for CRLM. TAMA at L4 superior seems to be the most discriminating anatomical measurement level for sarcopenia and SO. The preoperative CT scan can help to identify those patients who are at an increased risk of worse overall survival.

Longterm quality of life after anastomotic leakage following colorectal surgery. A multicentre, case-matched cohort.

J.J. van den Broek[1], D. Hogerzeil[2], K. de Valk[2], F. Daams[3], J.F. Lange[4], [1]Medical Center Alkmaar, Alkmaar, [2]Erasmus Medical Center, Rotterdam, [3]VU Medical Center, Amsterdam, The Netherlands

Aim: To investigate the long term effects of clinical anastomotic leakage (CAL) after colorectal surgery on surgical outcome and Health Related Quality of Life (HRQoL). Methods: A multicentre, case-controlled study was set up. Patients after CAL (group A; n = 49) were matched with patients without CAL (group B; n = 96) for sex, type of surgery, indication, time after surgery and hospital. Surgical outcome was scored in a standardized fashion, HRQoL was assessed by the SF 36, EORTC-QLQ-C30, EORTC-C29, EQ-5D-5L and the Body Image Scale. Results: There was no difference in all cause mortality after a follow up of 10 years after surgery (44.6% in group A; 38.3% in group B; p = 0.097). Reoperations, complications other than CAL, permanent stomas and scars were more frequent in group A. Using the SF-36, group B scored higher in the Physical Component Scale compared to group A (PCS group A: 42.1; group B: 46.3; $p < 0.05$). The EQ-5D-5L showed a significant difference between both groups when the VAS-score was compared between both groups (VAS group A: 69.9 vs group B: 77.2; $p < 0.05$). The index value for the 5 dimensions did not differ between both groups. Mean Body Image scores were significantly higher in group A (BIS group A: 8.9 vs group B: 4.8; $p < 0.01$). This difference was even more pronounced when patients with a stoma were not included in both groups (BIS group Ast-: 9.6 vs group Bst-: 4.3; $p < 0.05$). Cancer patients in group A (group Ac: n = 22) scored significantly worse than cancer patients in group B (group Bc: n = 66) in the Global Health Score (GHS) and the Functional Score (FS) of the EORTC questionnaires.
Conclusion: These results show detrimental effects on aspects of HRQoL for patients after colorectal anastomotic leakage even after 10 years, compared to patients after uncomplicated colorectal surgery. Understanding these poor patient reported outcomes and objective surgical outcomes should raise awareness of the treating surgeon for their patient's functional and emotional vulnerability even many years after this dreadful complication.

Trends in patterns of care for resectable esophageal cancer in the Netherlands: a population based study.

M. Koëter[1], M. van Putten[2], R.H.A. Verhoeven[2], V.E.P.P. Lemmens[2,3], G.A.P. Nieuwenhuijzen[1], [1]Dept of Surgery, Catharina Hospital, Eindhoven, [2]Comprehensive Cancer Center South, Eindhoven, [3]Dept of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands

According to the Dutch guidelines, patients with resectable esophageal cancer (EC) are treated with neoadjuvant chemoradiation followed by subsequent esophagectomy. Definitive chemoradiation (dCRT) can be an alternative option in patients not eligible for surgery. The objective of this study was to determine patterns of the use of surgery and dCRT for EC throughout the years in the Netherlands. All patients with resectable EC (T1-3, N0-1, M0-1A) diagnosed in the Netherlands between 2003-2012 (n=11326) were selected from the Netherlands Cancer Registry. Chi-square analysis was conducted to determine differences between patients with an adenocarcinoma (ADC) or a squamouscell carcinoma (SCC). Kaplan Meier curves with log rank test were used to determine overall survival (OS). Multivariable Cox regression analysis were performed to examine factors influencing survival. Throughout the years we observed a strong increase in the use of dCRT in patients with a SCC from 9 to 33%, while the use of surgery decreased from 39 to 30%. For ADC the use of dCRT increased moderately from 2 to 13%, and the use of surgery decreased from 58 to 51%. In patients with a SCC, 5-year OS was 40%, 22.7% and 6.7% for patients receiving surgery, dCRT or palliative treatment respectively. In patients with an ADC 5-Year OS for dCRT was less favourable with 36.0%, 12.6% and 14.1% in patients receiving surgery, dCRT or palliative treatment respectively. Despite no significantly different 5 year OS for dCRT in ADC when compared to palliative treatment, multivariable Cox regression analysis showed that dCRT for both SCC and ADC was still an independent predictor for a better survival when compared to palliative treatment. In conclusion, between 2003-2012 there is an marked increase in the use of dCRT in EC which is more prominent in SCC when compared to ADC. Parallel we observed a decrease in the use of surgical treatment. Five year survival for surgery was significantly better for both SCC as ADC when compared with other treatment modalities. Although multivariable analysis could not show a significant difference, 5 year survival for dCRT was comparable with palliative treatment in ADC.

Effect of co-morbidity on the probability to receive definitive chemoradiotherapy or surgery and the impact on survival in esophageal cancer patients: a population-based study.

Z. Faiz[1], M. van Putten[2], R.H.A. Verhoeven[2], J.W. van Sandick[3], G.A.P. Nieuwenhuijzen[4], V.E. Lemmens[2], B.P.L. Wijnhoven[5], J.T.M. Plukker[1], [1]Dept of Surgery, University Medical Center Groningen, Groningen, [2]Netherlands Comprehensive Cancer Organization (IKNL), [3]Dept of Surgery, Dutch Cancer Institute - Antoni van Leeuwenhoek, [4]Dept of Surgery, Catharina Hospital, Eindhoven, [5]Dept of Surgery, Erasmus Medical Center, Rotterdam, The Netherlands

Esophagectomy is still considered the treatment of choice for resectable esophageal carcinoma (EC). An alternative potentially curative treatment in patients who are unfit to undergo surgery is definitive chemoradiotherapy (dCRT).The aim of this study was to assess the effect of co-morbidity in the decision making between dCRT or surgery in the curative treatment and its impact on survival in EC patients. All 3943 patients diagnosed with EC (C15.1-C15.9) in the South East region of the Netherlands and registered in the Eindhoven Cancer Registry between 1995 and 2013 were selected. Only patients with potentially curative disease that could be treated with surgery or dCRT were selected (cT2-3, N0-3, M1a). Co-morbidity was assessed by a modified Charlson score and multivariate Cox proportional hazards analysis was used to assess the differences in overall survival. Of the 1855 eligible patients 33% had no co-morbidities, 28% one and 40% ≥ 2 co-morbidities. Forty-four percent of the patients underwent an esophagectomy (n=807), 15% received dCRT (n=278) and 15% neoadjuvant chemoradiotherapy and esophagectomy (n=315). Multivariable logistic regression analyses showed that ≥ 2 co-morbidities (OR=2.5. 95%CI 1.6-3.7), age >70 years, squamous cell carcinoma, lymph node metastasis, cardiovascular diseases and previous malignancies were significantly associated with a higher probability to receive dCRT instead of esophagectomy. Having ≥ 2 co-morbidities was significantly associated with a worse overall survival (HR=1.38, 95%CI 1.09-1.73) among patients who underwent an esophagectomy. However, overall survival and having ≥2 co-morbidities were not associated with dCRT.
Conclusion. Patients with ≥ 2 co-morbidities and aged > 70 years are more likely to be treated with dCRT. In contrast to the esophagectomy group, the dCRT group did not show any association between having ≥ 2 co-morbidities or older age and a worse overall survival.

Survival after Distal Pancreatectomy for Pancreatic Ductal Adenocarcinoma: a Nationwide Retrospective Cohort Study

T. de Rooij[1], J.A. Tol[1], C.H. van Eijck[2], D. Boerma[3], B.A. Bonsing[4], K. Bosscha[5], R.M. van Dam[6], M.G. Dijkgraaf[7], M.F. Gerhards[8], H. van Goor[9], E. van der Harst[10], I.H. de Hingh[11], G. Kazemier[12], J.M. Klaase[13], I.Q. Molenaar[14], G.A. Patijn[15], H.C. van Santvoort[1], J.J. Scheepers[16], G.P. van der Schelling[17], E. Sieders[18], O.R. Busch[1], M.G. Besselink[1] for the Dutch Pancreatic Cancer Group, [1]Dept of Surgery, Academic Medical Center, Amsterdam, [2]Dept of Surgery, Erasmus Medical Center, Rotterdam, [3]Dept of Surgery, St Antonius Hospital, Nieuwegein, [4]Dept of Surgery, Leiden University Medical Center, Leiden, [5]Dept of Surgery, Jeroen Bosch Hospital, Den Bosch, [6]Dept of Surgery, Maastricht University Medical Center, Maastricht, [7]Clinical Research Unit, Academic Medical Center, Amsterdam, [8]Dept of Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, [9]Dept of Surgery, Radboud University Medical Center, Nijmegen, [10]Dept of Surgery, Maasstad Hospital, Rotterdam, [11]Dept of Surgery, Catharina Hospital, Eindhoven, [12]Dept of Surgery, VU University Medical Center, Amsterdam, [13]Dept of Surgery, Medisch Spectrum Twente, Enschede, [14]Dept of Surgery, University Medical Center Utrecht, Utrecht, [15]Dept of Surgery, Isala Clincs, Zwolle, [16]Dept of Surgery, Reinier de Graaf Gasthuis, Delft, [17]Dept of Surgery, Amphia Hospital, Breda, [18]Dept of Surgery, University Medical Center Groningen, Groningen, The Netherlands

Introduction: Nationwide data on survival after distal pancreatectomy (DP) for pancreatic ductal adenocarcinoma (PDAC) with predictors for survival are lacking. Methods: Adult patients who underwent elective DP for PDAC in one of 17 Dutch pancreatic centers between January 1st 2005 and September 1st 2013 were analyzed retrospectively. Patients were excluded when DP was not the primary procedure or the histopathological diagnosis was not PDAC. Primary outcome was postoperative survival. Predictors for survival <1 year were identified. Results: In total, 761 consecutive patients were identified, of whom 620 patients were excluded because DP was not the primary procedure (n=124) or non-PDAC histopathology (n=496). Therefore, 141 patients (45% (n=63) male, mean age 64 years) who had undergone DP for PDAC were included, with a median number of 7 procedures per center [range 2 to 22]. Multivisceral resection was performed in 30% (n=43) and laparoscopic resection in 5% (n=7) of patients. In-hospital mortality was 4% (n=6). Mean tumor size was 44 mm [SD 23]. R0 resection was performed in 50% (n=70), R1 resection in 45% (n=64) and R2 resection in 5% (n=7) of patients. After DP, 45% (n=63) of patients received adjuvant chemotherapy without differences in age and ASA physical status between patients with and without adjuvant chemotherapy. Median follow-up was 14 [IQR 8-27] months. Postoperative median survival was 17 [IQR 13-21] months. One-year, three-year and five-year cumulative survival were 63%, 28% and 17%, respectively. Median survival of patients who had undergone multivisceral resection was significantly reduced compared with patients who had undergone DP only (10 [95% confidence interval (CI) 6-14] months versus 22 [95% CI 17-27] months, respectively; P < 0.001). Survival was 12 [95% CI 5-19] months after R0 and 8 [95% CI 3-14] months after R1 multivisceral resection. After multivariable analysis, AJCC (6th ed.) T-category (odds ratio 2.83 [95% CI 1.41-5.67]) and not receiving adjuvant chemotherapy (odds ratio 4.98 [95% CI 2.03-12.21]) were independent predictors for postoperative survival <1 year. Sex, age, ASA physical status, multivisceral resection, tumor size, lymph node ratio and resection margin did not predict postoperative survival <1 year.

Conclusion: In this nationwide series, DP for PDAC was associated with a similar in-hospital mortality, R1 resection rate and postoperative survival as seen after pancreatoduodenectomy for PDAC. These findings highlight the need for focus on adequate (neo-)adjuvant treatment strategies in these patients.

First experience with laparoscopic pancreatoduodenectomy in the Netherlands

M.W. Steen[1], M.F. Gerhards[1], S. Festen[1], [1]Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

Although laparoscopy has become a common surgical technique for many indications, laparotomy remains the standard surgical technique for pancreatic disorders. Laparoscopic pancreatoduodenectomy is not widely performed because it is a technically demanding procedure and there have been concerns regarding an increased risk of complications and unclear benefits of the laparoscopic procedure. The first minimal invasive pancreaticoduodenectomy (PD) was performed in 1992. The authors concluded that laparoscopy for pancreatic disorders should only be performed by surgeons highly experienced both in laparoscopy and open procedures for pancreatic disorders. In our center, we meet these criteria since many years. After extensive preparations, we performed our first laparoscopic PD in april 2014. The aim of this study was to demonstrate our first results with the laparoscopic PD. This was done by analyzing the prospectively gathered data of all patients with a periampullairy or pancreatic tumor that underwent a laparoscopic PD since april 2014. Seven patients were operated. Their median age was 65 years (range 54 – 76 years) with a 1:1 female:male ratio. Pathologic findings were cholangiocarcinoma in 3, duodenal carcinoma in 1, chronic pancreatitis in 1 and pancreatic ductal adenocarcinoma in 2 patients. The mean operation time was 395 minutes (6 hours and 35 minutes). No procedures were converted to open. The mean bloodloss was 765 milliliters. Complications were delayed gastric emptying in 2 patients, a grade B pancreatic fistula in 1 patient and a urinary tract infection in 1 patient. There was no mortality. The mean hospital stay was 14 days (range 9 – 21 days). The first results of laparoscopic PD are encouraging. No major per- or postoperative complications occurred except for one grade B pancreatic fistula This has resulted in a shortened postoperative length of stay of 4 days when compared to our open resections done between 2008 and 2013. Operation time was significantly longer, but we expect this to improve with experience.
In conclusion laparoscopic PD seems to be feasible and save and is likely to play an important role in pancreatic surgery in the near future in the Netherlands.

Impact of upsizing percutaneous catheters in patients with suspected infected necrotizing pancreatitis

J. van Grinsven[1,2], P. Timmerman[3], K.P. van Lienden[4], J.W. Haveman[3], D. Boerma[5], C.H. van Eijck[6], P. Fockens[1], H.C. van Santvoort[7], M.A. Boermeester[7], M.G. Besselink[7] for the Dutch Pancreatitis Study Group, [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Dutch Pancreatitis Study Group, St. Antonius Hospital, Nieuwegein, [3]Dept of Surgery, University Medical Center Groningen, Groningen, [4]Dept of Radiology, Academic Medical Center, Amsterdam, [5]Dept of Surgery, St. Antonius Hospital, Nieuwegein, [6]Dept of Surgery, Erasmus Medical Center, Rotterdam, [7]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

Infected necrotizing pancreatitis is nearly always an indication for invasive treatment. Percutaneous catheter drainage (PCD) is now well established as the first intervention in a 'step-up approach'. It has been suggested that a drain upsizing strategy might obviate the need for additional surgical necrosectomy and improve clinical outcome, but studies on this topic are lacking. We retrospectively identified patients with necrotizing pancreatitis from in-hospital databases (2004-2014) in four tertiary referral centers. Patients who underwent PCD as primary treatment for suspected infected necrosis were included. We compared patients' outcomes of a single center that attempted to routinely upsize in case of lack of clinical improvement with those of patients treated in the three centers where this strategy was not used routinely. Primary outcome was the need for additional surgical necrosectomy following PCD. Secondly, we compared complications including mortality and new-onset (multi) organ failure. Of 1427 consecutive patients with acute pancreatitis, 369 patients (26%) were diagnosed with necrotizing pancreatitis, of which 117 patients (32%) underwent primary PCD for suspected infected necrosis. Infected necrosis was ultimately proven in 82 of these patients (70%). In total 42 patients (36%) were treated in the drain upsizing strategy center versus 75 patients (64%) in the non-upsizing strategy centers. Patient characteristics were similar in baseline, except for differences in age and timing of first PCD for which we corrected in the analyses. The median of drain procedures was 3 (interquartile range (IQR) 2-4) in the upsizing strategy center versus 2 (IQR 1-2) in the non-upsizing strategy centers, P<.001. The maximal drain size was median 16 French (IQR 14-20) compared to 14 French (IQR 12-14), P<.001, respectively. Additional surgical necrosectomy was required in significantly less patients in the upsizing strategy center, 29% vs. 52% P=.045. Mortality was comparable in both groups, 17% vs. 19%, P=0.787. New onset (multi) organ failure after PCD occurred in 5% of patients in the upsizing strategy center compared to 20% of patients in the non-upsizing strategy centers, P=0.114.
Conclusion: A PCD upsizing strategy for patients with suspected infected necrotizing pancreatitis appears to reduce the need for surgical necrosectomy. Future studies will have to demonstrate the true clinical value of PCD upsizing and whether this should be performed on indication or preemptively.

Gamma-Delta T-Lymphocytes as diagnostic criterium in latent celiac disease

P. Nijeboer[1], T. van Gils[1], R. Ooijevaar[1], H.J. Bontkes[2], C.J. Mulder[1], G. Bouma[1], [1]Dept of Gastroenterology, and [2]Dept of Pathology, VU University Medical Center, Amsterdam, The Netherlands

An increase in Gamma-Delta intraepithelial lymphocytes (IEL) (CD3+TCRγδ+) is a characteristic finding in CD patients yet cut-off values for CD3+TCRγδ+ IEL in CD have not been determined. A validated cut-off value might be helpful in the establishing the diagnosis of CD, especially in those patients with minimal histological abnormalities (i.e., Marsh I) or individuals with positive serology in the absence of histological abnormalities. Flow cytometric immunophenotyping was performed on IELs isolated from fresh small bowel biopsy specimens obtained from histology and serology proven CD patients (n=219) (active CD: n=92, CD in remission: n=127), healthy controls without CD (n=89) and suspected CD (n=14), the latter being defined as Marsh I-II and/or positive serology. Thirty-one additional patients with non-celiac villous atrophy were included as a disease control group. Percentages of CD3+TCRγδ+ IEL from CD patients and healthy controls were used to calculate a cut-off value for CD3+TCRγδ+ IEL in suspected CD patients using a receiver operating characteristic (ROC) curve. A significantly higher percentage of CD3+TCRγδ+ IEL was found in biopsy and serology proven CD patients (median 19.0%, range 1-58%) compared to healthy controls (median 6.0%, range 1-15%) ($p<.001$). Active CD and CD in remission showed comparable percentages of CD3+TCRγδ+ IEL with a median of 18.5% and 19.0% respectively (range 1-58% and 1-53% respectively)($p=.78$). Follow-up immunophenotyping in patients with active CD revealed no significant decrease in CD3+TCRγδ+ IEL percentages despite histological recovery ($p=.12$). Patients with non-celiac villous atrophy showed a median CD3+TCRγδ+ of 5.0% (range 0.5-18%) which was comparable with healthy controls. The median percentage of CD3+TCRγδ+ IEL in suspected CD was 20.0% (range 11-66%) which was comparable compared to active CD patients ($p=.13$), and was significantly higher compared to healthy controls and non-celiac villous atrophy (both $p<.001$). A cut-off value of 15% for CD3+TCRγδ+ IEL resulted in 98% specificity and 61% sensitivity for a diagnosis of CD, with an area under the curve of 87% (95%-CI 83-91%).
Conclusion: CD3+TCRγδ+ IEL are increased in CD compared to healthy controls, also after the introduction of a gluten free diet (GFD). Patients with suspected CD without the characteristic villous atrophy display high percentages of CD3+TCRγδ+ IEL.
A percentage of >15% CD3+TCRγδ+ IEL might aid in a diagnosis of CD. Furthermore, Flow cytometric immunophenotyping might be helpful in cases of diagnostic doubt on CD in patients compliant to a GFD without the need for a gluten-challenge.

Medication-induced microscopic colitis: do recency and duration of use matter?

B.P.M. Verhaegh[1,2], F. de Vries[3,4], A.A.M. Masclee[1,2], A. Keshavarzian[3], A. de Boer[3], P. Souverein[3], D.M.A.E. Jonkers[1,2], M.J. Pierik[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [2]NUTRIM, School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, [3]Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht Institute of Pharmaceutical Sciences, Utrecht, [4]Clinical Pharmacology and Toxicology, Maastricht University Medical Center, Maastricht, The Netherlands

Microscopic colitis (MC) is a colonic disorder characterised by chronic watery diarrhoea. There is increasing evidence that exposure to commonly prescribed drugs like non-steroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors (PPIs), selective serotonin reuptake inhibitors (SSRIs), and statins is associated with an increased risk of MC. However, the attributive risk of recent or longer use and the effect of higher dosages has never been investigated, although this information would give more insight in the possible mechanism of medication-induced MC.A case-control study was conducted using the British Clinical Practice Research Datalink. Cases were diagnosed with microscopic, lymphocytic (LC) or collagenous (CC) colitis between 1992-2013. For each case, up to 5 randomly selected controls without MC were matched by year of birth, gender, and practice. The index date of the case defined that of the controls. Prescriptions within 60 days prior to index date were excluded to take into account a latency (lag) time and to minimize reverse causality. Exposure status was classified as current (61-90 days), recent (91-150 days), and past use (>150 days) according to the time since most recent prescription prior to index date. In current users, duration of continuous use and average daily dose was assessed. Conditional logistic regression analysis was applied to quantify the strength of the associations and to correct for confounders.In total, 1.211 cases with MC (394 CC, 292 LC, 525 undefined MC) and 6.041 controls were identified. Current use of NSAIDs (OR 1.79, 95% CI 1.36-2.36), PPIs (OR 3.93, 95% CI 2.25-4.74), and SSRIs (OR 2.27, 95% CI 1.79-2.89) was associated with an increased risk of MC compared to never and past use. Especially a 4-12 months continuous use of NSAIDs, PPIs, and SSRIs increased the risk of MC. Long-term use (>24 months) attenuated this risk. Exposure to more than 1.25 standardised daily dosages was associated with an elevated risk of MC in PPI (OR 6.90, 95% CI 3.82-12.49) and SSRI users (OR 4.15, 95% CI 2.47-6.97). Analysis per MC subtype showed a positive association between current use of NSAIDs (OR 2.28, 95% CI 1.46-3.54) and PPIs (OR 6.15, 95% CI 4.41-8.58) in CC and current use of PPIs (OR 2.40, 95% CI 1.60-3.59) and SSRIs (OR 2.65, 95% CI 1.69-4.15) in LC. Statin use was not associated with MC. A sensitivity analysis with a lag time of 90 days showed conclusions consistent with the primary analysis. In conclusion, use of NSAIDs, PPIs, and SSRIs is associated with an increased risk of MC. Especially in current users with continuous exposure duration for 4 to 12 months, drug exposure as cause for MC should be considered.

Incidence and treatment results of perianal and rectovaginal fistulizing Crohn's disease in a population-based cohort

K.W.A. Göttgens[1], S.F.G. Jeuring[2,3], R. Sturkenboom[1], M.J.L. Romberg-Camps[4], G.L. Beets[1], L.E. Oostenbrug[5], L.P.S. Stassen[1], M.J. Pierik[2,3], S.O. Breukink[1], [1]Dept of Surgery, and [2]Division of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [3]School for Nutrition, Toxicology and Metabolism (NUTRIM), Maastricht UMC, Maastricht, [4]Dept of Internal Medicine and Gastroenterology, Orbis Medical Center, Sittard-Geleen, [5]Dept of Internal Medicine and Gastroenterology, Atrium Medical Center, Heerlen, The Netherlands

Perianal fistulas (PF) and rectovaginal fistulas (RVF) frequently occur in Crohn's disease (CD) patients. These conditions can be very invalidating and are often refractory to (surgical) treatment. Despite their obvious relevance, little is known about the incidence of and risk factors for developing these conditions. Therefore, this study aimed to determine the incidence of and risk factors for PF and RVF in a large, unselected population of CD patients. Since 1991, incident IBD cases in a region of the Netherlands are included in a population-based IBD cohort. All 1162 CD patients were included for study. Incidences of PF and RVF were determined via Kaplan-Meier survival curves, and hazard ratios (HR) of potential risk factors were calculated using a Cox regression model. In total, 1162 CD patients were included, with a mean follow-up of 8.7 years (SD 5.7). In 161 cases, a PF developed after a median of 0.4 years (IQR 0.0-4.6) after diagnosis, corresponding to a cumulative probability of 21.5%. Ninety-nine (61.5%) patients underwent fistula surgery. The cumulative probability of recurrence of PF was 73.2%. Risk factors for developing PF were colonic (HR 3.1; 95%CI 1.9-5.2) and ileocolonic (HR 2.8; 95%CI 1.8-4.5) localisation of CD, and age <40 years at diagnosis (HR 1.7; 95%CI 1.2-2.5). In 17 cases, a RVF developed after a median of 4.7 years (IQR 0.8-8.4), corresponding to a cumulative probability of 3.9%.
Conclusion: This population-based study showed that the risk of developing a perianal or rectovaginal fistula is high in CD patients, and recurrences often occur. This finding underlines the importance of improving treatment strategies for these invalidating conditions.

Human splanchnic amino acid metabolism

E.P.J.G. Neis[1,2], S.S. Rensen[1], H.M.H. van Eijk[1], M. Arts[1], S.W. Olde Damink[1], E.E. Blaak[2,3], C.H.C. Dejong[1,2], [1]Dept of Surgery, NUTRIM, Maastricht University, Maastricht, [2]Top Institute Food and Nutrition, Wageningen, [3]Dept of Human Biology, NUTRIM, Maastricht University, Maastricht, The Netherlands

Various body compartments are thought to play distinct roles in amino acid homeostasis, through either net uptake or release. However, the separate roles of specific organs in determining amino acid balance in humans remain unclear, partly due to the fact that the portal vein is difficult to access for sampling in humans. As a result, most available data concern overall splanchnic balances. In this study, we aimed to evaluate interorgan amino acid exchange among the intestine, liver, spleen, and kidneys in patients undergoing upper abdominal surgery. Importantly, this human model gave us the unique opportunity to distinguish between the small intestine and colon in amino acid handling. Therefore, 20 patients planned to undergo a pylorus preserving pancreatico duodenectomy (PPPD) as treatment of benign or malignant tumors were included in this study. Under general anesthesia, blood from these patients was sampled during surgery from the portal vein, hepatic vein, superior mesenteric vein, inferior mesenteric vein, splenic vein, renal vein, and the radial artery. Subsequently, the difference between arterial and venous concentrations of 21 amino acids was determined by HPLC as a semi-quantitative measure of amino acid metabolism across a given organ. A p-value below 0.05 was considered statistically significant. Our data showed a net release of 32.7±7.3 µmol/L serine by the kidneys into the systemic circulation. Besides, we found a significant uptake of glutamine by the small intestine (124.8±21.0 µmol/L), accompanied by a net release of 36.4±5.8 µmol/L citrulline. This, however, was not seen for the colon. Interestingly, a trend of net hepatic uptake of citrul (9.7±1.6 µmol/L) was observed, next to a remarkable alanine, arginine, and methionine uptake (117.1±19.0 µmol/L; 26.1±4.2 µmol/L; 6.6±1.1 µmol/L). Glutamate, on the other hand, was significantly released by the liver into the circulation (67.9±11.0 µmol/L).
In conclusion, this design provided us with unique qualitative and quantitative information on integrative amino acid physiology. The well-known intestinal glutamine-citrul pathway appears to be present in the small intestine but not in the colon in vivo. In the future, this knowledge may be applied to optimize dietary supplementation of certain amino acids in critically ill patients.

Disease progression is a risk factor for colectomy in ulcerative colitis: 10-years of follow up in a tertiary care facility

S. Sahami[1,2], K. Konté[1], C.J. Buskens[2], P.J. Tanis[2], M.L. Lowenberg[1], C.J. Ponsioen[1], G.R. van den Brink[1], W.A. Bemelman[2], G.R. D'Haens[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

Ulcerative colitis (UC) is a chronic inflammatory bowel disease that is characterized by its relapsing and remitting behaviour. The disease pattern is hard to predict, but may influence the prognosis and the risk of colectomy. So far, literature on disease progression in UC patients is limited. Therefore, the primary objective of this study is to describe the ulcerative colitis proximal extension over time and to evaluate whether this is a risk factor for colectomy in UC patients. All patients recorded by our hospital registry, diagnosed locally with UC between 1 January 1990 and 31 December 2000 were included. Referred patients from other hospitals were excluded. Crohn's disease and IBDU patients were also excluded from the study. By chart review we identified additional data on disease progression, medication use and surgical outcomes. Disease progression is defined as mucosal inflammation that progresses from proctitis to left sided colitis, left sided colitis to extensive colitis or proctitis to extensive colitis, based on the Montreal classification. The cumulative risk of colectomy was estimated via the Kaplan-Meier method. The cox proportional hazards regression was used to identify predictive factors associated with colectomy. In total, 506 UC patients (252 male and 254 female) were included with a median follow up of 10 years (IQR, 5-15 years) since disease onset. The cumulative risk of colectomy was 11.7% at 5-years (95% CI, 8.8% - 14.6%), 17.2% (95% CI, 13.7% – 20.7%) at 10-years, 22.8% (95% CI, 18.2% – 27.3%) at 15-years and 27.6% (95% CI, 21.5% - 33.7%) at 20-years. The extent of disease at diagnosis was in 32.9% proctitis, 34.8% left sided colitis and 25.9% extensive colitis. Of these patients, 8.9% remained in prolonged remission after diagnosis, 68.3% had less than 1 relapse per year, 18.7% had more than 1 relapse per year and 11.6% had continuously active disease. In 44.9% of the patients, ulcerative colitis progressed to a more extensive location during the follow up. The cox proportional hazards regression analysis showed that proctitis at diagnosis (HR 0.41; 95%CI 0.19 – 0.88) was protective for colectomy, whereas disease progression (HR 2.19; 95%CI, 1.06 – 4.51) and the need for anti-TNF therapy (HR 2.03; 95%CI, 1.01 – 4.09) were independent risk factors. The cumulative colectomy rates were in with published data and have not changed over time despite the introduction of new therapies. In this historical cohort, the majority of patients diagnosed with distal colitis progress to a more extensive form. Disease progression is a risk factor for colectomy, which may imply that the disease behaviour is more aggressive and may become unresponsive to treatment.

Multiple in-hospitals transfers promote spread of Clostridium difficile infection in the hospital

Y.H. van Beurden[1,2], O.M. Dekkers[3,4], A.M. Kaiser[1], M.K. Bomers[5], R. van Houdt[1], C.W. Knetsch[6], C.J.J. Mulder[2], C.M.J.E. Vandenbroucke-Grauls[1], [1]Dept of Medical Microbiology and Infection Control, [2]Dept of Gastroenterology and Hepatology, and [5]Dept of Internal Medicine, VU University Medical Center, Amsterdam, [3]Dept of Clinical Epidemiology, [4]Dept of Endocrinology and Metabolic Diseases, and [6]Dept of Medical Microbiology, Leiden University Medical Center, Leiden, The Netherlands

Study design: Case-control study with 1:4 case-control ratio. Objective: to determine risk factors associated with hospital-wide spread of Clostridium difficile-infection (CDI). Background: An outbreak of a single clone of C. difficile ribotype 027 occurred at the VU University Medical Center, involving 19 medical departments. Several risk factors for CDI are known, but factors specifically associated with hospital-wide outbreaks are less well recognised. Methods: Outbreaksetting of CDI due to a single clone of C. difficile ribotype 027 in a 750-bed tertiary care medical centre. C. difficile isolates were characterised by ribotyping, Amplified Fragment Length Polymorphism, and Multi Locus Sequence Typing. A selection of strains (n= 10) was also characterised by Whole Genome Sequence analysis. Cases:all patients (n= 79) diagnosed with CDI due to C. difficile ribotype 027 hospitalized between May 2013 and March 2014. Controls: patients (n= 316), no known history of CDI, matched for age, and medical specialty, who stayed in the hospital within 48 hours of diagnosis of the case patient. Variables: medical charts were reviewed for demographic and clinical patient characteristics; wards where patients had stayed and transfers between wards were noted. All diagnostic and treatment procedures were recorded. Statistical methods: Odds Ratios (OR) and their 95% Confidence Intervals (95% CI) were calculated by univariate and multivariate conditional logistic regression (SPSS version 20). Results: All isolates belonged to a single clone. Almost all patients with CDI (75/79) had used antibiotics prior to CDI, compared to 176/316 of controls (OR for any antibiotic use: 14.70; 95% CI: 5.25-41.19). Several different classes of antibiotics contributed to the risk. Use of proton pump inhibitors was also associated with CDI (OR: 1.99; 95% CI: 1.12-3.31). Patients with CDI had been transferred between wards more frequently than control patients: mean 1.73 times vs. mean 0.94 times. Only one patient with CDI had a underlying gastrointestinal disease. The overall 30-day mortality was 17.7% for cases and 8.2% for controls.
Conclusion: In this large outbreak of CDI, caused by a single clone of C. difficile ribotype 027, antibiotic use appeared as a prerequisite for acquisition of this outbreak strain. We identified use of proton pump inhibitors as a risk factor for acquisition of C. difficile. Multiple in-hospital transfers of patients between different wards contributed to the hospital-wide spreadribotype 079het wel vinden, maar die zin moeten we denk ik weg laten.naar voren komt als RF. Reduction of patient transfers during hospital stay may be an important measure to prevent and control the spread of C. difficile.

Clinical and genetic characterization of patients with graft-vs.-host disease after allogeneic hematopoietic cell transplantation suggests a role for JAK2, IL2RA and HLA-DRB1

S. van Sommeren[1,2], H.M. de Jonge[3], J. Kuball[4], L. te Boome[4], E. Vellenga[5], G. Huls[6], R.K. Weersma[1], [1]Dept of Gastroenterology, University Medical Center Groningen, Groningen, [2]Dept of Genetics, University Medical Center Groningen, Groningen, [3]Dept of Gastroenterology, Isala klinieken, Zwolle, [4]Dept of Hematology, University Medical Center Utrecht, Utrecht, [5]Dept of Hematology, University Medical Center Groningen, Groningen, [6]Dept of Hematology, Radboud University Medical Center, Nijmegen, The Netherlands

Allogeneic hematopoietic cell transplantation (HCT) is the most effective tumor immune-therapy available for a variety of hematologic malignancies. Next to inducing graft-vs. -tumor effects, alloreactivity mediated by donor T cells can also be directed against normal host tissue (particularly the skin, liver and gastrointestinal (GI) tract), manifesting as graft-vs.-host disease (GVHD). GVHD, and especially GI-GVHD, is one of the major reasons for mortality and morbidity after allogeneic HCT. Clinically and endoscopically GI-GVHD resembles Crohn's disease, and genetic association studies have implicated several genes associated with GVHD, including NOD2, a well-known inflammatory bowel disease (IBD) gene. In this study, we characterized a Dutch cohort of GVHD patients and hypothesized that genetic risk variants, associated with IBD, also play a role in GI-GVHD. We extensively clinically characterized a cohort form two University Medical Centers and collected DNA from both recipients and donors. These were genotyped using the Immunochip which is a custom-made array including ~200.000 genetic variants with dense coverage of immune related genes. Cox regression analysis was used to correlate recipients and donor genotypes to GI-GVHD, including the time to development of GI-GVHD.The cohort consisted of 154 patients (recipients) undergoing HCT. 64 (42%) patients developed GVHD, of which 24 (38%) developed substantial GI-GVHD (grade II, III or IV). 32/64 (50%) GVHD patients died, of which 8 (25%) causes of death could directly be related to GVHD. The incidence and mortality resembles cohorts described in the literature. We did not replicate the previously reported genetic associations at NOD2 for GVHD in GI-GVHD or in overall GVHD. We identified suggestive signals (p-value < 1E-4) for six out of the 163 known IBD loci. Loci harbouring JAK2, IL2RA, and the HLA-DRB1 contained multiple genetic variants with signals for genetic association (JAK2 p-value 5.8E-5, IL2RA p-value 7.3E-6, HLA-DRB1 p-value 1.85E-5).In our Dutch cohort, GVHD is a frequently occurring complication of HCT, greatly diminishing the prognosis of these patients. We were not able to replicate the previously reported association with NOD2 although the sample size equals that of those reported in the literature. Due to insufficient power we were unable to detect genetic association signals at genome wide significance level but we found suggestive evidence for associations for multiple genetic variants at loci harbouring JAK2, IL2RA and the HLA locus. This implies that genetic variation in the immune system is likely to partly underlie the pathogenesis of (GI-) GVHD.

Arabinoxylans show distinct prebiotic properties and may affect intestinal barrier function

B. Salden[1], F.J. Troost[1], E. Wilms[1], F. Brüll[2], P. Truchado[3], T. Van de Wiele[3], S. Possemiers[3], A. Masclee[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, NUTRIM, Maastricht University Medical Center, Maastricht, The Netherlands, [2]BioActor BV, Maastricht, The Netherlands, [3]Laboratory of Microbial Ecology and Technology, Ghent University, Ghent, Belgium

Obesity is associated with alterations in microbial composition and an impaired gut barrier function. Defects in preserving the integrity of the gut barrier may contribute to chronic low-grade inflammation which is thought to play a role in the development of chronic metabolic diseases. Arabinoxylans (AXs) are the most abundant non-digestible carbohydrates present in wheat. AXs are thought to exert prebiotic effects although this has not yet been established. Aim of the study was to investigate the efficacy of daily AX supplementation over a 6-weeks period on gut barrier function, microbiota composition and activity, and metabolic control in overweight and obese subjects. In this randomized, double-blind, placebo-controlled trial, 45 subjects (24 male; mean age 49.2±15.6 years; mean body mass index 31.0±2.5 kg/m^2) were randomly assigned to groups that received either 7.5g/day AX (n=14), 15g/day AX (n=17) or 15g/day placebo ((maltodextrin) n=14), respectively, for 6 weeks. Segment specific intestinal permeability was assessed with a multi-sugar test, and sigmoid colon biopsies were obtained from a subgroup of participants for analyses of gene transcription and mucosal expression of tight junction (TJ) proteins. Peripheral blood mononuclear cells (PBMCs) were isolated and cultured to determine cytokine production capacity. Fecal samples were collected to assess microbiota composition and activity. Blood was sampled for measuring concentrations of glucose, insulin and lipids. All measurements were performed at base and at the end of the study period. Differences between AX and placebo groups were assessed using linear mixed models. AX treatment significantly increased the production of total fecal SCFAs in both the 7.5g AX and 15g AX group ($p<.025$). Fecal acetate concentrations were significantly higher in the 15g AX group ($p=.019$), and butyrate concentrations were significantly higher in the 7.5g AX group ($p=.001$), compared to placebo. Analyses of microbiota composition are ongoing. Gene transcription of claudin-3 was increased in sigmoid biopsies in the 15g AX group ($p=.018$); TJ protein expression was not altered. AX treatment did not alter intestinal permeability, cytokine production capacity of PBMCs or metabolic parameters.

Conclusion: Daily AX supplementation for 6 weeks increases fecal concentrations of SCFAs, including acetate and butyrate, in a group of overweight and obese subjects. The AX supplementation resulted in increased transcription of claudin-3, but did not induce changes in intestinal permeability or alter tight junction protein expression.

Early detection of necrotizing enterocolitis by faecal volatile organic compounds analysis by electronic nose compared to the intestinal microbiota

T.G.J. de Meij[1], M.P.C. van der Schee[2], M.E. van de Velde[1], D.J.C. Berkhout[1], A.E. Budding[3], E.F.J. de Groot[1], B.W. Kramer[4], A.H. van Kaam[5], M.M. van Weissenbruch[6], P. Andriessen[5], J.B. van Goudoever[6], P.H.M Savelkoul[3], H.J. Niemarkt[4], N.K.H. de Boer[7], [1]Dept of Pediatric Gastroenterology, VU University Medical Center, Amsterdam, [2]Dept of Pediatric Pulmonology, Academic Medical Center, Amsterdam, [3]Dept of Microbiology and Infection control, VU University Medical Center, Amsterdam, [4]Dept of Neonatology, University Medical Center Maastricht, Maastricht, [5]Dept of Neonatology, Academic Medical Center, Amsterdam, [6]Dept of Neonatology, VU University Medical Center, Amsterdam, [7]Dept of Gastroenterology and Hepatology, VU University Medical Center, Amsterdam, The Netherlands

Introduction: Necrotizing enterocolitis (NEC) is the most common severe gastro-intestinal disease in very low birth weight infants. Currently available biomarkers lack accuracy to detect NEC in pre-clinical stage. Furthermore, clinical symptoms of NEC are usually indistinguishable from sepsis, leading to delay in start of NEC-therapy, worsening its prognosis. Alterations in microbiota are considered an essential factor in the pathogenesis of NEC. We hypothesized that analysis of fecal volatile organic compounds (VOC), which reflect microbial composition, by electronic nose (eNose) allows for early discrimination between infants with NEC and controls. Methods: In three neonatal intensive care units in he Netherlands, fecal samples of infants born at gestational age <30 weeks were collected daily, up to the 28th day of life. Included infants were allocated in three matched groups: NEC, controls or sepsis. Fecal VOC profiles of collected samples in the 5 days before the clinical diagnosis of NEC, were analyzed by eNose. Furthermore, we investigated the intestinal microbiota composition, which largely contributes to the total fecal volatolome, by means of IS-pro. Results: Two to three days prior to clinical onset of NEC, fecal VOC profiles of affected infants (n=13) differed significantly from matched controls (n=26) and from subjects with sepsis (n=31), (AUC ± 95% CI, p-value, sensitivity, specificity: 0.79 ± 0.95, p=0.002, 83%, 75%) and (0.73 ± 1.0, p=0.015, 90%, 83%) respectively. Differences in microbial profiles were observed between the three groups at all time-intervals, which could largely be contributed to alterations within the phlylum Proteobacteria. Interestingly and in contrast with VOC profiles, microbiota profiles within each subgroup showed a fairly stable pattern over time.
Conclusion: Fecal VOC profiles of infants with NEC could firmly be discriminated from controls and sepsis, two to three days prior to onset of clinical symptoms. Microbiota profiles of NEC subjects differed from controls and sepsis already up to five days prior to NEC. Our observations suggest that microbiota profiling might select those neonates at risk for development of NEC. VOC-profiling has potential as non-invasive, predictive test for the onset of NEC.

Colorectal cancer resections in the oldest old between 2011 and 2013 in the Netherlands

N.M. Verweij[1], A.H.W. Schiphorst[1], A. Pronk[1], M.E. Hamaker[2], [1]Dept of Surgery, and [2]Dept of Geriatric Medicine, Diakonessenhuis, Utrecht, The Netherlands

Introduction: There is a growing number of elderly colon- and rectal cancer patients due to increasing life expectancy and ageing of the population. The purpose of this study was to compare the outcome of colorectal surgical resections in the oldest old (≥85 years old), elderly (70-84 years old) and younger patients (<70 years old). Methods: Data from the Dutch Surgical Colorectal Audit (DSCA) – a nationwide registry of all elective and emergency resections for colon- and rectal cancer in the Netherlands – for 2011-2013, were analysed. Results: Of the 27579 registered patients, 12847 (47%) patients were aged <70 years, 12714 (46%) were between 70 and 84 years old and the remaining 2018 (7%) of the patients were aged ≥ 85 years. The oldest old had higher ASA-scores, with an ASA 3 or higher in 46% (vs. 13% of the younger patients and 30% of the elderly, p<0.001). Cardiopulmonary comorbidity was seen in 47% of the oldest old patients, in 35% of the elderly and in 15% of the younger patients. Within the younger patients, the majority of resections (35%) were performed for stage 3 tumours while 14% had a stadium 4 tumour. The oldest old group received resections for mainly stadium 2 tumours (44%), stadium 4 tumour resections were performed in 7%. Laparoscopic resections were performed in 52% of the younger patients, 49% of the elderly and in 40% of the oldest old (p<0.001). There were more emergency resections in the oldest old group (22% vs. 14% of both younger patients and elderly, p<0.001). Postoperative complication rate was significantly higher in the oldest old and elderly (41% and 34% respectively, vs 29% in younger patients, p<0.001). Of these, surgical complication rates were similar for all age groups (18-19%). However, cardiopulmonary complications rates rose rapidly with age: 13% in younger patients, 25% in elderly and 40% for the oldest old.

Postoperative mortality rates (within 30 days of surgery) were the highest in the oldest old (10% vs. 4% in the elderly and 1% in the younger patients, p<0.001). Most postoperative deaths occurred in patients experiencing postoperative complications (87%).

Conclusion: In this study of 27579 patients undergoing colorectal surgery, including more than 2000 of the oldest old, we found that cardiopulmonary complications and mortality rates are much higher in the oldest old when compared to their younger counterparts, while the rate of surgical complications were quite similar. Strategies aimed at optimizing the patients' health status prior to surgery and tailoring of care to prevent cardiopulmonary complications could improve feasibility and outcome of colorectal surgery for these vulnerable patients.

MLDS VOORDRACHT: Differential induction of mucosal tolerance in the small and large intestine

S. Veenbergen[1], L.A. van Berkel[1], M. Fleur du Pré[1], J. He[2], Y. Simons-Oosterhuis[1], F. Luk[1], A.M. Mowat[3], B.L. Kelsall[2], J.N. Samsom, [1]Dept. of Pediatric Gastroenterology, Erasmus Medical Center - Sophia Children's Hospital, Rotterdam, The Netherlands, [2]Mucosal Immunobiology Section, Laboratory of Molecular Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, United States of America, [3]Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom

Mucosal tolerance to harmless antigens requires dendritic cells (DC) that sample these antigens and migrate into draining lymph nodes to activate naïve T cells. We previously demonstrated that the small and large intestine are drained by different lymph nodes. While T cell priming to orally applied ovalbumin (OVA) preferentially occurs in the mesenteric lymph nodes (MLN), presentation of rectally applied antigen to naïve T cells exclusively occurs in the iliac lymph nodes (ILN). Importantly, de novoinduced Foxp3+ Treg cells were detected after antigen delivery by both routes and were essential for the induction of tolerance. Here, we investigated whether distinct locally adapted regulatory mechanisms maintain tolerance in the small and large intestine. At steady state, the ILN-derived DC comprised two main DC subsets, CD103+CD11b- and CD103-CD11b+ DCs. The CD103+CD11b+ DCs known to be present in the MLN was strikingly absent in ILN. Rectal antigen administration was associated with an increase in CD103-CD11b+ and CD103+CD11b- DCs in the ILN, while CD103+CD11b+ and CD103+CD11b- DCs were the major migratory DC populations in the MLN after OVA feeding. Importantly, CCR7 was expressed by all these DC populations consistent with migration from the intestine. Interestingly, Batf3-deficient mice specifically lacking CD103+CD11b- DCs displayed a normally suppressed delayed-type hypersensitivity response after colonic OVA administration, demonstrating that CD103+CD11b- DCs are dispensable for tolerance induction in the large intestine. In agreement, ILN-derived CD11c+ DCs from Batf3-deficient mice were effective in driving TGFβ-mediated Foxp3+ Treg differentiation in vitro. Taken together, our data reveals that distinct sites and DC populations drive small intestinal and colonic tolerance.

MLDS VOORDRACHT: Epithelial to mesenchymal transition is not a factor in biliary atresia related liver fibrosis

C.M.G. Keyzer-Dekker[1], R.C. Lind[1], J.F. Kuebler[1], C. Petersen[1], M. Davenport[1], J.B.F. Hulscher[1], [1]University Medical Center Groningen, Groningen, The Netherlands

Background: Epithelial to mesenchymal transition (EMT) has been suggested to be an important factor in the development of liver fibrosis. There is still much unclear, however, about the role of EMT in biliary atresia (BA). BA is an inflammatory obliterative cholangiopathy which develops immediately around birth. Liver fibroses develops quickly, necessitating liver transplantation in ~70% of patients. We analyzed the presence of EMT in a murine model of BA and in liver biopsies of BA patients, and correlated these findings with clinical outcomes. Methods: We used both an animal model and human material. The murine Rhesus Rotavirus (RRV) induced model of BA was used. Pups (RRV and control) were sacrificed at 7 and 14 days after birth. We used immunohistochemistry (IHC) and rtPCR to investigate CK19, α-SMA, E-Cadherin, S100A4 and collagen type 1. Human liver biopsies of BA patients obtained during Kasai portoenterostomy were also analyzed using IHC. Results: In the RRV group CK19 staining of bile ducts was absent to weak, which was significantly different compared with the control groups at both time points ($p = 0.009$, $p = 0.003$). Although expression of α-SMA was present in portal tracts of healthy mice, there was greater expansion of α-SMA staining in the RRV group ($p < 0.001$). Portal staining of Collagen type I was pronounced in the RRV group ($p = 0.02$). E-Cadherin staining was moderate/strong in the RRV group versus weak/moderate in the control group ($p = 0.03$). rtPCR analysis showed an increase in CK7, CK19, E-Cadherin and S100A4 in 14 days old RRV mice when compared with 7 days old RRV mice. Liver biopsies were also obtained from 11 human BA patients. Median age at time of Kasai was 53 days. 25% of patients already had cirrhosis. CK7 and CK19 staining were weak in five patients, moderate in two, and strong in three patients. α-SMA portal and lobular expression was evaluated as none or weak in the majority of patients. There was no correlation between grade of liver fibrosis and CK7, CK19 or α-SMA expression. Age at Kasai was correlated to CK7 and CK19 expression: the older the patient the greater CK7 and CK19 expression ($r = 0.6$, $p= 0.08$). None of the markers were correlated to clearance of jaundice after Kasai.
Conclusion: This study shows that in murine model for BA there is an increase in both epithelial and mesenchymal markers. In liver biopsies of BA patients we demonstrated an increase in epithelial markers, whilst mesenchymal markers were not increased. There was no association between any of the markers and clinical outcome. This implies that EMT is not a factor BA related liver fibrosis.

Complications of botulinum toxin injections for treatment of esophageal motility disorders

F.B. van Hoeij[1], J.E. Pandolfino[2], J.M. Sternbach[2], S. Roman[3], J.F. Tack[4], A.J.P.M. Smout[1], A.J. Bredenoord[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands, [2]Dept of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, United States of America, [3]Dept of Physiology, Hospices Civils de Lyon, Lyon 1 University, Lyon, France, [4]Dept of Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium

Botulinum toxin (botox) injection in the lower esophageal sphincter (LES) or esophageal body is considered an effective and low-risk procedure for the short-term relief of symptoms in achalasia and spastic esophageal motility disorders. Therefore, endoscopic botox injection is mainly offered to elderly, medically high-risk patients as an alternative to surgical or endoscopic treatment. Besides case-reports, no systematic analysis of risks and complications of botox injections is available. The aim of this study is to inventory the occurrence of procedure-related complications after esophageal botox injections in a large, multi-center cohort of patients. We analyzed the records of all patients undergoing botox injection therapy for esophageal motility disorders at four tertiary referral hospitals in Europe and North America between 2008 and 2014. Complications were assigned grades according to the Clavien-Dindo classification. In total, 465 botox injection sessions were performed in 324 patients (mean age 63 years, range 18-98). The main indications were achalasia (176 patients; 54%), distal esophageal spasm, nutcracker esophagus or jackhammer esophagus (129 patients; 40%) and EGJ outflow obstruction (19 patients; 6%). Of the 176 of patients with achalasia, the distribution based on manometric subtype was: type I in 7% of patients, type II in 14%, type III in 26% and an undefined type of achalasia (by conventional manometry) in 53% of patients. Injections were delivered to the LES (23%), the body of the esophagus (26%) or a combination of both (51%). In nearly all patients 100 IU of botulinum toxin were injected, equally distributed over 4 to 10 injections. A total of 39 mild complications (Clavien-Dindo grade I) were reported by 32 patients (9.9%), consisting of chest pain or heartburn in 17 patients, epigastric discomfort in 7 patients, lightheadedness or nausea in 6 patients and other mild complications in 9 patients (fatigue, sore throat, difficulty breathing or acute urinary retention). No ulceration, perforation, pneumothorax, abscess or heart block was reported. One 64-year old patient died after developing acute mediastinitis (Clavien-Dindo grade V) following botox injections in the body of the esophagus for treatment of a spastic esophageal motility disorder. Early treatment failure was reported after 42 (9%) procedures. In four patients, the procedure was aborted due to restlessness, in one patient due to stasis of food.
Conclusion: Esophageal botox injection for the treatment of esophageal motility disorders is an off-label indication and should not be considered a completely safe treatment option, as at least one lethal complication has occurred.

Esophagogastric junction distensibility in the management of achalasia patients: relation to treatment outcome

F.G.M. Smeets[1,2], A.A.M. Masclee[1,2], D. Keszthelyi[1,2], E.T.T.L. Tjwa[3], J.M. Conchillo[1,2], [1]Division of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [2]NUTRIM, School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, [3]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands

Achalasia is characterized by a functional obstruction at the esophagogastric junction (EGJ). The functional luminal imaging probe (EndoFLIP) is a new method to assess EGJ distensibility. In a homogeneous group of newly diagnosed achalasia patients treated with pneumatic dilation, we aimed (1) to determine whether assessment of EGJ distensibility has added value in the management of achalasia patients, and (2) to evaluate whether EGJ distensibility differs between achalasia subtypes. Twenty-six newly diagnosed achalasia patients (14 males, mean age 52 years) were treated by graded PD (30-mm and 35-mm) separated by one week. EGJ distensibility was measured with the EndoFLIP technique before and after 30-mm PD. Good clinical outcome was defined as an Eckardt score <4 at one-year follow-up. Fifteen healthy controls (5 males, mean age 23 years) underwent an EndoFLIP measurement as control group. Newly diagnosed achalasia patients had reduced EGJ distensibility compared to healthy controls (50ml: 0.9 (0.7-1.5) vs. 3.4 (2.7-4.2) mm2/mmHg, p<0.01). The cutoff value for normality (10th percentile) of EGJ distensibility was 2.1 mm2/mmHg and 96% of newly diagnosed achalasia patients had an EGJ distensibility below this cutoff value prior to treatment. Nine patients had type I (35%) and 17 patients (65%) had type II achalasia according to the Chicago classification. Type II patients had a lower EGJ distensibility before treatment compared to type I patients (50ml: 0.8 (0.7-1.1) vs. 1.5 (0.9-1.9) mm^2/mmHg, p<0.05). Moreover, EGJ resting pressure was higher in type II compared to type I patients (49 (38-72) vs. 34 (23-46) mmHg, p<0.05). Treatment of newly diagnosed achalasia patients by single pneumatic dilation improved EGJ distensibility (50ml: from 0.9 (0.7-1.5) to 4.2 (3.0-5.7) mm^2/mmHg, p<0.01). Clinical outcome at one year follow-up was available for 22 patients. Sixteen patients (73%) had a good clinical outcome (i.e. Eckardt score <4), and no differences were found in EGJ distensibility both before and immediately after pneumatic dilation, between patients with a good or poor clinical outcome at one year follow-up. Only one out of six patients with a poor clinical treatment outcome had an abnormal EGJ distensibility (below 10th percentile) directly after the 30-mm pneumatic dilation.
Conclusions: Assessment of EGJ distensibility with the EndoFLIP technique is able to demonstrate the functional EGJ obstruction in newly diagnosed achalasia patients and EGJ distensibility differs between achalasia subtypes. Treatment by pneumatic dilation improves EGJ distensibility, but post-dilation EGJ distensibility did not predict clinical outcome at one-year follow-up.

Pediatric Achalasia in The Netherlands: diagnosis, management, follow-up and quality of life

R. Vrijlandt[1], M. Smits[1], M. van Lennep[1], M. Benninga[1], R. Houwen[2], F. Kokke[2], D. van der Zee[3], H. Escher[4], A. van den Neucker[5], T. de Meij[6], F. Bodewes[7], J. Schweizer[8], G. Damen[9], M. van Wijk[1], [1]Dept of Pediatric Gastroenterology, Emma Child's Hospital, Academic Medical Center, Amsterdam, [2]Dept of Pediatric Gastroenterology, Wilhemina Children's Hospital, University Medical Center Utrecht, Utrecht, [3]Dept of Pediatric Surgery, University Medical Center Utrecht, Utrecht, [4]Dept of Pediatric Gastroenterology, Sophia Children's Hospital, Erasmus Medical Center, Rotterdam, [5]Dept of Pediatric Gastroenterology, Maastricht University Medical Center, Maastricht, [6]Dept of Pediatric Gastroenterology, VU Medical Center, Amsterdam, [7]Dept of Pediatric Gastroenterology, Beatrix Children's Hospital, University Medical Center Groningen, Groningen, [8]Dept of Pediatric Gastroenterology, Willem-Alexander Child's hospital, University Medical Center Leiden, Leiden, [9]Dept of Pediatric Gastroenterology, Radboud University Medical Center, Nijmegen, The Netherlands*

Achalasia is a rare oesophageal motility disorder in childhood. Data on prevalence, incidence, presenting symptoms, treatment success, follow up and quality of life are scarce. Medical charts of all Dutch pediatric achalasia patients (<18yrs) diagnosed between January 1990 and December 2013, were retrospectively reviewed for data on presenting symptoms, treatment and relapses. Prospectively, severity of achalasia symptoms was assessed using the Eckardt score (suggestive for achalasia when >3) and the Reflux Disease Questionnaire (RDQ, suggestive for gastro-oesophageal reflux disease (GORD) when ≥mild heartburn/regurgitation occurred ≥2 days a week). Disease specific QoL was assessed with the Achalasia DS-QoL (when <18yr at time of study, 0= worst 100=best) or HRQoL (≥18yr, 0= worst 100=best). General QoL was measured with the KIDSCREEN-52 (<18yr, T-values over 10 domains relative to healthy norm, higher value suggests better QoL) or the SF-36 (≥18yr, 8 domains, 0= worst 100=best QoL per domain) and compared to healthy population norms. Eighty-seven (87) patients (mean age 11.44 +/- 3.43 years, 60% male) were included. Mean incidence was 0.10/100,000/year (range 0.03-0.21). Prevalence in 2012 was 0.90/100,000. Initial treatment (IT) was pneumatic balloon dilation (PD) in 68 (79%) patients and Heller's Myotomy (HM) in 18 (21%) patients. Complications of IT occurred more after HM compared to PD (10/18 vs 1/68 P<0.0001, n=4 perforations). Similarly, complication rate was higher for HM after relapse treatments (20/22 vs 3/135, P<0.0001, n=7 perforations). Re-treatment was required more often after initial PD (n=59, 88%) compared to initial HM (n=4, 22%), P<0.0001. Four years after IT 46% of patients <18 years were lost to follow up. Sixty-three of 87 (72%) patients were prospectively reached. Median Eckardt score was 3 (IQR 2-5) with 30 patients (47.6%) having a positive score. RDQ scores were higher for HM vs PD (1.71 (0.96 – 2.90) vs 0.58 (0 – 1.56), P=0.005). Overall adult HR-QoL score was 61.3 (45.1-80.0). General QoL (SF-36) in adults (n=52) was lower compared to healthy population norms for 7/8 domains. Pediatric achalasia DS-QoL score was 17.5 (8-29). Self-reported QoL (KIDSCREEN-52, n=20) was similar to population norms.

Conclusion: Pediatric achalasia is rare in the Netherlands. High relapse rates after predominant treatment PD indicate the need for prospective studies comparing HM and PD. Our study shows persistent symptoms after discharge and declined QoL in adulthood. Regarding the long term risks of uncontrolled achalasia, there is a need for a standardized follow up regime to improve clinical outcome and transfer to adult care.

Esophageal epithelial barrier function in Non-Erosive Reflux Disease (NERD) patients: a barrier defect?

N.F. Rinsma[1], R.M. Farré[2], F.J. Troost[1], M. Elizalde[1], A.A. Masclee[1], J.M. Conchillo[1], [1]Division of Gastroenterology and Hepatology, NUTRIM, Maastricht University Medical Center, Maastricht, The Netherlands, [2]Translational Research Center for Gastrointestinal Disorders, Catholic University Leuven, Belgium - Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, (Ciberehd), Instituto de Salud Carlos III, Spain

Background: Despite the absence of visible mucosal damage in patients with non-erosive reflux disease (NERD), we hypothesized that the esophageal epithelial barrier is functionally impaired and more vulnerable in response to acid exposure. We therefore investigated esophageal epithelial barrier function in NERD patients in comparison to patients with active erosive esophagitis (EE) and healthy controls (HC), both in the basal state and in response to acid exposure. Methods: 20 patients with chronic GERD - 10 patients with EE (mean age 63) and 10 with NERD (mean age 47) - and 10 HCs (mean age 35) were enrolled. NERD patients were well characterized with 24-h pH-impedance showing abnormal acid exposure (pH<4, >4% of time) and/or positive symptom association probability and no history of esophagitis on previous endoscopy. Before endoscopy, GERD patients discontinued PPI therapy for 7 days. Six esophageal biopsies from macroscopically normal mucosa were obtained at 5 cm above the gastroesophageal junction and directly transferred to a Ussing chamber system. After an equilibration period (40 min), base transepithelial electrical resistance (TEER) was assessed. Half of the biopsies were exposed to an acidic solution (pH1 – for 30 min). Changes in TEER during acid exposure and recovery were analyzed relative to base TEER. Permeation to the paracellular permeation marker fluorescein (375 DA - 1 mg/ml) was assessed in non-exposed biopsies for 120 minutes. Results: TEER was significantly lower in EE patients when compared to NERD patients (139±10 â„¦ vs. 175±10 â„¦, p<0.05) and controls (186±12 â„¦, p<0.01), however no difference was found between NERD patients and HCs. Ex vivo acid exposure provoked a comparable reduction in TEER in all groups (EE: -48±3 %, NERD: -40±5 %, HC: -50±6 % relative to base TEER, ns). Recovery of TEER towards base after acid exposure was more pronounced in NERD patients when compared to EE (AUC: 389 [347-400] vs. 310 [280-366], p<0.05). Mucosal permeability to fluorescein in non-exposed biopsies was not different between groups, indicating that only permeability to ions is increased in EE patients.
Conclusion: Esophageal epithelial barrier function in NERD patients evaluated ex vivo in Ussing chambers is not impaired. Therefore, other mechanisms may account for the high symptom burden in NERD patients.

Brain processing of rectal sensation in children with functional defecation disorders and healthy controls.

I.J.N. Koppen[1], S.M. Mugie[1], M.M. van den Berg[2], P.F.C. Groot[3], L. Reneman[3], A.J. Nederveen[3], M.B. de Ruiter[3], M.A. Benninga[1], [1]Dept of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Emma Children's Hospital, Amsterdam, [2]Dept of Pediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, [3]Dept of Radiology, Academic Medical Center, Amsterdam, The Netherlands

The pathophysiology underlying functional defecation disorders (FDD) in children is poorly understood. A loss of sensation of urge to defecate is often reported by both children with functional constipation (FC) and functional nonretentive fecal incontinence (FNRFI). We suggest that the loss of rectal sensation is related to impaired brain processing of visceral sensory stimuli. Brain imaging data are lacking in both adults and children with FDD. The aim of this study is to investigate the cerebral activity in response to rectal distension in children with FDD (FC and FNRFI) and in healthy controls (HCs).
Methods: 15 patients with FC (range 12-18 years), 10 patients with FNRFI (range 12-17 years) and 15 HCs (range 18-21 years) participated. A stepwise pressure-controlled distension protocol was used to determine the pressure threshold for urge sensation prior to the fMRI scan. During acquisition of blood oxygenation level-dependent (BOLD) fMRI, subjects received 2 sessions of 5 stimulations consisting of repetitions of 30 seconds of rectal stimulation with previous defined threshold pressures, followed by 30 seconds of rest. Images were acquired on a 3Tesla MRI scanner with an 8-channel SENSE head receive coil. Analyses were performed using SPM8 in Matlab, thresholded at $p<0.001$. Cerebral activation was defined as BOLD increase during rectal distension and cerebral deactivation as BOLD decrease during rectal distension. Results: FC and FNRFI patients had higher thresholds for urgency than HCs ($p<0.000$). The groups were differentiated by both activated and deactivated regions in response to rectal distension. FC patients showed activation in the anterior cingulate cortex, dorsolateral prefrontal cortex, inferior parietal lobule and putamen during rectal distension. No activations were observed in controls and FNRFI patients. FNRFI patients showed significant deactivation in the hippocampus, parahippocampal gyrus, fusiform gyrus, lingual gyrus, posterior parietal cortex and precentral gyrus. In HCs, deactivated areas were detected in the hippocampus, amygdala, fusiform gyrus, insula, thalamus, precuneus, and primary somatosensory cortex. In contrast, no regions with significant deactivation were detected in FC patients.
Conclusion: Children with FC differ from children with FNRFI and healthy controls, with respect to patterns of cerebral activation and deactivation during rectal distension, suggesting different neural processing of rectal urge sensation in brain regions previously implicated in adult studies using visceral pain stimuli. This confirms that FNRFI is a different clinical entity compared to FC.

Chait Cecostomy Catheter in adults for chronic obstipation: substantial morbidity and moderate functional results

A.K.E. Elfrink[1], B. van den Heuvel[1], M. Ankersmit[1], P.F. Vollebregt[2], R.F. Felt-Bersma[2], J.B. Tuynman[1], W.J.H.J. Meijerink[1], [1]Dept of Surgery, and [2]Dept of Gastroenterology, VU University Medical Center, Amsterdam, The Netherlands

Patients with slow transit constipation are faced with inadequate therapeutic interventions with a substantial impact on quality of life. Conservative therapy including lifestyle changes, medication or behavioural therapy fail to adequately relieve symptoms in the majority of patients. Retrograde rectal lavage as additional therapy has only limited success. In children a Chait Cecostomy Catheter (CCC) for antegrade flushing of the colon has proven to be effective restoring quality of life. Morbidity rates are low and reinterventions are uncommon as reported in these studies. For adults the appendical cecostomy used for antegrade flushing has shown to be associated with relative high morbidity rates and a high rate reinterventions. Other surgical options including subtotal colectomy and ileostomy have substantial more impact. Treatment of patients with chronic constipation without outlet obstruction with a CCC could be a good alternative as a first surgical step up procedure. Aim of this study was to evaluate feasibility, morbidity and functional outcome CCC as treatment for chronic constipation in adults. A prospective cohort of 18 patients, mean age 45 (range 23 – 68), diagnosed with slow transit constipation treated with a CCC, was evaluated. All patients failed conservative treatments as mentioned above. Median follow up was 10 months. Median hospital stay was 2.3 days (SD ± 2.7 days). Seven of 18 (39%) patients had complications within 30 days, for whom hospital readmission was needed. One had a serious complication requiring multiple reinterventions and ICU stay. Wound or peritoneal infection was reported in four patients. At 2 years follow-up 8 patients had a reintervention as result of luxation or leakage of the CCC. Four of these patients needed a colon resection due to other complications caused by the CCC. Eight of the 18 (44%) patients have good functional results of the CCC two years after placement. ConclusionsThe 30-day morbidity after laparoscopic placement of the CCC is relatively high. Although the short-term results were promising, after two year follow up the surgical and functional outcome was disappointing. Half of the patients needed a reintervention after placement of the CCC. Furthermore, in 40% of patients the CCC did not improve functional outcome.

Therefore we conclude that the CCC catheter for chronic idiopathic constipation may not be a good first surgical approach and alternatives including ileostomy should be discussed.

Utilising high-resolution colonic manometry to quantify dysmotility in children with slow transit constipation

S. Kuizenga-Wessel[1], I.J.N. Koppen[1], M.A. Benninga[1], L. Wiklendt[2], P.G. Dinning[2,3], [1]Dept of Pediatric Gastroenterology and Nutrition, Academic Medical Center, Emma Children's Hospital, Amsterdam, The Netherlands, [2]Human Physiology, Flinders University, Adelaide, SA, Australia, [3]Gastroenterology and Surgery, Flinders Medical Centre, Adelaide, SA, Australia

Slow transit constipation (STC) is associated with colonic motor abnormalities in both adults and children. Utilising high-resolution colonic manometry we have recently quantified the motor abnormalities in STC adults. Our aim in this study was to quantify the colonic motor abnormalities in children with STC and compare these data with STC adults to determine if the manometric signatures of abnormality were similar between the two groups. In 11 children (2 males; mean age 15.4 years; range 9-19 years) with marker study proven STC, after an overnight fast, a 36 sensors (spaced at 1.5cm intervals) water perfused manometry catheter was colonoscopically placed and the tip clipped in the region of the splenic flexure. Manometric recordings were taken for two hours pre and post a 700cKal meal. These data were compared to 12 healthy controls (5 men; median age 51 years; range 27-69 yrs) and 14 patients (2 men; median age 52 years; range 24-76 years) with scintigraphically defined STC. Data in adults were recorded with a 72 sensors (spaced at 1cm intervals) fibre-optic manometry catheter. Spectral analysis was used to determine any dominant frequency of pressure events prior to or after a meal. Propagating motor patterns were defined as i) cyclic (at 2-6/min); ii) short single motor patterns (<1 per min; extent 7 ± 2 cm) , iii) long single motor patterns (<1 per min; amplitude 48 ± 13 mmHg; extent 42 ± 9 cm); and iv) high amplitude propagating sequences (HAPS). The data are expressed as delta values (postprandial count – basal count). In healthy controls (HC) and adult STC patients, 2-3 cpm activity was prominent prior to and after a meal. This activity was not evident in children. The change in the count of long (HC, 0.7 ± 0.4; STC adults, 1.7 ± 1.1; children, 1.7 ± 0.6 / 2 hr) and short (HC, -1.5 ± 2.1; STC adults, 1.9 ± 2.4; children, 0.5 ± 0.6 / 2 hr) single propagating motor patterns did not differ between the 3 groups. In HC there was a significant increase in the count of retrograde cyclic motor patterns and this was not seen in either patient group (HC, 59.9 ± 25.4; STC adults, 4.9 ± 1.5; children, 2.4 ± 0.8 / 2 hr; ANOVA $P < 0.0001$). HAPS were not seen prior to the meal and after the meal were only identified in 5/12 HC, 1/14 adult STC and 0/11 children.

Conclusion: Neither patient group responded to a high calorie meal. The number of propagating events did not differ between STC adults and children, however in children the normal 2-3 cpm slow wave activity was not evident. The failed meal response and lack of prominent slow wave activity may indicate potential intrinsic and extrinsic abnormalities in children with severe constipation.

Yoga therapy for children with functional abdominal pain disorders; a randomized controlled trial

J.J. Korterink[1,2], L. Ockeloen[2], M. Hilbink[3], M.A. Benninga[2], J.M. Deckers-Kocken[4], [1]Dept of Pediatrics, Jeroen Bosch Hospital, 's Hertogenbosch, [2]Dept of Pediatric Gastroenterology and Nutrition, Emma Children's Hospital, Academic Medical Center, Amsterdam, [3]Jeroen Bosch Academy, Jeroen Bosch Hospital, 's Hertogenbosch, [4]Kinderbuik&co, Bilthoven, The Netherlands

Psychological distress is strongly associated with abdominal pain in children and plays a role in the development of abdominal pain related-functional gastronintestinal disorders (AP-FGIDs). Yoga therapy has shown its efficacy in stressmanagement and has been recommended as intervention in adults with irritable bowel syndrome (IBS). The aim of this study is to compare the effect of yoga therapy and standard care on the frequency and intensity of pain and quality of life (QoL) in children with AP-FGIDs.Sixty-nine patients, aged 8-18 years, with an AP-FGID, were randomized to either standard medical care complemented with yoga therapy (YT) or standard medical care alone (SMC). Hatha yoga was given once a week for 10 weeks. Sessions of 1.5h each were a mixture of classical yoga poses and relaxation exercises. SMC consisted of education, reassurance, dietary advice and fibers/mebeverine if considered necessary. Pain intensity (0-5) and pain frequency (0-4) were scored in a pain diary and QoL was measured with the KIDSCREEN-27 (5 domains). Patients were followed up for twelve months. Treatment response was defined as a 50% reduction of weekly pain scores. Between-group differences were analyzed with generalized estimating equations.From base to 1 year follow-up, mean pain intensity scores decreased from 17 to 8 ($p<0.01$) and from 16 to 12 ($p=0.83$) in the YT and SCM group, respectively. Mean pain frequency scores decreased from 16 to 8 ($p<0.01$) in the YT group and from 16 to 14 in the SMC group ($p=0.40$). However, YT was not significant superior to SMC. A trend towards a lower pain intensity in the YT group compared to the SMC group was found in children aged 13-18 years ($p=0.06$). At 1 year follow up, treatment response was accomplished in 58% of the YT group and 29% of the control group ($p=0.01$). Although children in the YT group and their parents reported larger improvement in QoL compared to the SMC group, difference proved to be non-significant ($p>0.05$ for all domains). A trend was reported for 'psychological well-being' in favor of YT ($p=0.06$). YT was significantly more effective in the reduction of children who reported monthly school absence at 1 year follow up, compared to SMC, from 55% to 7% after YT and from 65% to 33% after SMC ($p=0.03$).

Conclusion: At one year follow up, yoga therapy in addition to standard medical care was significant superior to SMC according to treatment success and reduction in school absence. However, YT was not more effective in the improvement of abdominal pain intensity, frequency and quality of life.

Laparoscopic ventral recto(vagino)pexy is a safe surgical procedure for elderly patients with a rectal prolapse or rectocele

S.C.N. Plasschaert[1], E.J.R. de Graaf[1], M.M.M. Bruijninckx[1], M. Vermaas[1], P.G. Doornebosch[1], [1]Dept of Surgery, IJsselland Hospital, Capelle a/d IJssel, The Netherlands

Full thickness rectal prolapse and associated symptoms is common in the elderly and can be debilitating. Several procedures have been described to treat this condition. Because of expected morbidity and mortality following transabdominal procedures, in the frail, elderly patient a perineal procedure is often chosen. However, the safety of this latter is matter of debate in current literature. As an alternative, a laparoscopic rectovaginopexy (LVP) is propagated. The purpose of this study is to investigate the safety of LVP in the elderly.Data from LVP surgery, performed in one general hospital, in young patients (<70 years, group I) and older patients (≥70 years, group II) was analysed retrospectively. Mean duration of the surgical procedure, mean amount of blood loss during surgery, conversion, morbidity (according to the Clavien-Dindo classification), mortality and the length of hospital stay were analysed.Between 2003 and 2014 a total of 115 LVP were performed (group I: 80 patients, group II: 35 patients). All procedures were performed under general anaesthesia with antibiotic prophylaxis. Group I had more patients with a higher BMI (p=0.01). In group II were more patients with a higher ASA score (p=0.00). Mean duration of the surgical procedure was longer in group II (116 minutes, range 60-180min) compared to group I (90 min, range 49-232 min) (p=0.01). Mean amount of blood loss was comparable in both groups (20cc SD 87cc vs. 30cc SD 163cc). There was one conversion in group II, none in group I (p=0.30). In group I were 12 complications in total (grade I:8, grade II:1, grade III:3), whereas there were 8 complications in total in group II: (grade I: 2, grade II: 1, grade IIIa+b: 4, grade IVa+b:1). Age proved not to be a predictor regarding morbidity (OR 1.57; 95% CI 0.541-4.529, p=0.41). There was no mortality in both groups. The median length of hospital stay was comparable for both groups (4vs 6 days, p=0.112).
Conclusions: A LVP surgical procedure is a safe procedure, even in the frail, elderly patient. Therefore LVP surgery should be the first choice of treatment in patients with a rectal prolapse or rectocele.

Evaluation of the proximal serrated polyp detection rate as a valuable colonoscopy quality parameter

J.E.G. IJspeert[1], S.C. van Doorn[1], B.A.J. Bastiaansen[1,2], P. Fockens[1,2], E. Dekker[1,2], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [2]Procolo center for colonoscopy, Bergman Clinics, Amsterdam, The Netherlands

The adenoma detection rate (ADR) is currently the most important surrogate quality parameter in the context of CRC prevention. However, also serrated polyps (SPs) are precursors of CRC. Large prospective studies comparing the detection rate of SPs among endoscopists in an era of awareness about the malignant potential of SPs have not yet been performed. We aimed to compare the proximal SP detection rate (PSPDR) and the detection rate of clinically relevant SPs (RSPDR) among endoscopists and to analyze the association between these parameters and the ADR. Colonoscopy data were retrieved in one expert center between January 2011 and June 2014 using a structured reporting system, enabling prospective and automatic quality assessment. Endoscopists who performed at least 50 colonoscopies within the timeframe were included for analysis. Multivariate logistic regression, adjusted for patient age, gender, quality of bowel preparation and colonoscopy indication, was used to compare the ADR, PSPDR and RSPDR among endoscopists. The association between these parameters was calculated using the Pearson's r correlation coefficient. Proximal colon was defined as proximal to the descending colon. Clinically relevant SPs were defined as all SPs, except for hyperplastic polyps (HPs) ≤5mm in the rectosigmoid. All lesions were assessed by an expert pathologist. In total 1485 adenomas and 841 SPs (582 HPs, 253 sessile serrated adenomas/polyps (SSA/Ps) and 6 traditional serrated adenomas) were retrieved in 2123 colonoscopies. Of all SPs, 304 (36.1%) were located in the proximal colon and 452 (53.7%) were regarded clinically relevant. Sixteen endoscopists were included for analysis. The PSPDR ranged from 2.8-18.6% (median 9.7%). Adjusted for confounders, the odds ratio for the detection of at least one proximal SP compared to the highest detector ranged from 0.78 (95% CI 0.41-1.51) to 0.12 (CI 0.03-0.54). The PSPDR was highly correlated with the RSPDR (0.871, $p<0.001$), ranging from 4.3-20.9% (median 12.9%). The PSPDR moderately correlated with the ADR (0.526, $p=0.036$), ranging from 23.9-49.2% (median 36.2%). The 25% highest clinically relevant SP detectors showed a significant higher detection rate for all SP subcategories. Most pronounced difference was found for the detection rate of at least one large SSA/P (2.2% vs 0.6%, OR 3.84 ($p<0.01$, CI 1.61-9.18)).

Conclusions: The PSPDR is widely variable among endoscopists, strongly correlated to the RSPDR and moderately correlated to the ADR. Measurement of the PSPDR, alongside the ADR, seems valuable and future research should determine the association between endoscopists' PSPDR and the risk of interval cancer.

Development and validation of a classification system for optical diagnosis of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps

J.E.G. IJspeert[1], B.A.J. Bastiaansen[1], M.E. van Leerdam[2], J. Wang[3], S. van Eeden[4], S. Sanduleanu[5], E.J. Schoon[6], T. Bisseling[7], M.C. Spaander[8], N. van Lelyveld[9], M. Bigirwamungu-Bargeman[10], G.A. Meijer[11], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, [3]Dept of Clinical Epidemiology, Biostatistics and Bioinformatics, and [4]Dept of Pathology, Academic Medical Center, Amsterdam, [2]Dept of Gastroenterology and Hepatology, Netherlands Cancer Institute, Amsterdam, [5]Dept of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht, [6]Dept of Gastroenterology and Hepatology, Catharina Hospital, Eindhoven, [7]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [8]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [9]Dept of Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, [10]Dept of Gastroenterology and Hepatology, Medical Spectrum Twente, Enschede, [11]Dept of Pathology, VU Medical Center, Amsterdam, The Netherlands

Accurate endoscopic differentiation would enable to resect and discard small and diminutive colonic lesions, thereby increasing cost-efficiency. Current classification systems based on Narrow Band Imaging (NBI), however, do not include neoplastic sessile serrated adenomas/polyps (SSA/Ps). We aimed to develop and validate a new classification method for endoscopic differentiation of adenomas (ADs), hyperplastic polyps (HPs) and SSA/Ps <10mm. We combined the NBI International Colorectal Endoscopic (NICE) classification and validated criteria for the differentiation of SSA/Ps to develop an integrative classification system. Ten consultant gastroenterologists, experienced with NBI and the NICE-criteria, evaluated and predicted lesion histology (including confidence level) of 45 colonic lesions (15 SSA/Ps, 15 HPs and 15 ADs), based on endoscopic images. Lesions were assessed before and after participation in a training of 20 minutes about the new classification system. After 6 months, the same endoscopists predicted lesion histology of a new set of 50 polyps, with a ratio of lesions that is comparable to daily practice (11 SSA/Ps, 16 HPs and 23 ADs). Performance of optical diagnosis was calculated with the histopathologic diagnosis as reference standard. All lesions were reviewed by two expert gastrointestinal pathologists. Both ADs and SSA/Ps were classified as neoplastic lesions. In the first validation phase, the pooled accuracy for optical diagnosis of lesions diagnosed with high confidence improved after training: 0.73 (95% CI 0.64-0.82) before vs 0.87 (CI 0.80-0.95, p<0.01) after training. Pooled accuracy increased from 0.83 (CI 0.75-0.91) to 0.93 (0.87-0.98, p = 0.02) for differentiation of SSA/Ps vs non-SSA/Ps and from 0.82 (CI 0.74-0.89) to 0.90 (CI 0.84-0.96, p<0.01) for differentiation of neoplastic lesions vs HPs. In the second validation phase, the pooled accuracy for optical diagnosis with high confidence was 0.84 (CI 0.81-0.88) for all lesions, 0.91 (0.88-0.94) for SSA/Ps and 0.89 (0.85-0.92) for neoplastic lesions. The pooled negative predictive value (NPV) with high confidence of diminutive neoplastic lesions was 0.91 (CI 0.83-0.96). Conclusions: We developed and validated the first integrative classification method for endoscopic differentiation of small and diminutive ADs, HPs and SSA/Ps. In a still image evaluation setting introduction of the WASP-classification showed a significant improvement of the accuracy of optical diagnosis overall as well as for SSA/Ps and neoplastic lesions in specific, which proved to be sustainable after 6 months. Future research is needed to validate this classification system during real-time colonoscopy.

Measuring gaze patterns during colonoscopy: a useful tool to measure colon inspection?

V.K. Dik[1], I.T.C. Hooge[2], M.G.H. Van Oijen[1,3], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Experimental Psychology and Helmholtz Institute, Utrecht University, Utrecht, [3]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Introduction: Considerable variation in adenoma detection rates has been shown between endoscopists, which at least partly may be explained by differences in extent of colon inspection. Eye tracking technology is an objective tool that may detect differences in quality of colon inspection between endoscopists. Aims & Methods: We investigated the feasibility of eye tracking technology during real-time, self-performed colonoscopies. Ten endoscopists each performed two procedures. A Tobii mobile eye tracking system was used consisting of light-weight eye tracking glasses, a pocket-sized recording assistant and infrared markers that register the right eye position at a sampling rate of 30 Hz. Data were used to determine the gaze time across four areas of interest (AOI) of the endoscopy monitor (upper, lower, left and right quadrant). To assess whether the measured gaze across the endoscopy monitor serves as a good measure for the gaze across the colonic surface we determined their correlation. In addition, we investigated whether these parameters depended on level of colonoscopy experience. Results: Gaze patterns were successfully measured in 18 of 20 procedures with only limited (3.9%) missing data. Endoscopists spent a mean of 790 milliseconds (range 676 – 981) per AOI before moving to another AOI (1.27 transitions per second, range 1.01 – 1.45). AOI to which endoscopists most frequently looked (transitions) were also the AIO to which they looked longest before moving to the next AIO (mean gaze time). The measured total gaze time per AOI correlated well with the time spent on the same area of the colonic surface (Pearson correlation coefficients ranging between 0.91 and 0.97). Endoscopists with more years of colonoscopy experience tended to have higher mean gaze times ($r = 0.52$, $p=0.06$) and demonstrated significantly higher percentages of overlap between the measured gaze position in the different AOI and the actual inspected area of the colonic surface ($r = 0.65$, $p = 0.02$).

Conclusions: The use of eye tracking technology to measure gaze patterns of endoscopists during real-time, self-performed colonoscopies is feasible and can be applied to measure and compare viewing behavior of individual endoscopists. Future studies should investigate whether differences in viewing behavior correlate with clinical relevant outcomes, in particular adenoma detection rate.

Colonoscopy with Robotic Steering and Automated Lumen Centralization Compared with Conventional Colonoscopy: Results of a Randomized In Vitro Pilot Study

H.J.M. Pullens[1,2], N. van der Stap[3,4], E.D. Rozeboom[3], M.P. Schwartz[1], F. van der Heijden[3], M.G.H. van Oijen[2,5], P.D. Siersema[2], I.A.M.J. Broeders[3,4], [1]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [2]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [3]Dept of Robotics and Mechatronics, University of Twente, Enschede, [4]Dept of Surgery, Meander Medical Center, Amersfoort, [5]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands

Background and aims: The steering mechanism of flexible endoscopes has been unchanged for many years, and is considered non-intuitive, non-ergonomic and has a long learning curve. We introduced a new platform for performing colonoscopy with robotic steering and automated lumen centralization (ALC), with the aim to study performance of this platform by both expert endoscopists and novices. Methods: We performed a randomized controlled crossover trial. Expert endoscopists (n=8) and novices (n=10) performed conventional colonoscopy and colonoscopy with robotic steering and ALC in a validated colon model with simulated polyps (n=21). Endpoints were cecal insertion time, number of detected polyps and subjective evaluation of the platform. Results: Novices intubated the cecum faster using robotic steering with ALC (median 8'56", interquartile range (IQR) 6'46"-16'34" vs. 11'47", IQR 8'19"-15'33", p=0.65), whereas experts were faster in intubating the cecum with conventional colonoscopy (2'9", IQR 1'13"-7'28" vs. 13'1", IQR 5'9"-16'54", p=0.12). Similarly, novices detected more polyps with robotic steering and ALC (88.1%, IQR 79.8-95.2% vs. 78.6%, IQR 75.0-91.7%, p=0.17), whereas experts detected more polyps during conventional colonoscopy (80.9%, IQR 76.2-85.7% vs. 69.0%, IQR 61.0-75.0%, p=0.03). All but one participant thought that robotic steering with ALC makes performing colonoscopy easier for novices. Novices were more positive about the new platform (p=0.023) than experts, experiencing an easier and faster introduction of the colonoscope compared with conventional colonoscopy.
Conclusions: Robotic steering with ALC allowed novices to intubate the cecum faster and to detect more simulated polyps in a colon model. Robotic steering with ALC was subjectively easier to learn for novices than conventional colonoscopy. This platform may be a next step towards a new way of performing colonoscopy.

Direct peroral cholangioscopic visualization can be helpful in differentiating benign and malign indeterminate bile duct lesions

A.B. de Vries[1], K.T. Buddingh[4], A.S.H. Gouw[2], V.B. Nieuwenhuijs[3], R.K. Weersma[1], [1]Dept of Gastroentrology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, [2]Dept of Pathology, University of Groningen, University Medical Center Groningen, Groningen, [3]Dept of Surgery, Isala, Zwolle, [4]Dept of Urology, Haga Ziekenhuis, Den Haag, The Netherlands

The assessment of indeterminate common bile duct lesions (IBL) as benign or malignant remains a challenging clinical problem, especially when conventional diagnostic modalities such as ERCPs, MRCPs and CTs are inconclusive. Single operator peroral cholangioscopy (POCS) is a technique that allows visualization and sampling of the larger bile ducts. Several studies have suggested POCS to be a promising diagnostic modality for IBL in this setting. The aim of the study was to investigate the diagnostic yield of POCS endoscopic appearance and targeted biopsies in the assessment of IBL. All patients receiving POCS for IBL between November 2007 and December 2013 were analysed retrospectively. Primary outcome was the presence of benign or malignant tissue in the surgical resection specimen. IBL in patients without surgery and not developing malignancy during follow-up were considered benign. Procedures consisted of an ERCP followed by POCS with the spyglass cholangioscope (Boston Scientific Netherlands) with the 'mother-baby' technique. Cholangioscopic assessment of the nature of the lesion was based on the presence of fibrotic appearance, neovascularisation and irregular and vulnerable aspect of the IBL. Sampling of the IBL was performed by POCS targeted biopsies (Spybite, Boston Scientific Netherlands). All POCS were performed by the same endoscopist. A total of 56 patients (36 males, median 59 year(IQR 43–66)) were included. Patients had received ERCP (>90%) or CT/MRCP (>70%) prior to POCS procedure that were inconclusive. Adverse events after POCS were seen in 2 cases. Malignant IBL was diagnosed in 16 patients (median follow-up 18 months(IQR 7-40)). Sensitivity and specificity of visual assessment for IBL was 68.7% and 82.5%, correctly identifying the nature of 44 IBL (accuracy 78%). POCS targeted biopsies were taken in 35 patients, including 14 with a malignant IBL. The diagnostic yield was low, with the pathologist reporting insufficient material available for assessment in 46% of the patients. Sensitivity and specificity of biopsies were 7% and 57%, correctly identifying 13 (accuracy 37%). Results for visual endoscopic assessment of IBL are in concordance with previous studies which showed POCS to be a good predictor of malignancy, especially when neovascularisation is observed. In contrast to previous studies the yield of POCS targeted biopsies was low and its role in assessing the nature of IBL remains unclear, warranting further research.

Conclusion: the visual assessment of IBL through POCS offers a relatively good diagnostic yield in the complicated group of patients with IBL in whom conventional diagnostics have not resulted in a definite diagnosis.

Endoscopic ultrasound-guided visualization of celiac ganglia and celiac ganglia neurolysis: results of a clinical cross-sectional and human cadaver study

W.F.W. Kappelle[1], R.L.A.W. Bleys[2], A.J.M. Van Wijck[3], R. Stellema[3], P.D. Siersema[1], F.P. Vleggaar[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Anatomy, and [3]Dept of Anesthesiology, University Medical Center Utrecht, Utrecht, The Netherlands

Endoscopic ultrasound guided celiac ganglia neurolysis (EUS-CGN), which is performed by injecting ethanol in individual celiac ganglia, has recently been introduced as an alternative to celiac plexus neurolysis. There is little evidence that the structures targeted during EUS-CGN are indeed celiac ganglia and that selective ethanol injection into ganglia is feasible. We aimed to assess the proportion of patients in which ganglia can be visualized with EUS, to evaluate whether these structures are indeed celiac ganglia and to visualize the spread of ethanol after EUS-CGN. In 100 consecutive patients (44 male [44%], median age 60, IQR 45-68) undergoing linear EUS, ganglia were sought and their characteristics recorded. Secondly, a linear echo-endoscope was placed next to the celiac trunk in a prosected human cadaver. A hypodermic needle was inserted into a ganglion after identification and the tissue surrounding the needle was removed, sectioned and stained. Finally, EUS-CGN was performed with ethanol 96%, mixed with orange dye, in a nonembalmed human cadaver. Thereafter, the entire region around the celiac plexus was removed and consecutive transverse sections were obtained with a cryomacrotome, whilst taking high-quality pictures every 75µm. Afterwards, a 3D-reconstruction was used to obtain sagittal and coronal images. In total, 211 ganglia were detected in 86/100 patients. Median number of ganglia was 2 (range 1-9), median size of the long and short axis were 6.2 mm (IQR 4.5-8.6 mm) and 2.8 mm (IQR 2.2-4.0 mm), respectively. Most often, the ganglia were located anteriorly (n=65, 31%), left (n=64, 30%) or anteriorly and left (n=75, 36%) of the celiac trunk. In the prosected cadaver, histology of the region around the needle showed numerous nerve cell bodies and no other structures with comparable echogenic characteristics. In total, two ganglia were visualized with EUS in the nonembalmed cadaver and both were injected with 1mL of ethanol using a 25G FNA-needle. More than 2200 images were taken during sectioning with the macrotome. 3D-reconstruction showed spreading of the dye in the celiac region, well beyond the ganglia. In total, a spread of 80 x 70 x 53 mm was seen.
Conclusion: Using EUS, it is possible to visualize celiac ganglia in the majority of patients. Histology confirmed that the visualized structures are indeed celiac ganglia. Ethanol may spread well beyond the injected celiac ganglia after EUS-CGN, even when using just 1 ml per ganglion, thus effectively resulting in a celiac plexus neurolysis. Therefore, it is doubtful whether selective celiac ganglia neurolysis is feasible.

A novel biodegradable non-covered self-expandable stent to treat pancreatic duct strictures in chronic pancreatitis; a pilot study

D.L. Cahen[1], S.W. van der Merwe[2], J.W. Poley[1], M. J. Bruno[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands, [2]Division of Gastroenterology and Hepatology, University Hospital Leuven, Belgium

In chronic pancreatitis (CP), fibrotic pancreatic duct (PD) strictures are a common complication and a therapeutic chalange. Dilatation by (progressive) plastic stent insertion requires multiple procedures and has limited success. Drainage with self-expandable metal stents seems more effective, but removal and migration problems limit their use. Biodegradable self-expandable stents (BD-SES) might be an attractive alternative, but have never been investigated in humans in this setting. The aim of this prospective pilot study was to evaluate the safety of non-covered BD-SES's (ELLA-CS) in CP patients with a fibrotic PD stricture. Patients were included if treatment with plastic stents for at least 6 months had failed and surgery was considered. Efficacy was a secondary endpoint. The two participating centers are academic hospitals in the Netherlands and Belgium. Stents were 6 mm in diameter, 3 or 4 cm in length, with an expected degradation time of 3-6 months. Patients were followed for one year. Stent and stricture resolution were evaluated by ERCP after 6 months. Stents were placed in 10 patients between January 2013 and October 2014 (median age 56, 6 male, median disease duration of 4 years). The median stricture length was 1 cm (IQR 0.5-3.5 cm). All stents were placed successfully, 9 after sphincterotomy and 6 after balloon dilatation. Nine were placed transpapillary and one intraductally. No peri-procedural complications were encountered, but one patient was admitted 4 days after stent placement because of self-limiting pancreatic pain. No stent-related complications occurred, but CP complications were frequent during follow-up (FU) (pain flares without evidence of stent occlusion, common bile duct (CBD) strictures, cholecystitis). In all seven patients that reached the 6-months FU, stent degradation was complete (100%). One patient received a plastic stent after three months, because of ongoing stricturing and pain. This patient has remained stent dependent. In the other six patients, stricture resolution was accomplished at ERCP (86%). Two patients underwent a Whipple procedure, 9 and 10 months after stent insertion; one because of a CBD stricture and recurrent flares, the other for a groove pancreatitis leading to gastric outlet obstruction (neither had evidence of a recurrent PD stricture). The remainder four patients are still stricture free after 1 year.

Conclusion: These preliminary results show that BD-SES's for fibrotic PD strictures in CP are easy and safe to place, degrade completely, and may even resolve strictures, resilient to conventional plastic stent treatment. These encouraging results warrant further testing.

Effects of radial and axial force of esophageal stents on occurrence of severe adverse events and recurrent dysphagia in patients with malignant dysphagia

W.F.W. Kappelle[1], M.C.W. Spaander[2], M.J. Bruno[2], M. Leenders[1], M.M.C. Hirdes[1], F.P. Vleggaar[1], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Erasmus Medical Center, Rotterdam, The Netherlands

Self-expanding stent placement is an effective palliative treatment for malignant dysphagia. However, serious adverse events (SAE's) and recurrent dysphagia are frequently encountered. Stent-related forces, radial force (RF) and axial force (AF), are thought to influence the risk of such events. A high RF is thought to decrease migration risk and increase stent related pain, while a high AF is thought to increase risk of perforation, bleeding and fistula formation. Furthermore, some esophageal stents elongate when compressed and this might be of clinical relevance. We aimed to evaluate whether RF, AF and the degree of elongation of esophageal stents affect the occurrence of SAE's and recurrent dysphagia in clinical practice. Data on eight types of esophageal stents, placed for malignant dysphagia between January 2006 and December 2013, were collected in two academic centers. Stent types included Ultraflex (n=50, 17%), fully covered (FC) Wallflex (n=32, 11%), Alimaxx-E (n=47, 16%), partially covered (PC) Wallflex (n=45, 15%), PC Evolution (n=40, 14%), Hanaro (n=40, 14%), Polyflex (n=11, 4%) and SX-Ella (n=27, 9%). Multivariate Cox regression analyses were performed to assess the effect of RF and AF on SAEs. In total, 292 patients (211 male [72%], mean age 66±11 years) were included. SAE's occurred in 67 patients (23%, after a median of 14 days, IQR 2-57), and included bleeding (n=17, 25%), fistula formation (n=17, 25%), pneumonia (n=12, 18%), severe pain (n=11, 16%), perforation (n=3, 5%) and other (n=7, 11%). Recurrent dysphagia was seen in 96 patients (33%, after a median of 52 days, IQR 18-125), mainly due to migration (n=35, 36%) and tumor in-/overgrowth (n=28, 40%). After correction for patient, tumor, treatment and stent characteristics, multivariable analysis showed no association between RF, AF or elongation and SAE's (P=0.18, P=0.36, P=0.20, respectively) and recurrent dysphagia (P=0.27, P=0.88, P=0.54, respectively). However, risk of stent migration was increased in esophageal stents with a higher RF (HR 1.03, 95% CI 1.00-1.05; P=0.02) and decreased in stents with a higher AF (HR 0.33, 95% CI 0.14-0.75; P=0.01) and a higher degree of elongation (HR 0.57, 95% CI 0.37-0.88; P=0.01). No association was found between stent forces and pain, perforation, bleed or fistula formation.

Conclusion: Placement of esophageal stents with a high RF is associated with an increased risk of stent migration, while a higher AF as well as a higher degree of elongation is associated with a lower migration risk. The exact mechanism of stent characteristics on stent migration needs further elucidation. Occurrence of an SAE is not associated with stent related forces.

FIT-based colorectal cancer screening: do we need to tailor screening for men and women?

E.J. Grobbee[1], E.M. Stoop[1], T.R. de Wijkerslooth[2], I. Lansdorp-Vogelaar[3], P.M. Bossuyt[4], E. Dekker[2], E.J. Kuipers[1], M.C.W. Spaander[1], [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [2]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, [3]Dept of Public Health, Erasmus University Medical Center, Rotterdam, [4]Dept of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, Amsterdam, The Netherlands

Colorectal cancer (CRC) screening programs are implemented worldwide, many of them are based on biennial fecal occult blood testing (FOBT). Despite well-known differences between men and women in incidence of CRC and its precursors, screening programs invariably use the same strategy for both genders. In recent years quantitative immunochemical FOBT (FIT) testing has become widely used. This allows gender-tailored screening by using different cutoffs for men and women to improve CRC screening efficacy. We aimed to evaluate whether different cutoffs should be used for men and women. Participants (50-75 years) in an invitational primary colonoscopy screening program were asked to complete one sample FIT (OC-sensor, Eiken, Japan) before colonoscopy. We estimated positivity rates, FIT sensitivity, specificity, detection rate and false-positivity rate in detecting advanced neoplasia (AN) for cutoff levels of 5 (FIT5), 10 (FIT10), 15 (FIT15) and 20 (FIT20) µg Hb/ g feces for both men and women, corresponding to 25, 50, 75 and 100 ng Hb/ml feces. A receiver-operating-characteristic (ROC) curve was calculated for men and women. In total 1,256 invitees underwent FIT and colonoscopy; 638 men and 618 women; median age of 61 years (IQR 56-66) and 60 years (IQR 55-65). AN was found in 10% (65/638) of all men, and in 8.4% (52/618) of all women. Sensitivity in men ranged from 55% (95%CI 43.2-66.9) for FIT5 to 34% (95%CI 23.4-46.1) for FIT20, and in women from 42% (95%CI 34.8-63.2) for FIT5 to 35% (95%CI 23.0-48.4) for FIT20. False-positivity rates in men ranged from 62% (59/95) to 45% (18/40) and from 70% (51/73) to 42% (12/31) for women and did not differ significantly for any of the cutoffs. The ROC curves had an area under the curve for detecting AN of 0.71 in men (95%CI 0.63-0.79) and 0.73 in women (95%CI 0.64-0.81). The absolute numbers of individuals with missed AN per 1,000 screenees significantly differed for higher cut-offs; 66 men versus 44 women at FIT15 ($p = 0.03$), and 67 men vs. 44 women at FIT20 ($p = 0.02$).

Conclusion: In FIT-based CRC screening women seem to have a lower sensitivity for advanced neoplasia than men when using a lower cutoff. In addition, women seem to have more false positive results than men when using the lowest cutoff. However, these numbers did not reach statistical significance. Yet when looking at absolute numbers, a significantly higher number of missed lesions in men was found using FIT15 and FIT20. When aiming for a same number of missed lesions per 1000 screenees, a lower cutoff should be used in men than in women in FIT-based CRC screening.

Surgical resection for T1 colorectal carcinoma is associated with improved recurrence free survival

T.D.G. Belderbos[1], F.N. van Erning[2], I.H.J.T. de Hingh[3], M.G.H. van Oijen[4], L.M.G. Moons[1], V.E.P.P Lemmens[2], P.D. Siersema[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Eindhoven Cancer Registry, Eindhoven, [3]Dept of Surgery, Catharina Hospital, Eindhoven, [4]Dept of Medical Oncology, Academic Medical Center, Amsterdam, The Netherlands

Controversy exists on the adequate management in case of pathologically confirmed T1 colorectal carcinoma (pT1 CRC). It is not well known whether recurrence free survival after pT1 CRC is improved by performing primary or secondary surgical resection. We aimed to compare recurrence free survival between patients undergoing surgical resection versus endoscopic resection or transanal endoscopic microsurgery (TEM) only. Secondary aims were to identify factors associated with surgery and recurrence free survival. We identified all patients diagnosed with pT1 CRC between 1995 and 2011 in the Eindhoven Cancer Registry. Data of these patients were linked to PALGA, the Dutch Pathology Registry. Recurrence was defined as subsequent occurrence of CRC at the same location or site of anastomosis, or distant metastasis originating from the index tumor. Surgery was defined as resection of at least a segment of the colon. Multivariable logistic regression was performed to evaluate patient- and tumor characteristics associated with surgery. Cox proportional hazard regression analysis was performed to assess the effect of surgery on the risk of recurrence after adjustment for relevant patient and tumor characteristics. A total number of 1,782 patients with pT1 CRC were identified, of whom 56% were male and mean age was 68 years (SD 11). Endoscopic resection only was performed in 510 patients (29%); TEM only in 86 patients (5%); and surgery in 1186 patients (67%), of whom 238 (20%) underwent prior endoscopic resection. Surgical resection was more often performed in younger patients (OR per 10 years increase 0.86, 95%-CI 0.78-0.95), between 1995 and 2000 (OR 1.65, 95%-CI 1.27 – 2.14), and in poorly differentiated (OR 1.71, 95%-CI 1.00 – 2.98) and right-sided tumors (OR 6.59, 95%-CI 3.95 – 11.00). One or more positive lymph nodes were found in 89 (8%) of 1186 patients undergoing surgery. In the endoscopic resection / TEM group, 48 recurrences (8%) were found versus 50 recurrences (4%) in the surgery group ($p<0.01$). Surgical resection was significantly associated with increased recurrence free survival (HR 0.51, 95%-CI 0.34 – 0.76). A higher recurrence rate was found for pT1 CRC in the rectum (HR 3.35, 95%-CI 1.19 – 9.45).

Conclusions: In a large cohort of pT1 CRCs, two thirds of patients underwent primary or secondary surgery, which was more likely to be performed in younger patients with poorly differentiated and right-sided tumors. Surgical resection was associated with improved recurrence free survival, but as not all risk factors were available, further studies are needed to elucidate which patients benefit from surgery.

Lower risk of metastatic disease in pedunculated polyps containing T1 colorectal carcinoma compared to lateral spreading tumors

A. van den Blink[1], A. Overwater[1], M.G.H. van Oijen[1], B.W.M. Spanier[2], T.C.J. Seerden[3], H.J.M. Pullens[4], W.H. de Vos tot Nederveen Cappel[5], G.J.A. Offerhaus[6], D.J. Bac[7], M. Kerkhof[8], K. Kessels[9], P.D. Siersema[1], M.M. Lacle[6], L.M.G. Moons[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Rijnstate, Arnhem, [3]Dept of Gastroenterology and Hepatology, Amphia Hospital, Breda, [4]Dept of Gastroenterology and Hepatology, Meander Medical Center, Amersfoort, [5]Dept of Gastroenterology and Hepatology, Isala, Zwolle, [6]Dept of Pathology, University Medical Center Utrecht, Utrecht, [7]Dept of Gastroenterology and Hepatology, Gelderse Vallei, Ede, [8]Dept of Gastroenterology and Hepatology, Groene Hart Hospital, Gouda, [9]Dept of Gastroenterology and Hepatology, Flevo hospital, Almere, The Netherlands

Although a lower incidence of lymph node metastasis (LNM) of T1 colorectal cancer (CRC) is suggested in pedunculated polyps compared to lateral spreading tumors (LSTs), no large cohort study has been performed comparing number of LNM, recurrence and complications of treatment. This study aimed to determine outcomes of T1 CRC in pedunculated polyps and LSTs. Patients diagnosed with a T1 CRC in 8 hospitals between January 2000 and July 2014 were extracted from the database of the Netherlands Cancer Registry. Patient characteristics, endoscopic and histological findings, treatment, and follow-up were collected of all patients. Recurrence was defined as the detection of metastasis or local recurrence during follow-up. Survival was estimated by Kaplan-Meier analysis and Cox proportional hazard regression analysis was used to adjust for gender, age, location in colon, polyp size, type of therapy and follow-up by radiologic imaging. A Chi-square test was used to compare rates of LNM, mortality and major complications. A total of 1026 patients with T1 CRC (410 pedunculated and 616 LSTs) were included. Polyps were treated with endoscopy only (pedunculated n=213 (52%) vs. LST n=155 (25%)), endoscopy followed by surgery (n=130 (32%) vs. n=123 (20%)) or primary surgery (n=67 (16%) vs. n=338 (55%)). Median follow-up was 41 months (IQR 18-74) in both groups. Pedunculated T1 CRCs had a more favorable 5-year disease free survival rate than LSTs (98% vs. 94%; adjusted HR 3.7 95%CI 1.4-9.4; p<0.01). Stratified to treatment, most survival benefit was observed for T1 CRCs treated with endoscopy only (98% vs. 89%). However, after adjustment for follow-up with imaging and location in rectum this was no longer significant (HR 3.0 95%CI 0.9-10, p=0.08). In the primary surgery group, the rate of LNM was lower for pedunculated polyps (3.0% vs. 10.4%, p=0.06). Recurrence was detected in 5/213 (2.3%) pedunculated polyps treated with endoscopy only. In patients treated with endoscopy followed by surgery, LNM were found in 11/130 (8.5%), and 2/130 (1.5%) patients developed a recurrence. Cumulative risk of recurrence or/and LNM for pedunculated polyps was 18/343 (5.2%), which was significantly lower than for LSTs (34/278 (12.2%), p<0.01). Major complications and mortality rates of surgery vs. endoscopy were 19.8% vs. 6.4% (p<0.01) and 2.5% vs. 0.03% (p=0.05), respectively.
Conclusion: Compared to LSTs, pedunculated T1 CRCs have a lower risk of developing LNM and recurrence and endoscopic resection is more often curative. This low risk closely approaches the risk of mortality from surgery, and benefits from surgery may easily disappear in the presence of risk factors for surgery.

Organ preservation for patients with a complete clinical response after neo-adjuvant chemoradiotherapy for rectal cancer: Selection and follow-up

M.H. Martens[1,2], L.A. Heijnen[1,2], M. Maas[2], D.M.J. Lambregts[2], L.P.S. Stassen[1], S.O. Breukink[1], J.W.A. Leijtens[3], C Hoff[4], R.G.H. Beets-Tan[2], G.L. Beets[1], [1]Dept of Surgery, and [2]Dept of Radiology, Maastricht University Medical Center, Maastricht, [3]Dept of Surgery, Laurentius Hospital, Roermond, The Netherlands

Standard treatment for locally advanced rectal cancer is neoadjuvant chemoradiotherapy (CRT) followed by standard surgery. Patients with a pathological complete response (15-20%) have excellent long-term outcome. Organ-preserving treatment options (Wait-and-See (W&S) or Transanal Endoscopic Microsurgery (TEM)) could be an alternative to standard surgery for patients with a clinical complete response (cCR). Adequate selection and follow-up of patients with cCR is crucial to minimize regrowth rates and to detect potential regrowth as early as possible. Aim of this prospective cohort study was to describe selection criteria and evaluate long-term follow-up of organ-preservation for rectal cancer post-CRT. Selection criteria ±8 weeks post-CRT were [1] no residual tumor with digital rectal examination, [2] normalized or fibrotic rectal wall on standard MRI, [3] absence of high signal on diffusion-weighted MRI, [4] absence of pathologic lymph nodes on contrast-enhanced MRI, and [5] typical white scar on endoscopy. Patients with a near complete response (4/5 criteria) were either reassessed after 3 months, or underwent TEM of the scar (only in ycN0). Standard follow-up for rectal cancer was performed (CEA, CT, and consults) with the addition of MRI and endoscopy every 3 months during the first year, and every 6 months during year 2-5. Long-term outcomes were estimated using Kaplan-Meier curves. One hundred patients were included with a median follow-up of 26 months (6-120). 85/100 in the W&S-group and 15 patients in the TEM-group (6 ypT1-2, 9 ypT0). Twelve patients developed a local regrowth, of whom 11 were detected within 1 year, and one patient at 23 months. Ten patients had a luminal regrowth (W&S n=9, TEM n=1), and 2 had a nodal regrowth (W&S n=1, TEM n=1). Two-year local regrowth-rate was 12%. Distant metastasis occurred in 5 patients, which were treated with curative intent in 4 patients. The remaining patient was diagnosed with peritoneal implants. Two-year disease-free and overall-survival were 84% and 99%, respectively.

Conclusion: Organ-preserving treatment for (near) complete responders after chemo-radiotherapy for rectal cancer, shows good long-term outcome. These experimental treatment strategies seem feasible if combined with strict selection criteria and follow-up. Additional optimization of selection tools and criteria may even further reduce local regrowth rates.

Systemic treatment of patients with metachronous peritoneal carcinomatosis of colorectal origin

T.R. van Oudheusden[1,2], Y.R. van Gestel[2], L. Razenberg[2,3], G.J. Creemers[3], V.E. Lemmens[2], I.H. de Hingh[1], [1]Dept of Surgery, and [3]Dept of Internal Medicine, Catharina Hospital, Eindhoven, [2]Dept of Research, Eindhoven Cancer Registry, Comprehensive Cancer Center The Netherlands (IKNL), Eindhoven, The Netherlands

Introduction: The introduction of systemic therapy combining chemotherapy and biologicals has resulted in enhanced survival in metastatic colorectal cancer patients in general. However, the result of this treatment in patients with peritoneal carcinomatosis (PC) remains questionable since these patients are usually not included in trials. For long, PC has even been regarded as refractory to systemic treatment but small studies have now shown a potential benefit also in these patients. The current study evaluates the results of systemic treatment in patients developing PC after initial curative treatment for colorectal cancer. Methods: Using the Eindhoven Cancer Registry, all consecutive patients with metachronous PC of colorectal origin, treated between 2003 and 2011 in a palliative setting were included, with follow up data until January 2014. Patient demographics and details concerning chemotherapeutic treatment were collected and compared.Results: Altogether 1042 patients were diagnosed with metachronous metastatic colorectal cancer and 197 patients (18.9%) had PC. From the latter, 92 patients received chemotherapy in a palliative setting. In 36 patients biologicals were added to the treatment. Overall survival was 7.1 months (95% CI 5.1-9.4 months) and was significantly increased to 13 months (95% CI 9.5-16.0 months) when receiving chemotherapy only and to 20.3 months (95% CI 13.7-29.3 months) when adding biologicals, to the chemotherapeutic regimen (P<0.001).
Conclusion: Biologicals in combination with systemic chemotherapy may increase survival in a patients with metachronous colorectal PC.

Systematic Assessment of Quality of Patient Information on Colorectal Cancer Screening on the Internet

E.H. Schreuders[1], E.J. Grobbee[1], E.J. Kuipers[1], M.C.W. Spaander[1], S.J.O. Veldhuyzen van Zanten[2], [1]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [2]Division of Gastroenterology, University of Alberta Hospital, Edmonton, Alberta, Canada

Efficacy of colorectal cancer (CRC) screening is dependent on patients' participation and adherence to surveillance guidelines. The internet is increasingly used for health information and disease management and may be a source for decision making. The aim was therefore to evaluate the quality, accuracy and readability of web-based patient focused information on CRC screening. Websites were searched by Google.com on April 9 2014, using the term: "colorectal cancer screening" OR "bowel cancer screening" OR "colon cancer screening". A Quality Evaluation Instrument (QIE) was developed and pretested, which awards points (0-44) on various aspects of CRC screening. In addition, websites were evaluated using a validated 5-point Global Quality Score (GQS), two validated internet quality instruments (LIDA; 0-100% and DISCERN;16-80) and two reading scores; Flesch Reading Ease (FRE) and Flesch-Kincaid Grade Level (FKG). Two raters independently assessed the first 30 websites. Clear portal links to other sites, duplicates and news articles were excluded. For QEI scores, consensus in case of disagreement was achieved through discussion with a third reviewer. For other quality parameters, mean score of both raters was used. Out of the first 30 hits, 20 websites were included for analysis. Most sites were published by a professional medical society (35%) or a governmental organization (30%). The mean QEI score was 25.5 (range 9-41) and the median GQS was three (range 2-5). There was a strong positive correlation between the QEI and the validated GQS (Spearman's r=0.81; p<0.001). Also the validated LIDA and DISCERN had a moderate correlation with the QEI; r_s=0.45 (p<0.05) and r_s=0.65 (p<0.01) respectively. There was no correlation between the Google rank and QEI (r_s=-0.36; p=0.12). The mean FRE was 48 (range 27–76). Only 30% of the websites had a reading level acceptable for the general public (FRE> 60). The mean FKG was 10.5 (range 5.4–15.9). The mean LIDA overall score was 68% (range 25-86%) and the mean DISCERN score was 46 (range 27-68).

There is marked variation in quality of websites on CRC screening. The developed QEI was strongly correlated with previously validated quality instruments, making it a valuable tool to identify high quality, accurate CRC screening websites. Notable was the poor correlation between quality and Google ranking. As people generally only read the first 10 hits, our findings suggest that patients will miss out on high quality websites related to CRC screening. Improvements in quality and readability are required to provide patients with reliable information to make informed decisions on CRC screening participation.

Tolerability of neo-adjuvant chemoradiotherapy with capecitabine and surgical outcomes in patients aged 70 years or older with locally advanced rectal cancer

L. Jacobs[1], E. van der Vlies[2], D. ten Bokkel Huinink[3], H.J. Bloemendal[4], P.D. Siersema[5], B.L.A.M. Weusten[1], N. van Lelyveld[1], M. Los[6], [1]Dept of Gastroenterology, and [2]Dept of Internal Medicine, St Antonius Hospital, Nieuwegein, [3]Dept of Oncology, Diakonessenhuis, Utrecht, [4]Dept of Oncology, Meander Medical Center, Amersfoort, [5]Dept of Gastroenterology, University Medical Center Utrecht, Utrecht, [6]Dept of Oncology, St Antonius Hospital, Nieuwegein, The Netherlands

Colorectal cancer (CRC) predominantly affects elderly patients. However, in studies on CRC, older patients are frequently underrepresented since comorbid conditions and functional status often lead to study exclusion. In elderly rectal cancer patients with an indication for neo-adjuvant chemoradiotherapy (nCRT) based on T/N stage, physicians decide on clinical grounds whether nCRT should be offered to individual patients. The aim of this study was to assess the proportion of patients aged ≥70 years with locally advanced rectal cancer actually undergoing nCRT, and to evaluate safety and efficacy of nCRT and subsequent surgery in this selected group of elderly patients. We used data from the Dutch Comprehensive Cancer Centre (IKNL) of 1704 patients with rectal cancer in four Dutch hospitals over the last 10 years. Data included patient characteristics, clinical TNM stages, preoperative treatment, surgery, pathological staging, adjuvant treatment, palliative treatment and vital statistics. All patients aged ≥70 years were included if treated with nCRT according to the ESMO Clinical Practice Guidelines. Patients were analysed for treatment deviations, postoperative morbidity, postoperative mortality and survival. Data were stratified for patient age (three groups: 70-74, 75-79, ≥80 years). Between 1-1-2002 and 31-12-2012, a total of 706 rectal cancer patients aged ≥70 years were identified. Of these, 42 patients with locally advanced disease received nCRT, median age 74 (IQR 72-78). Forty patients (95.2%) underwent subsequent curative surgery. Overall, 37 patients (88.1%) completed the planned nCRT without treatment deviations. The majority of patients (95.2%) experienced adverse events with radiation dermatitis (61.9%), fatigue (57.1%) and diarrhoea (42.9%) being most common. Forty patients (95.2%) were treated with surgery; one patient refused a resection and one patient died because of dihydropyrimidine dehydrogenase (DPD) deficiency during nCRT. Post-operative complications were observed in 11 patients (27.5%) and the 30-day mortality rate was 0%. Two- and five year overall survival rates were 82% (95% CI 70-94) and 49% (95% CI 23-75). Treatment deviations, post-operative morbidity and treatment efficacy were not different in the three age groups.
In conclusion, this multicentre study shows that only a minority of older patients with locally advanced rectal cancer are treated with nCRT. However, if selected on clinical grounds, nCRT is safe, well tolerated, and leads to a favourable surgical outcome even in patients aged ≥70 years. These results show that elderly should not be excluded from nCRT based exclusively on age.

Colorectal tumor prevention by progestins is critically dependent on postmenopausal hormone status

M.C.B. Wielenga[1], J. Heijmans[1], M. Schukking[1], B. Meijer[1], P.S. Montenegro-Miranda[1], P.B. Hoyer[2], J.M. Amos-Landgraf[3,4], W.F. Dove[3,4], G.R. van den Brink[1], [1]Tytgat institute for Liver and Intestinal Research and Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, the Netherlands, [2]Department of Physiology, University of Arizona, Tucson, USA, [3]McArdle Laboratory for Cancer Research, Department of Oncology, University of Wisconsin–Madison, Madison, USA, [4]Laboratory of Genetics, University of Wisconsin–Madison, Madison, USA

Large placebo controlled trials by the Women's Health Initiative (WHI) have shown that the combination of estrogen plus medroxyprogesterone acetate (MPA) but not estrogen alone protects from colorectal cancer (CRC) in postmenopausal women. Further in-depth animal research has thus far not been able to recapitulate these results, making it difficult to investigate the potential mechanism of action. We hypothesized that the reason for the lack of protective effect of female hormones in animal models of colorectal carcinogenesis may be related to the experimental approach. In all animal studies thus far, the menopause has been modelled by removal of the ovaries, the source of both female and male hormones. This fails to recapitulate the actual changes that take place in postmenopausal ovaries in which there is a steep drop in estrogen and progesterone production but male hormone production is maintained. Therefore we tested if the protective effect of MPA on colorectal tumorigenesis may be dependent on postmenopausal hormone status. To this aim we compared the effect of MPA on adenomagenesis in fertile mice to an ovary-intact mouse model of the menopause. In this model, menopause is induced with repetitive i.p. injections with 4-vinylcyclohexene diepoxide (VCD) leading to depletion of ovarial follicles, attenuated female hormone production but still intact male hormone production similar to human menopause. Colonic adenomas were chemically induced with the carcinogen azoxymethane (AOM) and MPA was replaced with subcutaneous slow release pellets. Effective induction of menopause was confirmed by the absence of ovarial follicles in the VCD treated postmenopausal mice. In fertile mice, MPA did not reduce adenoma formation, confirming previous research reporting lack of effect of MPA on adenomagenesis in fertile and ovariëctomized rodents. Induction of menopause resulted in a significant increase of adenoma number (2.6 vs 1.3 $P<0.05$). In contrast to fertile mice, MPA was able to significantly reduce adenoma formation (0.9 vs 2.6, $P<0.001$) to numbers observed in fertile mice. In the healthy colon, we did not observe differences in epithelial proliferation as assessed by BrdU incorporation, suggesting that the effects of menopause and MPA are specific for tumor initiation and not general epithelial proliferation.

From these data we conclude that the protective effect of progestins is critically dependent on postmenopausal hormone status. Future in vivo postmenopausal hormone research should be investigated using an appropriate postmenopausal mouse model. Our results suggest that MPA may be a chemopreventive agent specifically in postmenopausal women.

Multi Layered columnar epithelium (MLCE) induced by bile at the squamo-columnar junction in mice originates from squamous and columnar cells.

D. Straub[1,2], K. Parikh[1,2]; P. Fockens[1], K.K. Krishnadath[1,2], [1]Department of Gastro-enterology and Hepatology, Academic Medical Center, Amsterdam, Netherlands. [2]Center for Experimental and Molecular Medicine (CEMM), Amsterdam, The Netherlands

Barrett's esophagus (BE), a premalignant condition of esophageal adenocarcinoma (EAC) is defined as the replacement of normal stratified squamous epithelium of the lower esophagus by metaplastic columnar epithelium (Spechler 2014). The observation of multi-layered columnar epithelium regularly observed at the squamo-columnar junction (SCJ) in BE patients suggests a transitional stage between these two types of epithelia. Studies, in both human and rats, have shown that especially the combination of acid and biles can induce multilayered columnar epithelium (MLCE) and metaplasia at the SCJ (Vaezi 1995, Chen 2008, Glickman 2009). In this study we investigated if the diverse layers as observed in MLCE is a transitional stage between epithelia originating from one progenitor cell, or is a mix of different types of epithelia with diverse progenitors. 0.5% deoxycholic acid (DCA) was given to mice in drinking water for a maximum of 30 weeks. Animals were sacrificed and studied by immunohistochemistry (IHC) at different time points. The combination of bile and acid induced gland formation at the SCJ starting from week 10. The MLCE glands were positive in the outer layer for squamous markers K14, p63 and K5 and in the inner layer for columnar markers K19, TFF2 and Alcian Blue. In one of our previous studies we also observed Lgr5 positive cells (RNA in situ) in these multi-layered glands (Mari et al. 2014). To investigate if the multi-layered epithelium originates from a squamous or columnar stem cell, we performed lineage tracing experiments. A Cytokeratin 5 (K5)-cre (n=20) mouse specific for tracing squamous progenitor lineages, and a Leucine-G-coupled receptor (Lgr5)-cre mouse (n=20) were crossed with Rosa-lacZ mice. Lineage tracing was induced by tamoxifen injection prior to bile treatment at the age of 8 weeks. Mice were sacrificed 15 weeks after induction. K5-lacZ positive cells were present in the outer layer of the gland demonstrating that the origin of these cells is from squamous progenitors, which is in concordance with the IHC results. Negative K5 lineage tracing in columnar cells within the MLCE in mice excludes the transdifferentiation hypothesis in which squamous cells change into columnar cells, which has been a prevailing theory for many years. The negative lineage experiments for LGR5 suggests a columnar cell of origin, other than Lgr5 for the inner layer. Continuous acid and bile reflux changes the environment at the SCJ in mice and disrupts the natural homeostatic environment of squamous and columnar cells. It appears that MLCE is the result of competitive interactions between cell lineages driven by environmental changes.

Lipid phosphatase SHIP2 functions as oncogene in colorectal cancer by regulating PKB activation

E. Hoekstra[1], A.M. Das[2], M. Willemsen[1], C.J. van der Woude[1], T.L.M. ten Hagen[2], M.P. Peppelenbosch[1], G.M. Fuhler[1], [1]Department of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, [2] Department of Surgery, Erasmus MC, University Medical Center Rotterdam, The Netherlands

Background: Phosphatidylinositol phosphate lipids (PIPs) function as essential second messengers in cellular signaling, and careful regulation of their levels is therefore required. PI3-kinase phosphorylates $PI(4,5)P_2$ to produce $PI(3,4,5)P_3$, resulting in cell survival through PKB-mTOR signaling. The reverse reaction is catalyzed by the phosphatase PTEN, a known tumor suppressor. However, $PI(3,4,5)P_3$ is also dephosphorylated by the phosphatase SHIP2 (encoded by INPPL1), but the product of this reaction is $PI(3,4)P_2$. While it has been postulated that SHIP2 is a tumor suppressor, recent evidence has shown that unlike the PTEN product $PI(4,5)P_2$, $PI(3,4)P_2$ is required for full activation of PKB. This suggests that SHIP2, in contrast to PTEN, could function as an oncogene. Our aim was therefore to investigate the role of this lipid phosphatase in colorectal cancer. Methods: INPPL1 expression was analyzed using publicly available databases. SHIP2 protein expression was analyzed by immunohistochemistry on sections of 14 adenomas, 11 CRCs, and 8 controls. Phosphatase activity was assessed in 8 patients by immunoprecipitation of SHIP2 from freshly frozen cancer and normal adjacent tissue, followed by Malachite green assay. Cellular effects and downstream targets of SHIP2 were investigated by lentiviral transduction of two CRC cell lines with SHIP2 shRNAs or treated the cells with SHIP2 activity inhibitors. Cell survival assays, 2D time-lapse migration and 3D-invasion assays were performed. Results: SHIP2 expression in intestinal epithelial cells (IECs) is low in controls (3±5% positive IECs; mean intensity 0.13±0.23) and significantly increases from dysplasia (29% positive IECs; mean intensity 1.4±0.5) to carcinoma (81±29% positive IECs; mean intensity 1.6±0.8). This upregulation is mediated by an increased INPPL1 expression (1.4 fold increase). Likewise, SHIP2 enzymatic activity is increased in cancer compared to normal adjacent tissue. Chemical inhibition of SHIP2 activity results in a decreased phosphorylation of PKB, and reduces viable CRC cell numbers in a dose-dependent manner. Knockdown of SHIP2 also decreases phospho-PKB levels, and results in significant reduction of cell migration and invasion as shown by time-lapse microscopy and 3D-invasion assays.
Conclusions: The expression and intrinsic activity of the lipid-phosphatase SHIP2 is increased in colon cancer, which can promote the migration and invasion capabilities of CRC cells by increasing PKB signaling. These data provide evidence that SHIP2 functions as oncogene rather than tumor suppressor, making it a compelling target for future treatment, especially as SHIP2 inhibitors cause CRC cell death.

miR-511-3p, embedded in the macrophage mannose receptor gene, contributes to experimental colitis

S.E.M. Heinsbroekï€± §, M. Leonardo Squadrito[2] , R. Schilderinkï€±, F.W. Hilbersï€±, M. Hofmannï€±, A. Helmkeï€±, L. Boon[4], M.E. Wildenbergï€±, J.J.T.H Roelofs[3], C.Y. Ponsioenï€±, C.P. Petersï€± , A.A. te Veldeï€±, S. Gordon[5], M. De Palma[2], W.J. de Jongeï€±, [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, University of Amsterdam, AMC, Amsterdam, The Netherlands. [2] The Swiss Institute for Experimental Cancer Research (ISREC), École Polytechnique Fédérale de Lausanne (EPFL), Switzerland. [3]Department of Pathology, Academic Medical Center, University of Amsterdam, AMC, Amsterdam, The Netherlands. [4]Bioceros, Utrecht, The Netherlands. [5]Sir William Dunn School of Pathology, University of Oxford, Oxford, UK. §Corresponding author.

Introduction: miR-511-3p is embedded in intron 5 of the macrophage mannose receptor (CD206) gene Mrc1, that is expressed by M2 macrophages. Expression of CD206 and miRNA511-3p is co-regulated. CD206 is a pattern recognition receptor which recognises a broad range of microbes. The contribution of both CD206 and miRNA511-3p to colitis is unclear. We examined the role of CD206 and miR-511-3p in intestinal inflammation in both mouse and human systems. Methods: Colonic inflammation was induced by dextran sodium sulphate in CD206-deficient and WT mice, as well as mice in which the CD206 was blocked using a antagonists. Macrophages were stimulated with LPS, and cytokine responses measured. Expression levels of miR-511-3p were measured in macrophages from CD206-deficient mice using qPCR. Macrophages transduced to either overexpress or knock-down miR-511-3p were characterized. In addition, biopsies from Crohn's disease (CD) patients were analysed for miR-511-3p expression. Because the efficacy of anti-TNF treatment is associated with elevated CD206 expression, we correlated miR-511-3p expression to anti-TNF (adalimumab) treatment in patients with CD. Following the induction of experimental colitis, CD206-deficient mice showed ameliorated inflammation compared to WT mice. However, a CD206 blocking antibody and mannan antagonist did not affect the course of colitis, suggesting that CD206 was not involved in this response. Macrophages isolated from CD206-deficient mice had reduced levels of miR-511-3p and Tlr4, which was associated with reduced pro- inflammatory cytokine production upon LPS stimulation. Macrophages transduced to overexpress miR-511-3p showed 50% increase of Tlr4 mRNA, while knockdown of miR-511-3p reduced Tlr4 mRNA levels by 60%, compared to scrambled miRNA- transduced cells. Colon biopsies analysed before and 8 weeks into adalimumab showed a 4-fold reduction of miR-511-3p levels specifically in CD patients responding to the treatment.
Conclusion: Our results suggest that miR-511-3p controls macrophage-mediated microbial responses in mice and humans. Absence of miR-511-3p ameliorates colon inflammation in mice. In human CD patients that respond to adalimumab, miR-511-3p levels were reduced over the course of the treatment, suggesting that this miRNA is involved in the regulation of intestinal inflammation.

Homozygous disruption of the HNF1α-binding site in the UGT1A1 proximal promoter region results in Crigler-Najjar syndrome

R. van Dijk[1], I. Mayayo Peralta[1], S. Aronson[1], R. Oude Elferink[1], A. Kattentidt[2], U.H.W. Beuers[1] and P. Bosma[1], [1]Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands. [2]Department of Clinical Genetics, Erasmus MC, Rotterdam, The Netherlands

Hepatocyte nuclear factor 1α (HNF1α) is a liver specific transcriptional factor which is involved in the regulation of several liver specific genes involved in glucose and drug metabolism, including UDP-glucuronosyltransferases (UGT). Although several in vitro studies demonstrated that mutations of HNF1α binding sites present in the promoter regions resulted in reduced expression in hepatoma cells (HepG2), the implication of such mutations for liver function in man were lacking. Here we describe for the first time a severe inherited liver disorder caused by a mutation in an HNF1α binding site. Inherited unconjugated hyperbilirubinemia exists in a severe form due to reduced or absent UGT1A1 activity known as the autosomal recessive Crigler Najjar syndrome (CN) and in a mild form caused by a homozygous insertion of an extra TA repeat in the TATA box in the proximal UGT1A1 promoter, Gilbert syndrome. The UGT1A1 gene promoter is composed of two main regulatory regions, a proximal promoter region containing the TATA-box and a HNF1α-binding site. In a patient with CN syndrome phenotype that had no mutations in the UGT1A1 codon sequence the promoter region was analyzed. Besides an extra TA repeat in the TATA box, corresponding to Gilbert syndrome, a homozygous 3 nt insertion (CAT triplet) was found on position -85 to -83 of the proximal promoter, corresponding with the HNF1α binding site. To study the implications of this CAT triplet we cloned the patients and a wild type UGT1A1 proximal promoter in a luciferase vector. HepG2 cells were transfected with these luciferase vectors and activity was determined 48hrs after transfection. The patients promoter activity was reduced by more than 95% in comparison to the wild-type promoter, this was independent of the extra TA-repeat in the TATA-box. HNF1α was overexpressed in HEK293T cells, that lacks endogenous HNF1α expression, in order to clarify the role of HNF1α in enhancing UGT1A1 promoter activity. This showed that the transcriptional activity of wild-type promoter was significantly induced in a dose-dependent manner by HNF1α, the mutated promoter found in the patient did not respond to HNF1α at all. This demonstrates that the presence of CAT insertion within the HNF1α binding site abolishes UGT1A1 promoter transactivation by HNF1α.

In conclusion, we are the first to describe a patient with severe liver disorder caused by a mutation of the HNF1α binding site of the proximal promoter of a gene with a liver specific expression, underscoring the importance of HNF1α in the of transcriptional regulation of liver specific genes.

Normal mucus composition is essential in colonic anastomotic healing in mice

J.W.A.M. Bosmans[1,2], A.C.H.M. Jongen[1,2], G.M.H. Birchenough[3], M.J.J. Gijbels[4], E.E.L. Nyström[3], J.P.M. Derikx[1,2], N.D. Bouvy[1,2], G.C. Hansson[3], [1]Department of Surgery, Maastricht University Medical Center, Maastricht, the Netherlands. [2]NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University, Maastricht, the Netherlands. [3]Department of Medical Biochemistry, The Sahlgrenska Academy, University of Gothenburg, [4]Department of Pathology, Maastricht University Medical Centre+ Maastricht, Netherlands

Anastomotic leakage (AL) is one of the most dreaded complications after colorectal surgery causing high morbidity and mortality. Despite extensive research, it is unclear why the incidence of AL remains approximately 10%. We hypothesize that mucus plays a pivotal role in the healing of colorectal anastomoses, since the mucus layer forms the first of defense in the gastrointestinal tract. Previous research showed that Prostaglandin E2 (PGE2) suppletion in COX2$^{-/-}$ mice reduced the anastomotic leakage rate and ex vivo stimulation of the colon with PGE2 showed significant increase in mucus thickness. Therefore, we investigated if MUC2 (mucin 2, main component of mucus) depletion is associated with AL. Twenty-two male and 22 female mice of different Muc2 genotypes were subjected to a model of colonic AL. Mice were matched for age, gender and when possible littermates were used as controls. Half of the mice received daily administration of dmPGE2 to potentially stimulate mucus secretion, starting a day prior to surgery and follow-up was 3days. Mucus thickness measurements were performed ex vivo by measuring the distance between the epithelial surface and the mucus surface by a micropipette to ascertain presence of mucus at the anastomosis. Bacterial translocation in mesenterial lymph node (MLN) and spleen was determined by qPCR of bacterial 16S rDNA. Histological scoring of anastomosis, control proximal and distal colon was performed according to van der Ham et al. Of Muc2$^{-/-}$ mice, 91% developed AL, compared to 32% of control animals ($p<0.001$). An evident mucus layer could be found at the anastomotic site of control animals, but not on colonic tissue of Muc2$^{-/-}$ mice. DmPGE2 did not reduce the anastomotic leakage rate, neither in Muc2$^{-/-}$ nor in control mice. Histologically, normal healing could be found in control animals, while Muc2$^{-/-}$ showed more inflammation with granulocyte influx and less fibroblast activity and neoangiogenesis at the anastomotic site, although not significant. Of Muc2$^{-/-}$ 90% had bacterial 16S rDNA in their MLN and 27% in their spleen, while only 61% of the control animals had bacterial 16S rDNA in their MLN and no bacterial 16S rDNA could be found in spleens of these animals. Normal mucus composition is essential in the healing process of colonic anastomosis in mice. DmPGE2 cannot stimulate mucus secretion in vivo in order to promote anastomotic healing, at least not in this model. Further research on anastomotic healing should focus on positively influencing the mucus layer, to promote better postoperative recovery.

Mesalazine and cigarette smoke inhibit neutrophil extracellular trap formation in vitro

M.C. Buis[1], N. Sinnema[2], T. Blokzijl[1], K.N. Faber[1], J. Westra[2], G. Dijkstra[1], [1]Department of Gastroenterology and Hepatology, University of Groningen, University Medical Center, Groningen, The Netherlands. [2]Department of Rheumatology and Clinical Immunology, University of Groningen, University Medical Center, Groningen, The Netherlands

The mucosal infiltrate in ulcerative colitis (UC) is dominated by neutrophils. NET formation is a form of neutrophil cell death used to trap micro-organisms. These neutrophil extracellular traps (NETs) are not only involved in innate immunity, but also in proinflammatory responses. NETs are characterized by the release of DNA and other intracellular components. Citrullination of histones by PAD4 is one of the first steps in a cascade inducing NET formation. Both treatment with mesalazine and cigarette smoking are known to have a beneficial effect on UC, possibly through inhibition of NET formation. The aim of this study was to determine the effect of mesalazine and cigarette smoke extract (CSE) on NET formation in vitro. Neutrophils were obtained from the peripheral blood of 15 healthy volunteers and stimulated with Phorbol 12-myristate 13-acetate (PMA), after which they were treated with prednisolon (0-5 µg/ml), mesalazine (0-5mM), hydroxychloroquine (5- 20 µM) or CSE (0-30%). NET formation was quantified by measuring the amount of extracellular DNA. To visualize the presence of NETs we used immunofluorescence (IF) staining for neutrophil elastase (NE), myeloperoxidase (MPO), high-mobility group protein B1 (HMGB1) and citrullinated histone H3 (citr.h3). The results showed a dose-dependent inhibition of NET formation of both mesalazine and CSE, while prednisolon and hydroxychloroquine did not. IF showed the presence of MPO, NE and HMGB1 in the NETs. The inhibitory effect of mesalazine and CSE on NET formation was confirmed by IF: MPO and NE remained detectable in the cytoplasm, while HMGB1 and citr.h3 stayed within the nuclei. Pretreatment with mesalazine and CSE induced differences in the morphology of the neutrophils: after mesalazine the neutrophils were more stretched with round nuclei, while after CSE treatment the shape was more rounded with polymorphic shaped nuclei.
Conclusion: Mesalazine and CSE inhibit NET-formation in a dose-dependent manner in vitro. Inhibition of NET-formation for instance by blocking PAD4 activity, might be a promising target for future UC therapy.

Intestinal goblet cell and mucus alterations in obesity

N. van Best[1], F. Segers[1], F.J. Verdam[1], C. de Jonge[1], K. Lenaerts[1], J.W. Greve[1], W.A. Buurman[1], S.S. Rensen[1],[1]Department of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

Obesity is associated with changes in the composition and metabolic function of the intestinal microbiota. The factors that govern microbiota composition in obesity are largely undefined. Since microbiota composition is known to be influenced by goblet cell products, we hypothesized that altered intestinal goblet cell function could contribute to microbiota changes in obesity. Goblet cell numbers were quantified in jejunal biopsies of eleven obese and five normal weight human subjects (BMI 45.6±1.9 vs. 25.0±1.7 kg/m^2). Goblet cell numbers and mucus layer thickness were determined in the jejunum, ileum, and colon of 11 weeks old male obese and lean ZDF rats (weight: 350±7 vs. 305±5 g, n=6 in both groups) using histological and immunohistochemical techniques. Expression of goblet cell-derived mucus components and differentiation factors such as Klf4, Math1, and Hes1 was analyzed by qPCR. The total number of fecal bacteria as well as the relative abundance of Firmicutes and Bacteroidetes phyla and the mucus-degrading bacterium Akkermansia muciniphila were determined by qPCR. Localization of bacteria was assessed by FISH using a DNA probe detecting all intestinal bacteria combined with a mucin 2 staining on sequential sections. Obese subjects displayed a reduced goblet cell number in the jejunum compared with lean controls (6.4±0.4 vs. 8.1±0.2 cells/100 µm villus, $p<0.05$). This reduction was confirmed in rats (8.4±0.6 vs. 10.6±0.4 cells/100 µm villus, $p<0.01$) and was paralleled by lower expression of Klf4, a crucial goblet cell differentiation factor, in the jejunum and colon (0.22±0.05 vs. 0.61±0.07, $p<0.01$ and 0.40±0.05 vs. 0.60±0.05, $p<0.05$, respectively). Colonic mucus thickness appeared to be similar in both groups, but PAS and mucin 2 staining intensity were greatly reduced in obese rats. In with this, Muc2 gene expression was lower in the colon of obese rats (0.97±0.17 vs. 1.50±0.19, $p<0.05$). Bacteria appeared to be dispersed throughout the compromised mucus layer of obese rats, and were found in close proximity to epithelial cells. Interestingly, colonic Muc2 gene expression correlated with the abundance of both Firmicutes (r_s=-0.70, $p<0.05$) and A. muciniphila (r_s=0.78, $p<0.05$).

Taken together, the observed decrease in goblet cell number and Muc2 expression together with the reduced PAS and mucin 2 staining suggest that the mucus barrier is compromised in obesity, which could contribute to the observed microbiota composition changes and promote bacterial translocation. Future studies should be directed at elucidating whether altered goblet cell function in obesity is a cause or a consequence of microbiota composition differences.

Delayed bile acid uptake with metabolic consequences in Na$^+$-taurocholate cotransporting polypeptide knockout mice

D. Slijepcevic[1], J.M. Donkers[1], C. Kaufman[2,3], C.G.K. Wichers[4], E.H. Gilglioni[1], F.A. Lempp[2], S. Duijst[1], D.R. de Waart[1], R.P.J. Oude Elferink[1], W. Mier[3], B. Stieger[5], U. Beuers[1], S. Urban[2,6] and K.F.J. van de Graaf[1], [1] Tytgat Institute for Liver and Intestinal Research & Department of Gastroenterology & Hepatology, AMC, Amsterdam, the Netherlands, [2]Department of Infectious Diseases, Molecular Virology, University Hospital Heidelberg, Germany, [3]Department of Nuclear Medicine, University Hospital Heidelberg, Germany, [4]Department of Molecular Cancer Research, Section Metabolic Diseases, University Medical Center Utrecht, the Netherlands, [5]Department of Clinical Pharmacology and Toxicology, University Hospital Zurich, Switzerland, [6]German Center for Infection Research, Heidelberg University, Germany

Bile acids (BAs) are metabolic signaling molecules that improve glucose handling and decrease inflammation. We hypothesize that reduced hepatic BA uptake could lead to BA spillover into the circulation, thereby stimulating systemic BA signaling. The Na$^+$-taurocholate cotransporting polypeptide (NTCP) mediates uptake of conjugated BAs, implying a central function of this basolateral transporter in the enterohepatic circulation of BAs. Here, we investigated conjugated BA dynamics in vivo in the first NTCP-knockout mouse model. NTCP was recently also identified as the Hepatitis B Virus (HBV) entry receptor. The HBV entry inhibitor Myrcludex B is described as a potent NTCP inhibitory peptide. Therefore, we tested the specificity of this inhibitory peptide for NTCP in vivo.
We generated a conventional knock-out mouse by deletion of NTCP exon 1. BA kinetics were assessed using tritium-labelled taurocholate (TCA). Mice were fed 0.1% UDCA to challenge the hepatic BA uptake machinery. Bile flow was determined after cannulation of the gall bladder. Expression levels of BA transporters was analyzed by qPCR and Western blot. Mice were imaged by positron emission tomography (PET) to assess binding of gadolinium-labelled Myrcludex B. NTCP-knockout mice have markedly elevated serum total BA concentrations, mainly composed of conjugated BAs. The body weights of NTCP-knockout mice were significantly reduced directly post-weaning. A subset of knockout mice normalized serum total BA concentrations during maturation, although serum TCA clearance was reduced. The hypercholanemic phenotype was rapidly triggered by UDCA-feeding. Bile flow was slightly reduced, but biliary BA output remained intact. Fecal BA excretion was reduced in hypercholanemic NTCP-knockout mice. However, NTCP-knockout mice showed increased renal BA excretion and reduced Asbt expression in kidney. Hepatic uptake of conjugated BAs was potentially affected by downregulation of OATP1A1 and upregulation of OATP1A4. Finally, PET imaging showed a complete abrogation of hepatic binding of Myrcludex B in NTCP-knockout mice.
Conclusion: Chronic NTCP-deficiency causes (episodic) conjugated hypercholanemia, associated with a reduced hepatic BA uptake capacity and renal BA excretion. Finally, Myrcludex B is a specific tool to pharmacologically inhibit NTCP and the NTCP-knockout mouse is an interesting model to study the metabolic effects of conjugated BAs.

Clinical description and genetic analyses of a large cohort of 3402 PSC patients

R. Alberts[1], E.M.G. de Vries[2], C.Y. Ponsioen[2], R.K. Weersma[1] on behalf of the International PSC Study Group, [1]Dept. of Gastroenterology and Hepatology, University of Groningen and University Medical Centre Groningen, Groningen, [2]Dept. of Gastroenterology and Hepatology, Amsterdam Medical Centre, Amsterdam, The Netherlands

Primary Sclerosing Cholangitis is a severe and complex disease. To identify genetic components driving PSC sub-phenotypes, the International PSC Study Group has collected phenotypes for over 3400 PSC patients from 11 countries in Europa, the US and Canada. Collected phenotypes are dates of birth and diagnosis, date and cause of death (non PSC related, liver failure, cholangiosepsis, various cancers), diagnosis (PSC, small duct PSC or PSC with Autoimmune Hepatitis (AIH) overlap), dates of liver transplantations, co-occurrence with IBD, smoking status, date of diagnosis of cholangio-carcinoma (CCA), hepatocellular carcinoma (HCC) or colorectal cancer (CRC) and alka phosphatase levels upon diagnosis. To identify genetic variants underlying these phenotypes, we used genotype data of the same patients, obtained using the Illumina Immunochip. This single-nucleotide polymorphism (SNP) microarray interrogates 195,806 SNPs that were used for within-cases allelic association analysis. Classical HLA alleles were imputed using SNP2HLA. The cohort consists of 3159, 75 and 107 patients with PSC, small duct PSC and PSC with AIH overlap. 26% of patients underwent liver transplantation and 13% a proctocolectomy. 4% developed CRC, 1% gall bladder carcinoma, 6% CCA and 1% HCC. 61% had ulcerative colitis, whereas 11% had Crohn's disease and 3% IBD-U. Mean age at diagnosis for PSC was 39.4 years (SD 14.9) and mean time from diagnosis to first liver transplantation was 9.0 years (SD 10.1). We confirm published associations for AIH in our association analysis comparing PSC patients with and without AIH. The strongest published AIH signal in the HLA region is among the top 5 of our associations (rs2187668, $P = 7.3*10^{-10}$, OR = 2.4). This SNP tags the HLA-DR3-DQA1*05:01-DQB1*02:01 haplotype. The DQA1*05:01 and DQB1*02:01 alleles are the most significant HLA alleles in our study ($P < 5*10^{-7}$). We have suggestive evidence for IL12RB2 ($P = 1.3*10^{-6}$, OR = 2.5), implicated in several autoimmune diseases, to be associated with AIH in PSC patients. We have suggestive evidence for association of TAGAP ($P = 1.8*10^{-5}$, OR = 1.6) and several SNPs on chromosome 20 covering SPATA2, RNF114 and SNAI1 with liver transplantation. Small duct PSC is suggestively associated with a SNP next to BACH2 ($P = 7.5*10^{-6}$, OR = 2.1). Finally, we observe suggestive associations of rs17102823 with CRC ($P = 3.1*10^{-6}$, OR = 2.1) and of multiple SNPs in SLCO4C1 and one SNP ($P = 1.3*10^{-5}$, OR = 3.9) located between CD28 and CTLA4, both involved in T-cell regulation, with HCC.

Conclusion: we describe the largest PSC patient cohort available to date and identify genetic variants underlying important PSC sub-phenotypes.

Evaluation of the first results of the Dutch colorectal cancer (CRC) screening program in a general teaching hospital

A.G.E. van Meijel, L. van Meijel[1], R.P.R Adang[1], [1]VieCuri MC, Venlo, The Netherlands

February 2014 the nationwide colorectal screening program has been introduced in the Netherlands. Ultimately, all people between 55 and 75 years will be invited to participate by returning a faecal occult blood test (iFOBT). If the iFOBT is positive, the participants will be referred to a certified screening centre for a colonoscopy. The aim of this study was to describe the characteristics of and the endoscopic findings in the participants of the Dutch CRC screening program who were referred to our hospital for a colonoscopy between February 10th and October 8th 2014. Characteristics and endoscopic findings were systematically registered and all polyps were (if possible) removed for histopathological investigation. Correlations were assessed by means of chi-square tests and logistic regression analyses. During the study period 349 participants were referred, of whom 329 (94.3%) underwent a colonoscopy. This study population consisted of 200 males (60.8%), had a mean age of 72 years, only 0.9% was ASA 3, 10.3% had a history of polyps/CRC, 28.9% had a family history of CRC and 23,4% used anticoagulant drugs (acetylsalicylic acid excluded). Ultimately, 316 (96.0%) had a complete (first) colonoscopy, in 320 colonoscopies (97.3%) the BBPS was ≥ 6. In 32 participants (9.7%) 34 cancers were diagnosed, 14 (pT1) cancers were endoscopically removed, the remaining 20 cancers (pT1-4,N0-1M0-1) were surgically removed. In 124 participants (37.7%) advanced adenoma(s) (but no cancer) were found en in 104 participants (31.6%) non-advanced adenoma(s) (but no cancer/advanced adenoma) were found. The remaining 69 patients (21.0%) had no or miscellaneous endoscopic abnormalities. Male sex was an independent predictor for CRC (OR=3.074 (95% CI, 1.220-7.744)) and adenoma(s) (OR=2.308 (95% CI, 1.323-4.028)) in our study population. Overall, 698 adenomas were detected in 252 participants with the number of adenomas ranging from 1-20 adenomas per participant. Of these, 176 were advanced adenomas (25.2%) and 522 were non-advanced adenomas (74.8%). Diameters of polyps ranged from 1-70 mm. If polyps ≤ 6 mm had not been removed, this would have saved 470 endoscopical removals with subsequent histopathological investigations, at the cost of 20 missed advanced adenomas.

In conclusion, almost 10% of the participants of the Dutch CRC screening program referred to our hospital had colorectal cancer and in 40.6% of them the pT1 cancer could be removed endoscopically. Another 37.7% had advanced adenoma(s) and 31.6% had non-advanced adenomas. Efforts and costs could possibly be saved by leaving ≤ 6 mm polyps in situ, but this has to be proven in future studies.

Offering colonoscopy to participants with a negative FIT and a first degree relative with CRC increases the detection of advanced neoplasia in a screening program

F.G.J. Kallenberg[1], J.L.A. Vleugels[1], T.R. de Wijkerslooth[1], I. Stegeman[1], M.E. van Leerdam[2], P.M.M. Bossuyt[3], E.J. Kuipers[2], E. Dekker[1], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, [2]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, [3]Dept of Epidemiology and Biostatistics, Academic Medical Center, University of Amsterdam, The Netherlands

Background: In the Netherlands, fecal immunochemical testing (FIT) is used in colorectal cancer (CRC) population screening. However, FIT is known to have suboptimal sensitivity rates. Previous research suggested that having a first degree relative (FDR) with CRC increased the probability of detecting advanced neoplasia (AN). This study aimed to evaluate the diagnostic accuracy of adding family history (FH) of CRC to the FIT-based risk stratification by offering colonoscopy to participants with a positive FIT or FH. Methods: Data were collected in the colonoscopy arm of a previously reported trial in which colonoscopy and CT colonography were compared as primary screening methods. In this trial 6,600 randomly selected, asymptomatic individuals aged 50-75 years were invited to undergo colonoscopy. Participants were asked to complete a questionnaire on FH and to perform a one sample FIT (OC-sensor). Three commonly used FIT positivity-thresholds of 10, 15 and 20 µg Hb/g faeces (50, 75, 100 ng Hb/ml resp.) were used in our statistical analyses. A positivity threshold of 10 µg Hb/g was chosen for the description of results. 2x2 contingency tables were computed for calculating diagnostic test accuracy. AN was defined as CRC or advanced adenoma (AA; adenoma > 10mm, villous histology ≥ 25% or high grade dysplasia). A FH was defined as reporting ≥1 FDR with CRC. Results: of 6,600 invited individuals, 1,426 (22%) agreed to undergo colonoscopy. Both FIT and a complete questionnaire were provided by 1,071 of the participants prior to colonoscopy. Of these participants 100 (9%) had AN (7 CRC, 93 AA) detected during colonoscopy of whom 70 (70%) had a negative FIT (2 CRC, 68 AA). Overall, 173 (16%) individuals were identified as having a FH: AN was detected in 25 (14%) of them including 15 (60%) with a negative FIT, versus 75 (8%) of those without FH, including 49 (65%) with a negative FIT. The odds ratio for AN in participants with a FH but a negative FIT was 1.70 (95% CI: 0.93-3.12) versus participants without a FH and a negative FIT. The sensitivity of FIT-based screening in detecting AN was 36% (95% CI: 27–46) at a specificity of 93% (95% CI: 92–95). Adding FH to FIT-based stratification resulted in a sensitivity of 51% (95% CI; 41–61) at a specificity of 79% (95% CI; 76–82). Comparable trends were seen for higher thresholds of FIT. Conclusions: Amongst FIT negatives, having ≥1 FDR with CRC is associated with an increased risk of AN. Within a FIT-based screening program, identifying those at high risk of developing AN by assessing family history and offering them colonoscopy, increases sensitivity at the cost of specificity.

A family history questionnaire sent to patients undergoing outpatient colonoscopy enhances genetic counseling for hereditary colorectal cancer

K. Kessels[1,2], J.D. Eisinger[1], T.G. Letteboer[3], G.J.A. Offerhaus[4], P.D. Siersema[1], L.M.G. Moons[1], [1]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Flevohospital, Almere, [3]Dept of Clinical Genetics, University Medical Center Utrecht, Utrecht, [4]Dept of Pathology, University Medical Center Utrecht, Utrecht, The Netherlands

Background: Approximately 1 in 5 patients undergoing colonoscopy is at risk of hereditary colorectal cancer (CRC) after assessment of personal and family history (FH). However, assessment of a FH of cancer is known to be insufficient. AIM: To investigate whether introduction of a family history questionnaire (FHQ) sent to patients undergoing colonoscopy, results in an increased adherence to the Dutch guidelines for genetic evaluation and to evaluate adherence to the FHQ. Methods: A FHQ was sent by mail to all patients before undergoing outpatient colonoscopy in a university hospital in the Netherlands in 2013. In April 2014, all patients undergoing colonoscopy from 2010 to 2013 were matched with the database of the genetics department to determine who visited a geneticist. Additional characteristics and referral for genetic evaluation of all patients undergoing colonoscopy in 2013 were retrieved from the electronic medical record (EMR). Adherence to the FHQ was evaluated after exclusion of patients undergoing inpatient colonoscopy and with known hereditary CRC or inflammatory bowel disease. Results: A total of 6,163 patients underwent colonoscopy from 2010 to 2013. Of patients undergoing colonoscopy in 2013, 53/1,421(3.9%) had visited a geneticist by April 2014 compared to 75/4,742(1.6%) patients undergoing colonoscopy from 2010 to 2012 ($p<0.01$). No trend towards increasing visits over the years 2010 to 2012 was found. A total of 974 patients undergoing colonoscopy in 2013 were included to evaluate adherence to the FHQ. Of these, 282(29.0%) returned the FHQ. Personal history of CRC (OR 1.80, 95%CI 1.09-2.98) and previous colonoscopy (OR 1.37, 95% CI 1.03-1.81) were associated with returning the FHQ, whereas personal history of any cancer, age and gender were not. FH was not recorded in the EMR in 393/974(40.3%) patients. In 129/393(32.8%) of these, FH was obtained by a returned FHQ. Referral for genetic evaluation of patients who returned the FHQ was not significantly higher compared to patients who did not ($p=0.06$). In the absence of a recorded FH in the EMR, FH was obtained by a returned FHQ in 12/81(14.8%) referred patients. Eight of these 12(66.7%) were referred due to a positive FH and 4/12(33.3%) due to more than 10 adenomas at colonoscopy.

Conclusion: Introduction of a FHQ sent by mail to patients undergoing outpatient colonoscopy resulted in an increase in genetic evaluations of patients considered at risk for hereditary CRC. Nonetheless, only one-third of patients adhered to the FHQ and only 1% of patients undergoing colonoscopy was referred for genetic evaluation directly attributable to the returned FHQ, making it an ineffective screening tool.

Randomized comparison of surveillance intervals in Familial Colorectal Cancer: The Dutch FAmilial ColorecTal cancer Surveillance study (the FACTS study) Group

S.D. Hennink[1], A.E. van der Meulen-de Jong[1*], R. Wolterbeek[2], A.S.L.P. Crobach[3], M.C.J.M. Becx[4], L.F.S.J. Crobach[5], M. van Haastert[6], W.R. ten Hove[5], J.H. Kleibeuker[7], M.A.C. Meijssen[8], F.M. Nagengast[9], M.C.M. Rijk[10], J.M.J.I. Salemans[11], A. Stronkhorst[12], H.A.R.E. Tuynman[13], J. Vecht[8], M.L. Verhulst[11], W.H. de Vos tot Nederveen Cappel[8], H. Walinga[14], O.K. Weinhardt[15], B.D. Westerveld[8], A.M.C. Witte[5], H.J. Wolters[6], R.A. Veenendaal[1], H. Morreau[3], H.F.A. Vasen[1] *Both authors contributed equally tot this work, [1]Dept of Gastroenterology and Hepatology, [2]Dept of Medical Statistics and Bioinformatics, and [3]Dept of Pathology, Leiden University Medical Center, Leiden, [4]Dept of Gastroenterology, St. Antonius Hospital, Nieuwegein, [5]Dept of Gastroenterology, Diaconessenhuis, Leiden, [6]Dept of Gastroenterology, Martini Hospital, Groningen, [7]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [8]Dept of Gastroenterology, Isala Clinics, Zwolle, [9]Dept of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, [10]Dept of Gastroenterology, Amphia Hospital, Breda, [11]Dept of Gastroenterology, Máxima Medical Center, Eindhoven, [12]Dept of Gastroenterology, Catharina Hospital, Eindhoven, [13]Dept of Gastroenterology, Medical Center Alkmaar, Alkmaar, [14]Dept of Gastroenterology, Reinier de Graaf Gasthuis, Delft, [15]Dept of Gastroenterology, Scheper Hospital, Emmen, The Netherlands*

Colonoscopic surveillance is recommended for individuals with familial colorectal cancer (CRC). However, the appropriate screening interval has not yet been determined. The aim of this randomized controlled trial was to compare a 3-year with a 6-year screening interval. Individuals aged between 45 and 65 years with one first-degree relative with CRC <50 years or two first-degree relatives with CRC were selected. Subjects were excluded if they had 3 or more adenomas at base colonoscopy, while those with 0-2 adenomas were randomized into two groups: A) colonoscopy at 6 years and B) colonoscopy at 3 and 6 years. The primary outcome measure was advanced adenomatous polyps (AAP). Risk factors studied included gender, age, type of family history and base endoscopic findings. 528 patients with 0-2 adenomas at base colonoscopy, were randomized into two groups (A = 262, B = 266). The proportion of subjects with AAP at the first follow-up examination at 6 years in A was higher than the proportion of subjects with AAP at 3 years in B, however the difference was not statistically significant. There was also no statistically significant difference in the proportion of participants with AAP at the final follow-up examination between both groups. Male gender, age and (proximal) adenoma at base were significant predicting factors for adenoma. No significant predictors were found for AAP.
Our findings demonstrate that a 6-year surveillance interval in familial CRC is safe.

Cost-effectiveness of routine screening for Lynch syndrome in colorectal cancer patients up to 70 years of age

A. Goverde[1,2], C.H.M. Leenen[1*], E.W. de Bekker-Grob[3], A. Wagner[2], M.G.F. van Lier[1], M.C.W. Spaander[1], M.J. Bruno[1], C.M. Tops[6], A.M.W. van den Ouweland[2], H.J. Dubbink[4], E.J. Kuipers[1,5], W.N.M. Dinjens[4], M.E. van Leerdam[1,7], E.W. Steyerberg[3], On behalf of the LIMO study group, [*]Both authors contributed equally to this work, [1]Dept of Gastroenterology and Hepatology, [2]Dept of Clinical Genetics, [3]Dept of Public Health, [4]Dept of Pathology, and [5]Dept of Internal Medicine, Erasmus MC, University Medical Center, Rotterdam, [6]Dept of Clinical Genetics, Leiden University Medical Center, Leiden, [7]Dept of Gastroenterology and Hepatology, Antoni van Leeuwenhoek Hospital, Netherlands Cancer Institute, Amsterdam, The Netherlands*

Lynch syndrome (LS) is the most common hereditary cause of colorectal cancer (CRC). Identifying LS carriers among CRC patients is of great importance, since surveillance programs for their affected relatives can reduce CRC morbidity and mortality by 56-70%. However, many LS carriers are still not identified. The aim of this study was to assess the cost-effectiveness of routine molecular screening for LS in CRC patients up to 70 years of age. We routinely screened a population-based series of CRC patients aged ≤70 years for LS by analysis of microsatellite instability, immunohistochemistry and MLH1 hypermethylation, followed by germ mutation analysis in indicated cases. Effectiveness of screening was expressed in life years gained (LYG), based on the number of LS carriers detected among CRC patients and their relatives. Total costs consisted of LS diagnostics and surveillance, including gynaecological surveillance and prophylactic surgery for female LS carriers. We calculated incremental cost-effectiveness ratios (ICERs) comparing different age cut-offs and comparing age-targeted screening with the revised Bethesda guidelines. One-way sensitivity analyses were performed to test the robustness of ICERs. Screening among 1117 CRC patients identified 23 LS carriers, of whom 7 were ≤50, 7 were 51-60 and 9 were 61-70 years of age. Additionally, 70 LS carriers were identified among relatives (14, 42 and 14 per age category respectively). Overall, screening amounted to 76.0 LYG or 15.9, 43.9 and 16.1 LYG per age category. Total costs for LS screening and surveillance increased from €232,573 (€11,075 per LS carrier detected) for LS screening among CRC patients ≤50 years of age to €1,056,916 (€11,365 per LS carrier detected) for screening CRC patients ≤70 years of age. ICERs were €11,541/LYG for LS screening in CRC patients ≤60 years compared with ≤50 years and €19,699/LYG for screening CRC patients ≤70 years compared with ≤60 years. The revised Bethesda guidelines identified 17/23 (74%) LS carriers among CRC patients and 53/70 (76%) LS carriers among relatives. The ICER for LS screening in CRC patients ≤70 years of age was €20,174/LYG compared with LS screening according to the revised Bethesda guidelines. The ICERs were most sensitive to the assumed LYG by relatives. All ICERs remained <€27,000/LYG in sensitivity analyses.

In conclusion, routine LS screening by analysis of microsatellite instability, immune-histochemistry, and MLH1 hypermethylation in CRC patients up to 70 years of age is a cost-effective strategy according to currently accepted standards, with important clinical benefits for LS carriers among CRC patients and their relatives.

Small-bowel surveillance in patients with Peutz-Jeghers syndrome: comparing magnetic resonance enteroclysis and double balloon enteroscopy

A. Goverde[1,2], A. Wagner[2], S.E. Korsse[1], M.E. van Leerdam[1,6], N. Krak[3], J. Stoker[4], H. van Buuren[1], R.M.W. Hofstra[2], M.J. Bruno[1], P. Dewint[1,7], E. Dekker[5], M.C.W. Spaander[1], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Clinical Genetics, and [3]Dept of Radiology, Erasmus MC, University Medical Center, Rotterdam, [4]Dept of Radiology, and [5]Dept of Gastroenterology and Hepatology, Amsterdam Medical Center, Amsterdam, [6]Dept of Gastroenterology and Hepatology, Antoni van Leeuwenhoek Hospital, Netherlands Cancer Institute, Amsterdam, [7]Dept of Gastroenterology and Hepatology, Maasstad Hospital, Rotterdam, The Netherlands

Surveillance of the small-bowel with polypectomy of significant polyps (SP, defined as polyps ≥15mm in diameter) prevents polyp-related complications in Peutz-Jeghers syndrome (PJS). However, evidence for the optimal imaging technique for these patients is lacking. Therefore, we aimed to compare the diagnostic yield and patient preference of Magnetic Resonance Enteroclysis (MRE) and Double Balloon Enteroscopy (DBE) in PJS. Adult PJS patients recruited from two academic centers underwent MRE followed by a proximal DBE with polypectomy of SP within 20 weeks. The endoscopists were blinded for the MRE results. For DBE patients were consciously sedated using midazolam and fentanyl intravenously or were under general anaesthesia with propofol. We compared the number of SP and total number of polyps detected by MRE and DBE. Patients' perception regarding shame, pain, burden and duration of both procedures were assessed through questionnaires, as well as their preference for future surveillance. Fifteen PJS patients, 67% males with a median age of 47 (IQR 39-53) years underwent both MRE and DBE. The median maximal insertion depth for DBE was 270cm (IQR 160-340cm). SP were identified by MRE and/or DBE in 12/15 (80%) patients. Agreement between MRE and DBE on the presence of SP was 87% (13/15) and both methods identified 11 patients with SP. Significantly more polyps were detected by DBE compared with MRE (154 vs. 93, p=0.03), however the number of SP was comparable for both techniques (both 47, p=0,37). Patients' perception regarding shame and burden at preparation and during both procedures did not differ significantly between MRE and DBE. However, patients reported significantly more pain during the preparation for MRE compared to DBE (moderate vs. no pain, p=0.02), although perception of pain during the procedures was comparable (both mild, p=0.89). Significantly more patients perceived the procedure as taking much time for MRE compared with DBE (38.5% vs. 8.5%, p=0.05). For future small-bowel surveillance 10/13 (77%) patients preferred DBE over MRE (p=0.09).

Conclusion: Our results suggest that MRE and DBE have comparable diagnostic yield of clinically relevant polyps ≥15mm in diameter. Although DBE resulted in incomplete small-bowel visualization in all patients, it allows for direct intervention and was preferred over MRE by patients in this series. Based on the MRE results, 11/15 (73%) patients had an indication for DBE with polypectomy. Larger cohorts of PJS patients are needed to fully evaluate the diagnostic yield of DBE compared with other diagnostic modalities.

Frequent use of antibiotics and colorectal cancer risk – results of a nested case-control study

V.K. Dik[1], M.G.H. Van Oijen[1,2], H.M. Smeets[3,4], P.D. Siersema[1], [1]Dept of Gastro-enterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Medical Oncology, Academic Medical Center, University of Amsterdam, Amsterdam, [3]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, [4]Achmea Health Insurance, Amersfoort, The Netherlands

Introduction: Microbiotical dysbiosis induced by a Western diet seems to be associated with an increased risk of developing colorectal cancer (CRC). Few studies have also evaluated other factors with an effect on the colonic microbiota and their association with CRC risk. Aims & Methods: We investigated whether chronic use of antibiotics is associated with an increased risk of developing CRC. Data on the use of antibiotics and comedication were extracted from a health insurance database for subjects with a Diagnostic Related Group (DRG) for CRC between 2006-2011 and four age- and sex-matched controls without CRC. Antibiotic use was categorized according to the number of prescriptions during a 5-year follow-up period (1-6 years prior to CRC). Multivariable conditional binary logistic regression analysis was used to estimate odds ratios (OR) and 95% confidence intervals (95%CI) for different levels of use. Results: A total of 4,029 cases (47% male, mean age at diagnosis 71±11 years) and 15,988 controls were included. Cases and controls only differed by more NSAIDs prescriptions in cases ($p<0.01$). Antibiotics had been prescribed to 2,630 (65.3%) cases and 10,234 (64.0%) controls ($p=0.13$). An increasing number of prescriptions for antibiotics was associated with an increasing risk of CRC (multivariable OR for high (≥8 prescriptions) vs. no prescriptions: 1.26, 95%CI 1.11–1.44, p-trend<0.01). For each increase of 5 prescriptions (on average 1 per follow-up year), the OR for CRC was 1.05 (95%CI 1.01–1.09). Both anti-aerobic agents (multivariable OR for high (≥8 prescriptions) vs. no prescriptions: 1.25, 95%CI 1.08–1.45) and anti-anaerobic agents (multivariable OR for high (≥5) vs. no prescriptions: 1.45, 95%CI 1.07–1.97) were associated with CRC risk.
Conclusions: We found a dose-dependent association between the use of antibiotics, especially when used frequently, and an increasing risk of developing CRC. Future studies need to establish under which conditions the use of antibiotics increases the risk of developing CRC.

Are we missing serrated polyposis syndrome patients?

Y.J. van Herwaarden[1], P. Dura[1], S. Pape[1], F.M. Nagengast[1], T.M. Bisseling[1], I.D. Nagtegaal[2], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands

Serrated polyposis syndrome (SPS) is a new and under recognised colorectal cancer (CRC) predisposition syndrome. Previous studies reported miss-rates of SPS diagnosis varying from 40 to 82%.[1, 2] Since SPS patients and their first degree relatives have an increased risk of CRC, early recognition is important. We aimed to determine the miss-rate of SPS during follow-up. We retrospectively identified patients diagnosed with ≥1 colorectal polyp or carcinoma detected at our center between 1986 and 2013 using the nation-wide pathology registry. A cumulative polyp count was scored for adenomatous and serrated polyps per patient. Size and location of serrated polyps was recorded to assess if patients fulfilled the WHO criteria for SPS. Based on the available diagnosis in the patient files, miss-rate and 95% confidence interval (CI) were calculated. We randomly assessed 4000 patients of which 1587 (39.4%) had ≥ 1 serrated polyp. Sixteen patients fulfilled the WHO criteria with a median number of 24 serrated polyps (range 15-59) and 2 adenomas (range 0-9). In four patients no prior SPS diagnosis was made, leading to a miss-rate of 25.0% (95%CI 3.7-46.2). Duration of follow-up varied from 2 to 16 years in these missed cases. In three out of these four patients familial CRC was diagnosed instead of SPS. These patients were under strict follow-up with surveillance intervals ranging from 1 to 6 years. The diagnosis in the other patient was probably missed because the majority of serrated polyps had been removed before the formulation of the WHO criteria for SPS in 2000 and the pathology reports were not easily available. Of the patients diagnosed with SPS only one had a delay of 2 years before diagnosis, however, the surveillance interval (every 2 years) was adequate. A fifth patient fulfilling the SPS criteria was diagnosed with Lynch syndrome based on a MSH2 mutation, and as such was not marked as a missed case.

Conclusions: The miss-rate for diagnosis of SPS is significant, even during longer follow-up with repeated colonoscopies. Failure to recognize SPS was the result of not systematically applying the WHO criteria or the unavailability of older pathology reports to the clinician. Awareness of this CRC predisposition syndrome needs to be raised to lower the miss-rate of SPS.

Training on detection and resection of nonpolypoid colorectal neoplasms reduces the postcolonoscopy colorectal cancer

R.J.J.M. Marx[1], C.M.C. le Clercq[1], R.M.M. Bogie[1], B. Winkens[2], J.W. Kruimel[1], J. Conchillo[1], R.J.J. de Ridder[1], T. Kaltenbach[3], R. Soetikno[3], A.A.M. Masclee[1], S. Sanduleanu[1], [1]Dept of Internal Medicine, Division of Gastroenterology and Hepatology, and [2]Dept of Methodology and Statistics, Maastricht University Medical Center, Maastricht, The Netherlands, [3]VA Healthcare System, Palo Alto, Stanford School of Medicine, United States of America

Nonpolypoid colorectal neoplasms (NP-CRN) contribute to the development of PCCRC. Data is lacking if training in the detection of NP-CRN can lead to the reduction of PCCRC rate. We hypothesized that such training can lead to a measurable reduction of PCCRC rate. In this prospective cohort study, we examined the PCCRC rate and etiology after implementation of systematic training on the detection and endoscopic resection of NP-CRN. Before the commencement of the study, we trained all endoscopists, faculty and trainees at our university hospital on the detection and endoscopic resection of NP-CRN, using lectures, video training and individual feedback. We then prospectively studied all patients undergoing elective colonoscopy, from February 2008 to February 2012. We excluded patients with IBD, hereditary CRC syndromes or a history of CRC. We retrieved all newly diagnosed CRC cases from February 2008 to October 2014, using the Nationwide Pathology Database and the Netherlands Cancer Registry. We cross-linked extensive patient information from hospital registry to CRC data. We defined a PCCRC as a CRC diagnosed 6-60 months after a colonoscopy which excluded CRC. We applied an algorithm based on the time period from previous colonoscopy to CRC diagnosis, the stage of the tumor and index colonoscopic findings, to ascertain the potential reasons of PCCRCs: missed lesions, inadequate examination/surveillance, incomplete resection or newly developed CRC.After training, the PCCRC rate was lower than before (0.7 PCCRCs/1,000 colonoscopies vs 2.0 PCCRCs/1,000 colonoscopies). Indication for colonoscopy was symptoms (84.5%), screening (6.6%) or surveillance (8.9%). After training, 9 patients (mean age (SD): 78.6 (4.0) yrs, 56% male) from a cohort of 8,217 patients (mean age (SD): 59.1 (15.8) yrs, 46% male) enrolled were diagnosed with a PCCRC during 35,428 PYFU, corresponding to 0.25 PCCRC/1,000 PYFU. Five of the 9 PCCRCs were proximally located and 8 were early stage (I and II); all 3 T1-2N0 PCCRCs were NP-CRNs. On histopathology, 2 were poorly and 7 moderately differentiated; 2 were mucinous adenocarcinomas. PCCRCs were diagnosed on average 35 months after the index colonoscopy. The most likely reasons for PCCRC included: non-adherence to surveillance (n=1), inadequate bowel examination (n=2), missed lesions (n=4) and newly developed CRC (n=2). We could not attribute any PCCRC to incomplete resection.

Conclusion: The PCCRC rate declined after training on detection and endoscopic resection of flat neoplasms. Development of practical skills to recognize and treat nonpolypoid neoplasms is a useful intervention to minimize the PCCRC rate.

Statin use after diagnosis improves survival in colon cancer patients.

**P.W. Voorneveld[1], *M.S. Reimers[2], E. Bastiaannet[2,3], R.J. Jacobs[1], R. van Eijk[4], M.M.J. Zanders[5], R.M.C. Herings[6], M.P.P. van Herk-Sukel[6], L.L. Kodach[1], T. van Wezel[4] , P.J.K. Kuppen[2], H. Morreau[4], C.J.H. van de Velde[2], **J.C.H. Hardwick[1], **G.J. Liefers[2,1] Gastroenterology & Hepatology, Leiden University Medical Center, [2]Surgery, Leiden University Medical Center, [3]Gerontology & Geriatrics, Leiden University Medical Center, [4]Pathology, Leiden University Medical Center, Netherlands, [5] Research, Comprehensive Cancer Centre the Netherlands, [6]PHARMO Institute for Drug Outcomes Research, The Netherlands, * § These authors contributed equally*

The use of statins has been associated with a reduced incidence of colorectal cancer. Potentially, statins may also have an influence on survival of colon cancer patients when used after diagnosis. The primary aim of this observational study was to evaluate the influence of statin use after diagnosis of colon cancer on overall survival. The secondary aim was to investigate the molecular background in which statins are effective adjuvant therapeutic agents, specifically KRAS mutational status and Bone Morphogenetic Protein pathway functionality. Data was derived from the PHARMO database network (PHARMO, Netherlands) and was linked to a colon cancer cohort (Eindhoven Cancer Registry). A Tissue Micro Array (TMA) consisting of 999 colon cancer specimens was constructed from patients who had a surgical resection between 2002 and 2008. Survival was analyzed with statin user status after diagnosis as a time-dependent covariate. Multivariate Poisson regression survival models were used to study the effect of statins on overall survival (OS). The tumours were analyzed for SMAD4, BMPR1a, BMPR1b and BMPR2 expression and KRAS mutations to perform stratified analyses for intact BMP signaling status and KRAS mutation status. In this cohort, 21.0% (210/999) of the patients were defined as statin users after colon cancer diagnosis. Statin use after diagnosis was significantly associated with an improved OS with an adjusted Rate Ratio (RR) of 0.67 (95% CI 0.51-0.87, P=0.003). When stratified for intact BMP signaling status, survival benefit of statin use after diagnosis was stronger in tumors with intact BMP signaling (adjusted RR 0.46, 95% CI 0.29-0.74, P=0.001) than in tumors with a non-intact BMP signaling pathway (adjusted RR 0.75, 95% CI 0.53-1.06, P=0.106). Statin use after diagnosis was not associated with an improved OS in KRAS wild-type tumors (Adjusted RR 0.81, 95% CI 0.56-1.18, P=0.273) or KRAS mutated-tumors (Adjusted RR 0.59, 95% CI 0.35-1.03, P=0.062).

Conclusion: Statin use after diagnosis is associated with an improved overall survival in colon cancer patients. This survival benefit is more prominent in tumors with intact BMP signaling. The survival benefit is independent of KRAS mutation status.

The efficiency and efficacy of a multidisciplinary team meeting

Y.L. Basta[1,2], O.L. Baur[3], S. van Dieren[2], J.H. Klinkenbijl[4], P. Fockens[1], K.M. Tytgat[1], On behalf of GIOCA team, [1]Dept of Gastroenterology, and [2]Dept of Surgery, Academic Medical Center, Amsterdam, [3]Student of Medicine, Academic Medical Center, Amsterdam, [4]Dept of Surgery, Gelre Hospitals, Apeldoorn, The Netherlands

Background: Many healthcare settings have accepted multidisciplinary care as best practice. Therefore, avenues towards improving the efficiency and efficacy of Multidisciplinary teams (MDTs) should be investigated. This study aimed to identify and quantify variables that influence the efficiency and efficacy of an MDT in a tertiary referral center in the Netherlands. Methods: Consecutive MDT meetings were prospectively studied, during 6 months. Efficiency was assessed by measuring the duration of the meeting. Efficacy was assessed by determining the proportion of accurately diagnosed patients by the MDT. Variables influencing the efficiency and efficacy of MDT meetings were identified with linear and logistic regression models, supplemented with a modified Poisson regression. Results: In 74 MDT meetings with a mean duration of 63 min (SD +/-14), 691 discussions of 551 patients took place. A median of 10 (IQR 6 – 14) patients with a mean discussion time of 05:43 min (SD +/- 2) were discussed per MDT meeting.
Of all referrals, the diagnosis was accurately altered for 120 (21.8%) patients. The MDT accurately diagnosed 94.0% of all referrals, of which 88.9% at the first MDT. This was not influenced by the duration of the MDT or number of patients discussed (95%CI 0.99 – 1.0; p=0.75; 95%CI 0.9 – 1.1; p=0.87, resp.). The chance of a correct diagnosis increased when patients' cases were presented by the treating doctor (RR 1.2 95%CI 1.0 – 1.5). At every MDT meeting a median of 19 interruptions took place, each adding 0:12 minutes to the duration (95%CI 0:0018 – 0:18; p=0.046). Late arrival of surgeons or medical oncologists drastically increased the time per MDT spent not discussing patients (12:54 and 24:54 minutes, respectively).
Conclusion: The duration of the meeting or the number of patients discussed, did not influence number of correct diagnosis made by the MDT. A presentation by the treating doctor increased the chance of an accurate diagnosis. Late arrival of surgeons or medical oncologists drastically increased the time per MDT not discussing patients.

Higher prevalence of cystic lesions of the pancreas in first degree relatives of familial pancreatic cancer cases than in carriers of pancreatic cancer-prone gene mutations

I.C.A.W. Konings[1], F. Harinck[1], J.W. Poley[1], C.M. Aalfs[2], A. van Rens[3], N.C. Krak[4], A. Wagner[5], C.Y. Nio[6], R. Sijmons[7], H. van Dullemen[8], F.P. Vleggaar[9], M.G.E.M. Ausems[10], P. Fockens[11], J.E. van Hooft[11], M.J. Bruno[1], On behalf of the Dutch research group on pancreatic cancer surveillance in high-risk individuals, [1]Dept of Gastroenterology and Hepatology, Erasmus MC, University Medical Center, Rotterdam, [2]Dept of Clinical Genetics, Academic Medical Center, Amsterdam, [3]Family Cancer Clinic, The Netherlands Cancer Institute, Amsterdam, [4] Dept of Radiology, Erasmus MC, University Medical Center, Rotterdam, [5]Dept of Clinical Genetics, Erasmus MC, University Medical Center, Rotterdam, [6]Dept of Radiology, Academic Medical Center, Amsterdam, [7]Dept of Clinical Genetics, University Medical Center Groningen, Groningen, [8]Dept of Gastroenterology and Hepatology, University Medical Center Groningen, Groningen, [9]Dept of Gastroenterology and Hepatology, University Medical Center Utrecht, Utrecht, [10]Dept of Clinical Genetics, University Medical Center Utrecht, Utrecht, [11]Dept of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

Individuals at high risk for developing pancreatic cancer (PC) include: (1) first degree relatives (FDR) of familial PC cases (FPC), and (2) carriers of a known PC-prone gene mutation. The genes involved in the development of FPC are unknown. Consequently, given the presumed autosomal dominant inheritance pattern of FPC, by definition half of these FPC-individuals are not at increased risk. The distribution of detected abnormalities in both risk groups is unknown. The aim of this study was therefore to compare detected abnormalities between both risk groups.Individuals with an estimated lifetime risk of developing PC>10% underwent annual pancreatic surveillance with magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) in an ongoing prospective multicenter study. Individuals included are: (1) FDR of FPC cases, defined as families with PC in ≥2 FDR, in ≥3 relatives, or in ≥2 relatives with ≥ 1 case aged <50 at diagnosis, and (2) mutation carriers of PC-prone gene mutations (all CDKN2A mutation carriers and Peutz-Jeghers patients; BRCA1 or 2 mutation carriers, p53 mutation carriers and Lynch syndrome patients with ≥2 family members affected with PC). A total of 172 individuals were included; 82 FPC-individuals and 90 mutation carriers. FPC-individuals were significantly older at inclusion than the mutation carriers (mean age 54 vs 49 respectively, P=0.001). There was no significant difference in follow-up between groups (mean 44 months in FPC-individuals vs 41 months in mutation carriers, P=0.350). A total of 47 cysts were detected in 82 FPC-individuals (57%) and 36 cysts in 90 mutation carriers (40%, P=0.023). There was no difference in the detection of cystic lesions <10 mm (n=43 (52%) vs. n=36 (40%), P=0.102), however, cysts ≥10 mm were significantly more prevalent in FPC-individuals than in mutation carriers (n=12 (15%) vs n=4 (4%), P=0.022) as well as presumed side-branch IPMNs (n=24 (29%) vs n=14 (16%), P=0.030). The number of lesions per individual, the presence and number of chronic pancreatitis features, and the age of individuals at diagnosis of a cystic lesion did not differ between both groups.

In conclusion, cystic lesions are more frequently detected during surveillance for pancreatic cancer in FPC-individuals (57%) compared to PC prone gene mutation carriers (40%), more specifically cysts ≥10 mm and presumed side-branch IPMNs. This is remarkable given the fact that half of these FPC-individuals are probably not at increased risk to develop pancreatic neoplasia (presumed autosomal dominant inheritance of unknown mutation) and our finding might imply a difference in pathophysiology between both groups.

Endoscopic ultrasound based surveillance of non-functioning pancreatic neuroendocrine tumors in multiple endocrine neoplasia type 1 syndrome; a retrospective cohort study to assess growth-rate

W.F.W. Kappelle[1], G.D. Valk[2], M. Leenders[1], P.D. Siersema[1], F.P. Vleggaar[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Internal Medicine, University Medical Center Utrecht, Utrecht, The Netherlands

In multiple endocrine neoplasia type 1 (MEN1), endoscopic ultrasound (EUS) is used to identify pancreatic neuroendocrine tumors (PNETs). The role of surveillance in small (<20 mm), non-functioning tumors is unclear, mostly because the natural course of these lesions is largely unknown. Therefore, current advice is to perform EUS at regular intervals (6-12 months). We aimed to assess the incidence of small, asymptomatic PNETs in MEN1 syndrome using EUS and to assess the growth rate of the largest lesion per patient.All linear array EUS procedures in patients with MEN1 syndrome between May 2002 and November 2014 at the UMC Utrecht were identified in our endoscopy database. Number, size and location of PNETs were recorded. Average growth rate of lesions <20 mm at initial EUS and the association between time and number of lesions was calculated with mixed model linear regression analysis.Forty-eight patients were included (17 males [35%]); mean age at the first procedure was 41.4 years (SD 13.8). A total of 156 lesions were identified (median 2, IQR 1-5); median size of the largest lesion was 11 mm (IQR 7-18 mm) x 10 mm (IQR 6-16 mm). Thirty-nine patients (81%) had >1 EUS-procedure, with a total of 166 EUS procedures (median 4, IQR 2-5) and a median follow-up of 37 months (IQR 13-63). 6/39 patients (15%) had a lesion ≥20 mm during the first EUS. In 4 of the remaining 33 patients (12%), a lesion ≥20 mm was found during surveillance EUS-procedures after a median of 27 months (range 12-30)(number needed to test: 8.3). Mean growth rate of the largest lesion per patient was 0.16 mm per year (P=0.26). New PNETs were observed with a mean incidence of 0.69 lesions per patient per year (P<0.001). Nonetheless, the 4 lesions that were found to be ≥20 mm during surveillance were already seen at the initial EUS. In total, 8/48 patients underwent surgery (16.7%); 3 patients (6%) after the first EUS-procedure and 5 patients after a later EUS-procedure (13%). In 5/8 patients (63%), size of the largest lesion was ≥20 mm at first EUS-procedure. In one of the other three patients, size of the largest lesion had increased to ≥20 mm at a subsequent EUS-procedure (933 days after the first EUS-procedure).

Conclusions: Annual growth rate of small PNETs is low and the interval between EUS procedures could probably be prolonged without compromising safety. Clinical relevance of new small lesions found during surveillance appears limited, as all lesions ≥20 mm during surveillance EUS were already found during the initial EUS.

Hospital of diagnosis for pancreatic cancer influences surgery rate and survival in a nationwide analysis: a plea for further centralization

M.J.A.M. Bakens[1,2], Y.R.B.M. van Gestel[2], M. Bongers[1], M.G.H. Besselink[3], C.H.C. Dejong[4], V.E.P.P. Lemmens[2], I.H.J.T. de Hingh[1], On behalf of the Dutch Pancreatic Cancer Group (DPCG), [1]Dept of Surgery, Catharina Hospital, Eindhoven, [2]Netherlands Cancer Registry, Comprehensive Cancer Organisation Netherlands, Eindhoven, [3]Dept of Surgery, Academic Medical Center, Amsterdam, [4]Dept of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

Since surgical resection is the only chance for long-term survival, determining the resectability of a pancreatic tumor is a crucial step. Although centralization for surgical expertise has improved the resection rates of pancreatic cancer in recent years, diagnostic work-up for M0-pancreatic cancer patients is not centralized in the Netherlands. The current study investigated whether the hospital of initial diagnosis influenced the chance of undergoing surgery and the effect on survival. All patients diagnosed with M0-pancreatic cancer between 2005 and 2012 in The Netherlands were included. Population-based data were obtained from the nationwide Netherlands Cancer Registry.All 97 hospitals were classified as either “pancreatic center” or “non-pancreatic center”, based on high-volume (>20/year) pancreatoduodenectomies performed in 2012. Groups were compared using chi-square tests. The relationship between diagnostic center and the chance of undergoing surgery was analysed by multivariable logistic regression. The influence of hospital of diagnosis on overall survival was assessed using multivariable Cox regression analysis. Seventeen hospitals were designated as a pancreatic center (17.5%). Of the 7276 included patients, 2657 (36.5%)underwent surgery with a curative intent. This proportion was 51% of patients diagnosed in pancreatic centers and 30% for non-pancreatic centers. Actual resection was done in 42% for pancreatic centers and 23.2% for non-pancreatic centers.In multivariable analysis, patients diagnosed in a pancreatic center were more likely to undergo surgery with a curative intent (OR 2.11 95%CI 1.88-2.36). Diagnosis in a pancreatic center was associated with improved survival compared to diagnosis in a non-pancreatic center (HR 0.93; 95%CI 0.88–0.99).

Conclusions: In this nationwide analysis, patients diagnosed with M0-pancreatic cancer in a pancreatic center were more likely to undergo a potentially curative resection and had better survival. This suggests that patients with M0-pancreatic cancer who are not referred for resection should undergo assessment by a specialized team.

Clonal diversity based on single-cell analysis predicts progression in Barrett's esophagus

M.R. Timmer[1,2], P. Martinez[3], C.T. Lau[1,2], P. Fockens[1], J.J.G.H.M. Bergman[1], C.C. Maley[4], T.A. Graham[3], K.K. Krishnadath[1,2], [1]Dept of Gastroenterology and Hepatology, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [2]Center for Experimental and Molecular Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [3]Centre for Tumour Biology, Barts Cancer Institute, London, United Kingdom, [4]Center for Evolution and Cancer, University of California, San Francisco, United States of America

Barrett's esophagus (BE) is associated with a low annual risk of developing esophageal adenocarcinoma (EAC). Predictive biomarkers would be of great clinical value in facilitating more cost-effective surveillance. Here we attempted to evaluate the predictive value of clonal diversity in a large prospective multi-center cohort of Barrett's patients without dysplasia at baseline. We have performed single-cell genetic analysis on brush cytology specimens from patients with non-dysplastic BE. Genetic abnormalities were detected by DNA fluorescence in situ hybridization using two probe sets including probes for CEP17, Her-2, P53 and P16 (Set 1) and 20q, MYC and the chromosomal centromeric probes 7 and 17 (Set 2). For each individual cell, a 'per cell' signal pattern was recorded for each set to provide detailed information on genetically different clones. Clones were defined as the collection of cells with the same genotype. We then aimed to risk stratify patients according to measures of clonal diversity (i.e. richness, Simpson diversity, Shannon diversity and average pairwise distance) using Cox proportional-hazard models. Endpoints were progression to high-grade dysplasia (HGD) or EAC. Thresholds for each variable (e.g. a threshold to distinguish normal from abnormal) were determined by a bootstrap-resampling procedure. A total of 320 patients (81% men; mean age 59 years ±12; median BE length 2 cm) were followed for a median of 43 (95% CI 40-46) months during which 20 patients progressed to HGD (n=8) or EAC (n=12). Only 30 patients displayed a single genotype throughout their respective cell population in set 1, and 107 in set 2 (9.4 % and 33.4%, respectively). The diversity obtained from set 1 was significantly higher than the one obtained from set 2 (p=0.0001, paired t-test), owing to the prominence of P16 and P53 abnormalities which were assayed in set 1. All measures of clonal diversity, except for the Simpson diversity (set 1), were significantly associated with progression.

Conclusion: Quantification of genetic diversity can be considered a proxy measure of the evolutionary process that underpins carcinogenesis in Barrett's Esophagus. In our cohort, measures of clonal diversity based on single-cell genetics predict progression to high-grade dysplasia or adenocarcinoma. Our data support the hypothesis that Barrett's segments with higher levels of genetic diversity likely indicate more evolvable lesions.

High prevalence of Barrett's esophagus and histological inflammatory changes in patients after esophageal atresia repair

F.W.T. Vergouwe[1,2], H. IJsselstijn[2], K. Biermann[3], R.M. Wijnen[2], M.J. Bruno[1], M.C. Spaander[1], [1]Dept of Gastroenterology and Hepatology, and [3]Dept of Pathology, Erasmus MC, University Medical Center, Rotterdam, [2]Dept of Pediatric Surgery, Erasmus MC, University Medical Center, Sophia Children's Hospital, Rotterdam, The Netherlands

Esophageal atresia (EA) is a rare congenital anomaly (1:3500 live births) and requires surgical correction shortly after birth. Survival rates now exceed 90%. After EA repair gastroesophageal reflux (GER) is reported in 25-62% of children and adults. High incidence of GER and increased survival in EA patients raises concerns about the possibility of an increased risk of Barrett's esophagus (BE) and esophageal cancer. Incidence of BE amongst adults in the general population is 1.6% and predominantly diagnosed in middle-aged males (±55 years). In this follow-up study we assessed the prevalence of GER and BE after EA repair. EA can be classified according to the Gross classification: Type A: EA without trachea-esophageal fistula (TEF), type B: EA with proximal TEF, type C: EA with distal TEF (most common) and type D: EA with proximal and distal TEF. Since 2011, all patients (age≥17years) with a history of EA repair are invited for gastroscopy with random biopsies at the gastroesophageal junction (GEJ) and 4-quadrant biopsies in case of BE. Clinical, endoscopic and histological data are prospectively collected. To date 70 adults (61.4% male) with a median age of 21.6 years (range 16.8-52.8 years) underwent a gastroscopy. Type of EA according to Gross: type A was found in 9 (12.9%) patients, type C in 60 (85.7%) patients and type D in 1 (1.4%) patient. History of GER, confirmed by pH metry, X-esophagus or gastroscopy in childhood, was present in 53 (75.7%) patients, 20 (28.7%) of whom underwent fundo-plication surgery. At baseline, 22 (31.4%) patients had GER complaints and 8 (11.4%) patients used PPIs. Endoscopic findings were: BE in 17 (24.3%) patients with a circumferential extent up to 2cm and maximum extent up to 6cm, active esophagitis in 7 (10%), inlet patch in 8 (11.4%) and no abnormalities in 37 (52.9%) patients. Histology revealed BE in 6 (8.6%) patients all without dysplasia with a median age of 31.7 years (range 20.9-45.3 years) (83.3% male). Chronic inflammation was found in 41 (58.6%) patients, active esophagitis in 4 (5.7%) patients and in 16 (22.9%) patients inflammatory changes were absent. One male had developed squamous cell carcinoma of the distal esophagus at the age of 44 years.

Conclusions: More than half of the adult patients after EA repair have significant inflammation at the GEJ. In these patients the prevalence of BE is fivefold increased compared to the general population and is present at a much younger age. These findings may signify important and relevant clinical implications including use of PPI and lifelong endoscopic follow-up by experts to facilitate early diagnosis of clinically relevant lesions.

T1b esophageal adenocarcinoma: retrospective cohort study on patient management and risk of metastatic disease

D.W. Schölvinck[1,2], H.T. Künzli[1,2], S.L. Meijer[3], C.A. Seldenrijk[4], J.J.G.H.M. Bergman[2], B.L.A.M. Weusten[1,2], [1]Dept of Gastroenterology and Hepatology, and [4]Dept of Pathology, St. Antonius Hospital, Nieuwegein, [2]Dept of Gastroenterology and Hepatology, and [3]Dept of Pathology, Academic Medical Center, Amsterdam, The Netherlands

Esophagectomy for submucosal (T1b) esophageal adenocarcinoma (EAC) is generally advised in order to optimize patient outcome given the risk of concurrent (occult) LN metastasis (LNM). However, severe comorbidity might preclude these patients from surgery. The aim of our study was to assess the proportion of patients referred for surgery, and to evaluate the incidence of metastatic disease in T1b EAC. Between 2001 and 2011, all patients undergoing diagnostic endoscopic resection (ER) for EAC in two centers in the Netherlands were reviewed. Only patients with histopathologically proven submucosal tumor invasion were included. Based on the ER specimen, T1bEAC's were divided into tumors which were removed radically (R0; tumor-negative vertical resection margin (VRM)) and irradically (R1; tumor-positive VRM). Subsequently, in the R0-group, EAC's were classified as either low-risk (LR; submucosal invasion <500nm, G1-G2, no lymphovascular invasion (LVI)) or high-risk (HR; deep submucosal invasion >500nm, and/or G3-G4, and/or LVI). Data on patient management (esophagectomy versus conservative management) and outcome were assessed. Metastatic disease was defined as either LNM in surgical resection specimen, or evidence of malignant disease during follow-up (FU). 62 patients (49 male, median age 70 years) with a T1b EAC were included, of which 21 patients underwent an endoscopic R1-resection, and 41 a R0-resection. Of the R0-resections, 13 were classified as LR, and 28 as HR. Esophagectomy was performed in 10/21 (48%) of the R1-resections, in 10/28 (36%) of R0-HR patients, and in only 1 in the R0-LR group. In patients not undergoing surgery (n=41), the median FUuntil metastatic disease or end of study was 52 (IQR 23 - 74) months. In the R1 group, metastatic disease was diagnosed in 6 (28,5%) patients (3/10 esophagectomy patients, 3/11 non-surgical patients). In the R0-HR group, evidence of metastatic disease was found in 4 (14.3%) patients (1/10 esophagectomy patients, 3/18 non-surgical patients). None of the 13 R0-LR patients developed metastatic disease. During FU, 20 (49%) of the 41 non-surgical patients died: 5 due to disease progression (median survival 8 [range 4-68] months), and 15 due to unrelated causes (median survival 34 (IQR 17 – 62) months).

Conclusions: In low-risk T1b EAC, the risk of metastatic disease after a radical ERappears to be very low. In high-risk T1b EAC, even after irradical ER, esophagectomy is performed in less than 50% of patients. Given the reasonable disease-free survival, conservative management of these patients seems to be a valid alternative when surgery is not an option due to co-morbidity.

SOX2 and P53 protein expression predicts response to preoperative chemo-radiotherapy in patients with esophageal adenocarcinoma

S. van Olphen[1,2], K. Biermann[2], B.P.L. Wijnhoven[3], M.C.W. Spaander[1], A. van der Gaast[4], J.B. van Lanschot[3], M.J. Bruno[1], L.H.J. Looijenga[2*], *Both authors contributed equally to the work, [1]Dept of Gastroenterology and Hepatology, [2]Dept of Pathology, [3]Dept of Surgery, and [4]Dept of Medical Oncology, Erasmus University Medical Center, Rotterdam, The Netherlands*

Objective: Preoperative chemoradiotherapy has recently become common practice in treatment of esophageal cancer with a gain in 5- year survival of 10-15%. However, a significant proportion of patients do not respond well and experiencing unnecessary severe side-effects. Accurate risk-stratification of patients using informative biomarkers before therapy may help to avoid unnecessary morbidity due to ineffective treatment. The aim of this study was to investigate the correlation between the expression of SOX2 and P53 in pre-treatment tumor biopsies and grade of pathological tumor response in resected specimen of patients with esophageal adenocarcinoma (EAC) treated with neoadjuvant chemoradiotherapy (nCRT). Methods: All EAC patients who received nCRT according to the CROSS regimen followed by esophagectomy, between January 2003 and July 2011 at the Erasmus University Medical Center, were included. SOX2 and P53 protein expression was detected by immunohistochemistry on all pre-treatment tumor biopsies and scored independently by two investigators who were blinded for clinical outcome. Aberrant expression was defined as negative expression of SOX2 and overexpression or complete loss of P53 expression. The overall Tumor Regression Grade (TRG) was evaluated using the Mandard scoring system. Patients with TRG 1 or TRG 2 were classified as major responders (ie, < 10% of tumor cells remaining), whereas patients with TRG 3 or TRG 4 were classified as minor responders (ie, > 10% of tumor cells remaining). Results: In total 77 consecutive patients were included. Forty (53%) patients had a pathological major response (TRG 1-2) and 37 (47%) a minor response (TRG 3-4). In pre-treatment biopsies aberrant SOX2 and P53 expression was seen in 40% (31/77) and 83% (64/77), respectively. A major response was significantly associated with an aberrant SOX2 expression (OR 3.9, 95% CI: 1.5 - 10.2, p=0.005) and aberrant p53 expression (OR 4.5, 95% CI: 1.15 – 18.2, p=0.031). Aberrant expression of both biomarkers increased the probability of a major response in the individual patient (OR of 5.6; 95% CI: 2.1 - 14.9, p= 0.001), with a sensitivity of 68%, specificity of 73% and a positive predictive value of 73%.

Conclusion: SOX2 and P53 expression in the pre-treatment biopsies predict response to nCRT in patients with EAC. These biomarkers might help to identify patients who are likely to benefit most from this multimodality treatment.

The impact of organ failure on mortality in necrotizing pancreatitis

O.J. Bakker[1], N.J. Schepers[2,3*], M.G. Besselink[4], U. Ahmed Ali[1], T.L. Bollen[5], H.G. Gooszen[6], H.C. van Santvoort[4], M.J. Bruno[2], For the Dutch Pancreatitis Study Group, *Both authors contributed equally to this work, [1]Dept of Surgery, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, [3]Dutch Pancreatitis Study Group, St. Antonius Hospital, Nieuwegein, [4]Dept of Surgery, Academic Medical Center, Amsterdam, [5]Dept of Radiology, St. Antonius Hospital, Nieuwegein, [6]Dept of Operation Rooms and Evidence Based Surgery, Radboud University, Nijmegen Medical Center, Nijmegen, The Netherlands*

Mortality in necrotizing pancreatitis is driven by the type, timing and duration of organ failure. This study aims to further specify the current knowledge on the impact of these determinants of organ failure on mortality and the association with infected necrotizing pancreatitis. We performed a post-hoc analysis of a prospective database of 639 consecutive patients with acute necrotizing pancreatitis from 21 hospitals. During the entire hospital stay, all data regarding organ failure were registered including type (i.e. respiratory, cardiovascular and renal failure), duration and sequence of organ failure. The relation between persistent multiple organ failure (i.e. failure of 2 or more organ systems for more than 48 hours) and mortality was analyzed. Finally, the association between organ failure with infected necrotizing pancreatitis was studied. In total, 240 of 639 patients with necrotizing pancreatitis (38%) developed organ failure. Mortality in 106 patients with renal failure was 47%, in 197 patients with cardiovascular failure 40%, and in 221 patients with pulmonary failure mortality was 37%. Persistent organ failure started in the first week in 47% of patients (41% mortality), in 14% during the second week (43% mortality), and in 39% after the second week (32% mortality) (P=0.51). During hospital stay, patients developed a median of 2 episodes of organ failure (interquartile range (IQR) 2–3). The longest episode persistent organ failure lasted a median of 9 days (IQR 3–17 days). Mortality in persistent multiple organ failure lasting less than 1 week, 1 to 2 weeks, 2 to 3 weeks or longer than 3 weeks was 43%, 38%, 46% and 52% respectively (P=0.68). Persistent simultaneous failure of all 3 organ systems occurred in 52 patients with 63% mortality. Overall, patients with organ failure but without infected necrosis had a higher risk for mortality (44% of 108 patients) than patients with organ failure and infected necrosis (29% of 132 patients) (RR2.6; 95% CI:1.7-4.0; P<0.001). However, when only mortality occurring after 10 days of admission was considered, this difference was no longer significant (28% vs. 30%, respectively, RR1.3, P=0.4). In 70 patients with infected necrosis who had no organ failure mortality was 4%.

Conclusion: Mortality in patients with necrotizing pancreatitis and persisting organ failure is high. Nevertheless, even after several weeks of organ failure, half of patients survive. Mortality was higher in patients with organ failure alone compared to patients with organ failure and infected necrosis. We believe that these results strongly support intensive and prolonged treatment of organ failure in these patients.

Outcome in patients with presumed groove pancreatitis: long-term follow-up from a single center

S.J. Lekkerkerker[1], C.Y. Nio[2], Y. Issa[3], P. Fockens[1], O.R.C. Busch[3], T.M. van Gulik[3], E.A.J. Rauws[1], M.A. Boermeester[3], J.E. van Hooft[1], M.G.H. Besselink[3], [1]Dept of Gastroenterology and Hepatology, [2]Dept of Radiology, and [3]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

Groove pancreatitis (GP) is a focal form of pancreatitis located between the duodenum and pancreatic head. Differentiating GP from cancer can be challenging. Data on the outcome and prevalence of cancer in patients with the suspicion of GP are lacking. Our aim was to answer the following questions: (1) What is the prevalence of cancer in patients with the suspicion of GP? (2) Are there valid descriptors to differentiate cancer from GP? (3) What are the outcomes in patients with GP after conservative, endoscopic or surgical treatment? Patients presenting between 2001 and 2014 with the suspicion of GP were retrospectively included. Patients with GP received questionnaires evaluating clinical symptoms, including pain and gastric outlet obstruction. Of 38 patients who met the radiological criteria of GP, 10 (26%) patients were diagnosed with cancer during initial work-up. Compared to patients with cancer, patients with GP were more often smokers (24/27 (86%) vs 4/9 (44%), p=0.019), who presented with abdominal pain (25/28 (89%) vs 5/10 (50%), p=0.01) and had cysts in the groove area (22/28 (79%) vs 1/10 (10%), p<0.001), without jaundice (3/28 (11%) vs 6/10 (60%), p=0.002). In total, 20/38 patients had cysts in the groove area without jaundice; 19 of these 20 patients had GP (95%), one had cancer (5%). After excluding the 10 patients with cancer, 28 patients with GP remained (median age 52 (range 33-76), 17/28 men, 26/28 alcohol abuse, 24/27 smoking). In total, 14/28 patients were treated conservatively, with a median follow-up of 36 months (range 7-127 months). This resulted in complete symptom relief in 5/14 patients and improvement in 6/14 patients. Endoscopic intervention was performed in 6/28 patients, with a median follow-up of 36 months (range 10-92 months). In 3/6 patients complete symptom relief was reported, 2/6 patients showed improvement. Surgery was performed in 8/28 patients, with a median follow-up of 24 months (range 10-127 months). Indication for surgery was either treatment failure (3/8) or inability to exclude malignancy (5/8). One patient died post-operatively. Symptoms improved in all other patients who underwent surgical resection, with complete symptom relief in 4/7 patients.

Conclusions: If a patient presents with possible GP, there should be a high suspicion of cancer. It is therefore advisable to perform EUS with FNA in every patient, although negative cytology does not exclude malignancy. In patients with cysts in the groove area without jaundice, GP is the most likely diagnosis. Since conservative, endoscopic and surgery can all lead to symptom improvement in a large proportion of patients, a ‘step-up approach’ seems advisable.

Validation of a 9-microRNA panel in pancreatic cyst fluid for the risk stratification of pancreatic cysts in a prospective cohort

W.K. Utomo[1], L.H. Looijenga[2], M.J. Bruno[1], M.P. Peppelenbosch[1], H. Braat[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Pathology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

Introduction: Pancreatic cancer remains a disease with a poor prognosis, even in potentially resectable disease. Pancreatic cystic neoplasms (PCNs) are regarded as one of the precursors of pancreatic cancer. With the widespread use of radiologic cross-sectional imaging, PCNs are discovered more frequently. However, not all PCNs will undergo malignant transformation. Thus, it is imperative to discriminate between the PCN that will follow a benign course or develop into invasive carcinoma. MicroRNAs (MiRs) have been shown to be a promising biomarker for this prediction. In 2012, Matthaei et al. published a 9-miR signature to discriminate between high risk from low risk pancreatic cyst with a sensitivity of 89% and specificity of 100%. In this study, we aim to validate this 9-miR panel in a prospective cohort of European patients. Experimental design: We included all patients who underwent EUS-FNA in the clinical workup of a pancreatic cyst. Pancreatic cyst fluid was collected and total microRNA was isolated using Taqman® miRNA ABC Purification Kit. The obtained miR elution was then used in a RT-reaction and expression analysis was performed using a singleplex Taqman® MicroRNA Assay. The expression of miR-18a, miR-24, miR-30a-3p, miR-92a, miR-99b, miR-106b, miR-142-3a, miR-342-3p, and miR-532-3p were measured and specific diffpairs were generated as described by Matthaei et al. Logistic regression using these diffpairs were then used to evaluate the performance as predictors of high risk cysts. Finally, using the published regression coefficients, we calculated a risk score for risk stratification. Result: A total of 80 patient samples were analyzed. During follow-up, 29(36.3%) patients underwent resection, of which 6 (7.5%) patients had developed at least high grade dysplasia. The diffpairs 18-92, 24-30, 30-532, 24-99, 106-92, 142-92, and 24-342 were computed as a self-normalizing biomarker. Univariable and multivariable logistic regression did not show any diffpair as significant predictor of high risk cysts. There were no differences in the distribution of the calculated risk scores between high risk and low risk cysts. Sub analysis in resected cysts did not show significant differences between benign and malignant cysts.

Conclusions: We attempted to validate a previously published, promising, 9-microRNA panel to identify high risk cysts measured in pancreatic cyst fluid. However, in our European prospective cohort, we did not find any of the markers to be suitable for the risk stratification of pancreatic cysts.

Malignant progression during long-term follow-up of pancreatic cysts: how often do we change treatment strategy?

S.J. Lekkerkerker[1], P. Fockens[1], M.G.H Besselink[2], E.A.J. Rauws[1], J.E. van Hooft[1], [1]Dept of Gastroenterology and Hepatology, and [2]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands

Patients presenting with a cystic lesion in the pancreas without worrisome features or high-risk stigmata often enter a surveillance program. The natural history of pancreatic cysts is still largely unknown. Our aim was to evaluate the resection rate and rate of malignancy in patients with pancreatic cysts who had entered a surveillance program. From our prospective database (2006-present) of patients with pancreatic cysts (n=321), we extracted all patients with pancreatic cysts with ≥6 months of follow-up, who were not referred for surgery and did not have pancreatic cancer at presentation. A total of 132 patients (median age 62 (range 29-79), 75% female) with pancreatic cysts were followed for a median of 31 months (range 6-143). In 120 patients (91%) there was no suspicion of malignancy or indication for surgery during a median follow-up of 32 months (range 6-143). In 12 patients (9%) significant changes occurred, leading to an indication for surgery after a median follow-up of 26 months (range 7-86). Two of these patients were not referred for surgery because of extensive comorbidity and patient preference; one had a side branch (SB)-IPMN which had increased from 2.4 to 5.4 cm in 1 year, the other patient developed a mural nodule of 26 mm. Ten patients (8%) were referred for surgery. Surgery was indicated because of changed presumptive diagnosis (n=3), a nodule (n=3), PD dilation (n=3), more than 10 mm increase in cyst size (n=4) and/or recurrent pancreatitis (n=2). One patient underwent surgery for a symptomatic serous cystic neoplasm (SCN). Histology showed 3 mixed type (MT)-IPMN, 1 SB-IPMN, 2 mucinous cystic neoplasms (MCN), 1 neuroendocrine tumor (NET), 1 SCN, 1 inflammatory cyst and 1 lymphangioma. In 7 (70%) of the cases the presumed diagnosis was correct and in 8 (80%) of the cases the correct differentiation between benign and (pre)malignant was made. One patient had the suspicion of a MCN, but surgical histology showed a SB-IPMN. In 2 patients with the suspicion of a neoplastic cyst (1 SB-IPMN and 1 MCN) a non-neoplastic lesion was found; 1 inflammatory cyst and 1 lymphangioma, respectively. No high-grade dysplasia or invasive cancer was found, 2 patients had cysts with border dysplasia. No surgery-related mortality occurred.

Conclusions: Most pancreatic cysts that undergo surveillance do not show substantial changes during follow-up. In our cohort, 7% of patients underwent surgery because of suspicion of malignant progression. No malignancy or high-grade dysplasia was found, suggesting that additional markers are needed for tailored treatment of “suspicious” pancreatic cysts during surveillance.

Are the current diagnostic criteria for acute cholangitis (TG13) applicable in patients with acute biliary pancreatitis?

N.J. Schepers[1,2], O.J. Bakker[3], U. Ahmed Ali[3], E.J.M. van Geenen[4], H.C. van Santvoort[5], M.G. Besselink[5], M.J. Bruno[1*], For the Dutch Pancreatitis Study Group, [*]Co-senior authorship, [1]Dept of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, [2]Dutch Pancreatitis Study Group, St. Antonius Hospital, Nieuwegein, [3]Dept of Surgery, University Medical Center Utrecht, Utrecht, [4]Dept of Gastroenterology and Hepatology, Radboud University, Nijmegen Medical Center, Nijmegen, [5]Dept of Surgery, Academic Medical Center, Amsterdam, The Netherlands*

In patients with acute biliary pancreatitis and suspected cholangitis, early endoscopic retrograde cholangiography (ERC) has shown to reduce mortality and morbidity. However, a uniform definition for cholangitis in acute pancreatitis is lacking. Recently, the revised Tokyo Guidelines (TG13) for diagnosis of acute cholangitis were published. The aim of this study was to evaluate these TG13 diagnostic criteria for acute cholangitis in patients with acute biliary pancreatitis. We performed a post hoc analysis of a prospective database of 731 patients with acute pancreatitis included in 15 Dutch hospitals between 2004 and 2007. Patients characteristics on admission, characteristics of ERC and clinical outcomes were available. An ERC within 72 hours after admission was considered an ´early ERC´. The TG13 criteria consist of 3 categories (systemic inflammation, cholestasis and imaging) from which 2 or 3 items are required for the suspected or definitive cholangitis diagnosis, respectively. We evaluated which patients fulfilled these criteria, described the findings during ERC and described the clinical outcome. In total 418 out of 731 patients suffered from acute biliary pancreatitis. Within the first three days of admission, classification according to the TG13 criteria was as follows: 1. no cholangitis (n=147, 35%); 2. suspected cholangitis (n=212, 51%); and 3. definitive cholangitis (n=59; 14%). An 'early ERC' was performed in 34 patients (23%) with no cholangitis, 110 patients (52%) with suspected cholangitis, and 54 patients (92%) with definitive cholangitis according to TG13. Purulent bile during ERC was observed in similar frequency in all 3 groups (3% vs. 9% vs. 11%, P=0.24). Patients with suspected cholangitis according to TG13 in whom an early ERC was performed had similar outcomes compared to patients who were treated conservatively in terms of mortality (16% vs. 15%, P=0.74), length of hospital stay (median 13 vs. 13, P=0.56), pancreatic necrosis (16% vs. 25%, P=0.11), infected pancreatic necrosis (15% vs. 15%, P=0.97), bacteremia (18% vs. 15%, P=0.50) and intensive care unit admission (17% vs. 21%, P=0.54). Also, no significant differences in outcomes were observed between early ERC or conservative treatment in patients who had definitive or no cholangitis according to TG13.

Conclusion: Acute cholangitis in the early phase of acute biliary pancreatitis tends to be over-diagnosed when using the TG13 diagnostic criteria. Accordingly, a more accurate tool is needed for the assessment of acute cholangitis in the setting of acute biliary pancreatitis.

Patient-reported outcomes of uncomplicated symptomatic cholecystolithiasis patients following cholecystectomy: A prospective multi-center cohort study

M.P. Lamberts[1,2,3], B.L. Den Oudsten[4], J.J.G.M. Gerritsen[5], A.J. Roukema[6], G.P. Westert[1], J.P.H. Drenth[2], C.J.H.M. van Laarhoven[3], [1]Scientific Institute for Quality of Healthcare (IQ healthcare), Radboud University Medical Center, Nijmegen, [2]Dept of Gastroenterology and Hepatology, and [3]Dept of Surgery, Radboud University Medical Center, Nijmegen, [4]Dept of Medical and Clinical Psychology, CoRPS, Tilburg University, Tilburg, [5]Dept of Surgery, Medisch Spectrum Twente, Enschede, [6]Dept of Surgery, St. Elisabeth Hospital, Tilburg, The Netherlands

Up to 33% of uncomplicated symptomatic cholelithiasis patients report persistent pain after cholecystectomy despite that pain relief is initially the main objective to perform the procedure. We aimed to determine characteristics associated with patient-reported absence of abdominal pain after cholecystectomy, with improved abdominal symptoms, and with a positive surgery result. Patients ≥ 18 years of age with symptomatic cholelithiasis that received cholecystectomy were included. Patients were sent a questionnaire consisting of the Gastrointestinal Quality of Life Index (GIQLI) and the McGill Pain Questionnaire (MPQ) preoperatively. In addition, patients received the GIQLI and Patients' Experience of Surgery Questionnaire (PESQ) at 12 weeks after cholecystectomy. Logistic regression analyses were performed to determine associations. Questionnaires were sent to 552 patients and returned by 342 (62.0%) patients (78.4% female, mean age at surgery 49.7 ± 14.3 years) preoperatively and postoperatively. Postoperative absence of abdominal pain was reported by 60.5% of the patients. A high preoperative GIQLI score (OR 1.02, 95% CI 1.01-1.03), episodic pain (OR 2.22, 95% CI 1.25-3.94), and duration of pain ≤ 1 year (OR 2.23, 95% CI 1.26-3.94) were associated with postoperative absence of pain. These factors were not associated with the 91.5% of patients who reported improved abdominal symptoms and with the 92.4% who positively rated the cholecystectomy result. Preoperative characteristics determine the odds for relief of abdominal pain after cholecystectomy. However, these factors were not associated with the rating of patient-reported improved abdominal symptoms or a positive result of cholecystectomy, highlighting the variation of internal standards and expectations of patients prior to cholecystectomy.

Nomogram to predict recurrent disease after curative pancreatic resection for patients with grade 1 or 2 non-functional neuroendocrine tumor

A.P.J. Jilesen[1], C.H.J. van Eijck[2], F.J. van Kemenade[3], S. van Eeden[4], J.Verheij[4], S. van Dieren[5], D.J. Gouma[1], E.J.M. Nieveen van Dijkum[1], [1]Dept of Surgery, [4]Dept of Pathology, and [5]Dept of Methodology and Statistic CRU, Academic Medical Center, Amsterdam, [2]Dept of Surgery, and [3]Dept of Pathology, Erasmus Medical Center, Rotterdam, The Netherlands

Background: Compared to other types of cancers, adjuvant therapy after curative resection is not standard in patients with pancreatic neuroendocrine tumor (pNET). The aim of this study was to predict recurrent disease in patients with grade 1 or 2 non-functional pNET (NF-pNET). Methods: Retrospectively all resected NF-pNET from 1997-2013 of two academic institutions were included. Patients with distant metastases or hereditary syndromes were excluded. Pathology was revised according WHO classification 2010. Grade 3 tumors were excluded for risk factor analysis. Recurrent disease was defined as local tumor recurrence, tumor localization in lymph nodes or distant metastases. Significant predictors for recurrent disease from the multivariable Cox regression were used to make the nomogram. The nomogram was internally validated by calculating the Harrel's c-statistic and Hosmer–Lemeshow Chi-square test. Results: Overall 107 patients were suitable for analysis and during follow-up, median 52 months (IQR 29-81), 31 (30%) patients developed recurrent disease and 12 patients died by tumor progression. Overall 5-year disease specific survival was 91%. Risk factors for recurrent disease were tumor size > 2cm, positive lymph nodes in resected specimen and perineural invasion. Patients with a nomogram score ≥ 14 were high risk patients for recurrent disease with a c-statistic of 0.79 (CI95% 0.70-0.88) and Hosmer–Lemeshow test of 6.45 (p=0.694).
Conclusions: the nomogram showed a good fit to predict recurrent disease after curative resection in grade 1 and 2 NF-pNET. High risk patients for recurrent disease should be monitored more closely and they may benefit from adjuvant treatment after their resection.

Diagnostic workup for small subepithelial upper gastrointestinal tumors is inadequate in guiding management

J.R. ten Hove[1], N. van Lelyveld[2], F.P. Vleggaar[1], L.M.G. Moons[1], [1]Dept of Gastro-enterology and Hepatology, University Medical Center Utrecht, Utrecht, [2]Dept of Gastroenterology, St. Antonius Hospital, Utrecht, The Netherlands

Background: The occurrence of a subepithelial tumor (SET) of the upper gastrointestinal tract prompts a possible diagnosis of GIST, carrying malignant potential. Current guidelines uphold conservative management as one of the possible strategies for SETs <2cm, necessitating tissue acquisition to reach a definitive diagnosis. Tissue acquisition of SETS <2 cm can be difficult, resulting in long term follow-up of benign SETs without malignant potential. Aim: To assess the currently used tissue sampling techniques for small upper gastrointestinal SETs and their efficacy in daily practice. Methods: All patients undergoing an endoscopic ultrasound (EUS) for a suspected SET in either esophagus, stomach or duodenum in an academic and a community hospital between 2001 and 2013 were retrospectively studied. Intramural tumors <5cm were included for further analysis, irrespective of the suspicion of a malignant diagnosis or wall layer of origin. Pathology reports for each obtained tissue sample were analyzed and assessed for the presence of a definitive diagnosis. Results: Out of 259 patients who underwent EUS for evaluation of a suspected SET, 143 had a subepithelial tumor < 5cm (39 in esophagus, 91 in stomach, 13 in duodenum) with a mean initial size of 19.1 mm (SD 10.3). Mean age was 60.3 years (SD 12.6) and 83 patients (58%) were male. A total of 197 tissue samples was obtained during endoscopy or EUS. The rate of diagnostic samples was low in both the first 12 months; 23/163 samples (14.1%), as in the follow-up period; 6/34 samples (17.6%). The proportion of diagnostic samples was 17.1% (12/70) for EUS guided fine needle aspiration (EUS-FNA), 14.7% (5/34) for key hole biopsies and 6.3% (5/80) for endoscopic biopsies without further specification. Trucut, fine needle biopsy (FNB) and de-roofing techniques led to a definitive pathologic diagnosis in 2/3 (66%), 3/5 (60%) and 2/3 cases (66.7%), respectively. The proportion of diagnostic samples increased for each subsequent size category: 5.1% (0-1cm), 5.7% (1-2cm), 19.4% (2-3cm), 44.1% (3-5cm). Size ≤ 2cm was a significant predictor of a nondiagnostic biopsy (5.5% vs. 31.4% diagnostic samples, OR 7.8; 95% CI 3.2-19.6). Assessment of the mitotic index in 50 high-power fields was not possible in any of the obtained tissue samples. No complications were observed in any of the used tissue sampling techniques.

Conclusion: The yield of diagnostic tissue sampling of small SETs during EUS or upper endoscopy is disappointingly low, with small size of the tumor being a significant predictor of poor outcome. Trucut and fine needle biopsy show higher outcome, and should be considered as an alternative to FNA.

Nutrition before, during, and after surgery increases the arginine/ADMA ratio and relates to improved myocardial glucose metabolism: a randomized controlled trial

M. Visser[1,2,3], M. Davids[4], H.J. Verberne[5], W.E.M. Kok[6], R. Tepaske[7], R. Cocchieri[2], E.M. Kemper[8], T. Teerlink[4], M.A. Jonker[9], W. Wisselink[1], B.A.J.M. de Mol[2], P.A.M. van Leeuwen[1], [1]Dept of Surgery, VU University Medical Center, Amsterdam, [2]Dept of Cardio-thoracic Surgery, Academic Medical Center, University of Amsterdam, Amsterdam, [3]Research Unit, Gelderse Vallei Hospital, Ede, [4]Dept of Clinical Chemistry, VU University Medical Center, Amsterdam, [5]Dept of Nuclear Medicine, [6]Dept of Cardiology, and [8]Dept of Pharmacy, Academic Medical Center, University of Amsterdam, Amsterdam, [7]Intensive Care Unit, Academic Medical Center, University of Amsterdam, Amsterdam, [9]Dept of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

Nitric oxide (NO) is essential for optimal perfusion of the heart and its vasculature. NO may be insufficient in surgical patients as its precursor arginine is decreased and the inhibitor of its synthesis asymmetric dimethylarginine (ADMA) is increased. Besides arginine, the presence of other amino acids essential for proper metabolism of cardiac cells may be decreased too. Supplementation of these amino acids with (par)enteral nutrition before, during, and after surgery may augment myocardial and plasma arginine/ADMA ratio and the availability of amino acids. Myocardial glucose metabolism and nutritional conditioning may result in a reduction of cardiac injury and may support rapid recovery after major surgery. Therefore, we investigated the effect of nutrition before, during, and after surgery on amino acids and the myocardial arginine/ADMA ratio and its relation to myocardial glucose metabolism. In this trial, 33 patients undergoing off-pump coronary artery bypass grafting (CABG) were randomized between enteral, parenteral or no nutrition (control) from 2 days before, during, until 2 days after surgery. Both enteral and parenteral solutions were prepared with commercial available products and included proteins or amino acids, glucose, vitamins and minerals. Concentrations of amino acids including ADMA were analysed in myocardial tissue and plasma samples. ^{18}F-fluorodeoxyglucose positron emission tomography (PET) was performed before and after surgery to assess myocardial glucose metabolism.The myocardial arginine/ADMA ratio increased during surgery and was significantly higher in the enteral and parenteral group compared to the control group (median(IQR) 115.0 (98.0-142.2), p = 0.012, 116.9 (100.3-135.3), p = 0.004, and 93.3 (82.7-101.1) respectively). Furthermore, the change in pre- to postoperative plasma arginine/ADMA ratio correlated with the change in myocardial glucose metabolism in PET (r=0.427, p=0.033).
In conclusion, enteral or parenteral nutrition before, during, and after CABG may positively influence myocardial glucose metabolism by increasing plasma and myocardial arginine/ADMA ratio.

Patients with a positive SNAQ score stay 1.4 days longer in hospital

H.M. Kruizenga[1,2], F. Neelemaat[1], C.Bijl[1], A. Thijs[1,3], P. Weijs[1], [1]Dept of Nutrition and Dietetics, VU University Medical Center, Amsterdam, [2]Dutch Malnutrition Steering Group, Amsterdam, [3]Dept of Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands

Introduction: In the VU University medical center (VUmc), Amsterdam, The Netherlands, screening on undernutrition, using the Short Nutritional Assessment Questionnaire (SNAQ), is common practice since 2007. Using the screening data of the past eight years two questions will be answered: 1. What is the percentage of patients with a SNAQ score "undernutrition" (≥ 3points) in the general hospital population and per medical specialism? 2. Are SNAQ score and Length of Hospital Stay (LOS) related? Methods: All in-patients of the VUmc who were admitted for at least 24 hours in the period of 1-1-2007 until 1-11-2014, were included. SNAQ score, admitting medical specialism, LOS, age and sex were extracted from the digital hospital chart system. Since LOS was skewed to the right, natural logarithmic transformation was applied to distribute the data more symmetrically. Regression analysis was used to test the relation between SNAQ score and LOS. Results: 101.653 patients were included (51% male, age 58 ± 17). It took 2 years to implement the screening, starting with only 2 wards in 2007. The percentage of screened patients improved in time (2007: 15%; 2008: 44%; 2009: 68%; 2010: 71%; 2011: 70%; 2012: 70%; 2013: 76%; 2014: 76%). In the patients admitted from 2009-2014, 15.2% of the patients had a SNAQ score "undernourished" (≥3 points). Medical specialisms with the highest percentage of SNAQ score "under-nourished" were Geriatrics (35%), Oncology (34%), Gastroenterlogy (34%) and Internal medicine (22%). Patients with SNAQ≥ 3 points had a higher LOS (median 6.0 days vs. SNAQ 0 and 1 points median LOS 3.9 days ($P<0.001$)). Regression analysis, with LnLOS as a dependent variable and SNAQ≥ 3 points and age as independent variables, points out that SNAQ≥ 3 points is a significant determinant of LOS ($\beta 1,4$, $p<0.001$)
Conclusion and plans for 2015: In a large hospital population 15,2% of the population has a SNAQ screening result "malnourished". These patients' hospital stay is 1.4 days longer. The Dutch Malnutrition Steering Group (DMG) will ask all Dutch hospitals to extract these data out of their medical chart system. DMG will analyse these results per hospital and combine it, resulting in national hospital malnutrition prevalence data and unique data on the relation between malnutrition and length of hospital stay.

The prebiotic inulin enhances fat oxidation in overweight males

C.M. van der Beek[1,2], E.E. Canfora[1,3], E.E. Blaak[1,3], C.H.C. Dejong[1,2], K. Lenaerts[1,2], [1]Top Institute Food and Nutrition, Wageningen, [2]Dept of Surgery, and [3]Dept of Human Biology, NUTRIM School for Nutrition, Toxicology and Metabolism, Maastricht University Medical Center, Maastricht, The Netherlands

Human gut microbiota are suggested to play an important role in maintaining metabolic health by fermentation of dietary fibers into short-chain fatty acids (SCFAs). Specifically, the prebiotic inulin has been proven to increase SCFA production in vitro, and long term inulin intake has been shown to exert beneficial effects on human metabolism and body composition. However, acute effects of inulin intake on human substrate oxidation and metabolism are still unknown. The aim of this study was to investigate the metabolic effects of a single dose of inulin in overweight males. In this double-blind, randomized controlled crossover study fourteen healthy, overweight males (age 34±3 y, BMI 30.4±0.7 kg/m^2) underwent two experimental test days. During one test day the subjects ingested a high-fat milkshake containing U-^{13}C-labeled inulin (0.5 g) combined with a load of unlabelled inulin (23.5 g), and during the other test day the subjects consumed the same milkshake containing the placebo maltodextrin (24 g). Fat and carbohydrate oxidation were measured via an open-circuit ventilated hood and blood samples were collected up to 7 h after ingestion. Breath samples for $^{13}CO_2$ measurements were collected via a mixing chamber and analyzed using gas chromatography-isotope ratio mass spectrometry. Visual analogue scale (VAS) scores for hunger and satiety were collected for 7 h. Values are presented as mean±SEM. Repeated measures ANOVA was used to detect differences between treatment groups and differences are shown as incremental area under the curve (iAUC) for the early (0-3 h after ingestion) and the late postprandial phase (4-7 h after ingestion). $^{13}CO_2$ enrichments in exhaled breath continuously increased from 2 hours after the ingestion of U-^{13}C inulin, indicating an early fermentation process by gut microbiota. Fat oxidation transiently increased in the early postprandial phase (0-3 h) after inulin ingestion when compared with placebo ($P<0.05$), whereas carbohydrate oxidation decreased ($P<0.05$). Plasma free fatty acids increased after inulin ingestion ($P<0.05$) when compared with placebo. Plasma glucose increased ($P<0.05$) immediately after maltodextrin ingestion. There were no effects on plasma triglycerides, free glycerol, and hunger and satiety.

In conclusion, inulin ingestion acutely affects whole-body metabolism in overweight males, with a pronounced increase in fat oxidation and increase in plasma free fatty acids. Microbial fermentation of inulin into SCFAs may be responsible for this effect, which will be assessed by determining plasma SCFA concentrations in these volunteers.

The impact of different diagnostic criteria on the prevalence of sarcopenia in healthy elderly individuals and geriatric outpatients

E.M. Reijnierse[1], M.C. Trappenburg[1,2], M.J. Leter[1], G.J. Blauw[3], S. Sipilä[4], E. Sillanpää[4], M.V. Narici[5], J.Y. Hogrel[6], G. Butler-Browne[6], J.S. McPhee[7], H. Gapeyeva[8], M. Pääsuke[8], M.A.E. de van der Schueren[9,10], C.G.M. Meskers[11], A.B. Maier[1,2], [1]Dept of Internal Medicine, Section of Gerontology and Geriatrics, VU University Medical Center, Amsterdam, The Netherlands, [2]Dept of Internal Medicine, Amstelland Hospital, Amstelveen, The Netherlands, [3]Dept of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, The Netherlands - Dept of Geriatrics, Bronovo Hospital, The Hague, The Netherlands, [4]Gerontology Research Center and Dept of Health Sciences, University of Jyväskylä, Jyväskylä, Finland, [5]Division of Medical Sciences and Graduate Entry Medicine, MRC-ARUK Centre of Excellence for Musculoskeletal Ageing Research, University of Nottingham, Royal Derby Hospital Centre, Birmingham-Nottingham, UK, [6]UPMC UM 76, INSERM U974, CNRS 7215, Institut de Myologie, Paris, France, [7]School of Healthcare Science, John Dalton Building, Manchester Metropolitan University, Manchester, UK, [8]Institute of Exercise Biology and Physiotherapy, University of Tartu, Centre of Behavioral and Health Sciences, University of Tartu, Tartu, Estonia, [9]Dept of Internal Medicine, Section Nutrition and Dietetics, VU University Medical Center, Amsterdam, The Netherlands, [10]Dept of Nutrition, Sports and Health, Faculty of Health and Social Studies, HAN University of Applied Sciences, Nijmegen, The Netherlands, [11]Dept of Rehabilitation Medicine, VU University Medical Center, Amsterdam, The Netherlands

Sarcopenia, low muscle mass and muscle function, is a frequent syndrome in elderly and is associated with physical disability and mortality. Optimization of physical and nutritional intervention has shown significant efficacy in increasing muscle mass. Prevalence rates vary between 0% to 20% in a middle aged population, due to the use of different criteria for sarcopenia encompassing different measures, correction factors and cut-off points. Previous diagnostic criteria for sarcopenia incorporated measures of muscle mass, but proposed consensus definitions characterize sarcopenia by the combination of low muscle mass, muscle strength and/or physical performance. However, consensus on diagnostic criteria for sarcopenia has not been reached yet. This cross-sectional study compared prevalence rates of sarcopenia using nine frequently used sets of diagnostic criteria applied in two different elderly populations, encompassing 308 healthy elderly individuals from the MYOAGE study (152 males, 156 females; mean age 74 years, 7.0 SD) and 123 geriatric outpatients (54 males, 69 females; mean age 81 years, 3.2 SD). Diagnostic criteria for sarcopenia included relative and absolute muscle mass,, muscle strength and physical performance. Prevalence rates of sarcopenia varied between 0% and 15% in healthy elderly individuals and between 0% to 34% in geriatric outpatients, dependent on the applied set of diagnostic criteria. Agreement between the applied sets of criteria was minimal: only one of the geriatric outpatients was classified as sarcopenic according to all applied sets of diagnostic criteria; this was true for none of the healthy elderly individuals. The lack of agreement can be explained by the use of different measures (i.e. muscle mass, muscle strength, physical performance), correction factors (height, body mass, BMI), cut-off points and by methodological issues.
This study clearly demonstrates the dependency of sarcopenia prevalence rates on the applied diagnostic criteria and indicates the importance of defining sarcopenia and the need to reach consensus on the diagnostic criteria. Consensus on the diagnostic criteria for sarcopenia should be based on evidence on the relation of diagnostic measures and clinically relevant muscle-related outcomes, useful correction factors and valid cut-off points.

Incidence of non-alcoholic fatty liver disease in a large population cohort in the North of the Netherlands: a LifeLines Cohort analysis

E.H. van den Berg[1], M. Amini[2*], R.P.F. Dullaart[3], K.N. Faber[1], A. Timmer[4], The LifeLines Cohort Study[5], B.Z. Alizadeh[1,2*], H. Blokzijl[1*], *These authors contributed equally, [1]Dept of Gastroenterology and Hepatology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [2]Dept of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [3]Dept of Internal Medicine (Endocrinology), University of Groningen, University Medical Center Groningen, Groningen, The Netherlands, [4]European Medical School Oldenburg-Groningen, Oldenburg, Germany, [5]The LifeLines Cohort Study, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands*

Background: Non-alcoholic fatty liver disease (NAFLD) is an increasing health issue, being part of the worldwide epidemic of obesity. The aim of this study was to investigate the prevalence of biochemical characteristics in people with NAFLD in a large population-based cohort study. Methods: The study is conducted in the LifeLines Cohort Study (N=167,000), of which 13,301 independent participants with biomedical data were included. The LifeLines Cohort Study is a multi-disciplinary prospective population-based cohort study examining the health and health-related behaviors of participants living in the Northern region of The Netherlands in a unique three-generation design. Base and bio-clinical information were collected person-to-person and through mail, using extended structured and validated questionnaires. Out of laboratory measurements available in LifeLines, we studied a priori-defined liver function tests, lipid profile, leucocyte count, serum CRP, hemoglobin A1c (HbA1c) and fasting glucose (FG). NAFLD was defined by using the validated Hepatic Steatosis Index (HSI): HSI>36 was categorized as NAFLD, HSI 30-36 as suspected NAFLD and HSI<30 as no NAFLD. Prevalence and biochemical characteristics were compared using ANOVA, chi-square test and regression analyses when appropriate. A p-value <0.01 was considered to be significant. Results: Among all participants, 38% had NAFLD, 39% were suspected of NALFD and 23% had no NAFLD. More men (62%) than women (38%) had NAFLD (p<0.001). Individuals with NAFLD were significantly older, had higher waist circumference, higher levels of HbA1c, FG, liver function tests, including ALT, AST, ALT/AST ratio, GGT and ALP, total and differential leucocyte counts, serum CRP, triglycerides, low-density lipoprotein cholesterol and lower high-density lipoprotein cholesterol, when compared to the other participants (all p-values <0.001). People with NAFLD showed a significantly higher prevalence of the metabolic syndrome (35% vs 7%, p<0.001).

Conclusion: NAFLD is a common disease in the Northern part of the Netherlands, affecting 38% of the population, and is associated with the metabolic syndrome and inflammatory indexes. Future population-based studies on genetic and environmental causes of NAFLD and its consequences, such as fibrosis, are mandatory.

Percutaneous transhepatic feeding tube placement: a single-center experience in 37 patients

A. Gerritsen[1], J. Damstra[1], K.P. van Lienden[2], O.M. van Delden[2], O.R.C. Busch[1], T.M. van Gulik[1], M.A. Boermeester[1], J.S. Laméris[2], M.G.H. Besselink[1], [1]Dept of Surgery, and [2]Dept of Radiology, Academic Medical Center, Amsterdam, The Netherlands

Enteral nutrition can be administered via several routes (e.g. nasonenteral or jejunostomy feeding tubes), but all routes have their specific downsides. In patients with a percutaneous transhepatic biliary drainage (PTBD) catheter and the need for enteral access, transhepatic feeding tube placement may offer a suitable alternative, but data regarding this technique are lacking. The aim of this study was to determine the feasibility of percutaneous transhepatic feeding tube placement in patients with PTBD. We performed a retrospective monocenter cohort study in patients with PTBD undergoing percutaneous transhepatic feeding tube placement (April 2003-October 2014). The feeding tube was placed by an interventional radiologist alongside the PTBD. Primary endpoint was successful tube placement, defined as a correct position (in the duodenum or jejunum) and successful administration of nutrition or bile via the tube. Overall, 40 patients underwent transhepatic feeding tube placement, of whom 3 were excluded because data were lacking. Indications for tube placement were severe gastroparesis or malnutrition requiring enteral feeding (n=29) or bile restitution (n=8). 35 of 37 (95%) initial tube placements were successful. Failure was due to pain during the procedure or recurrent dislodgement of the tube. Median procedure time was 43 ± 13 minutes. The primary tube remained in the correct position for a median of 30 (15–83) days. Tube related complications included blockage (n=11), dislodgement (n=6), and cholangitis (n=1) and led to the need for replacement in 8 (22%) patients.
Conclusions: Transhepatic feeding tube placement alongside a pre-existent PTBD was safe and successful in this series and may be considered in patients with PTBD requiring prolonged enteral access.

The association of nutritional status with brain atrophy and cerebrovascular lesions on MRI in a cohort of geriatric outpatients

M.A.E. de van der Schueren[1], S. Lonterman-Monasch[2], M.A. Chung[1,5], W.M. van der Flier[3], A.B. Maier[4], M. Muller[5], [1]Dept of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, [2]Dept of Internal Medicine, Haga Hospital, The Hague, [3]Alzheimer Center, Dept of Neurology, Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, [4]Dept of Gerontology, Internal Medicine, VU University Medical Center, Amsterdam, [5]Dept of Gerontology and Geriatrics, Leiden University Medical Center, Leiden, The Netherlands

Earlier studies have shown that patients with dementia are at increased risk of malnutrition, due to difficulties managing their budget, shopping, preparing meals or recognizing their need to eat. Little information is available on the relation between malnutrition and alterations in brain structure. This study investigates the association between malnutrition and White Matter Hyperintensities (WMHs), Global Cortical brain Atrophy (GCA) or Medial Temporal lobe Atrophy (MTA) on MRI. Cross-sectionally, 488 geriatric outpatients were included, and in 359 MRI's were made on indication by the geriatrician. Nutritional status was assessed by the Mini Nutritional Assessment (<17 malnourished, 17-23,5 risk of malnutrition, >23,5 well-nourished) and by laboratory values of vit B1, B6, B12, D and folic acid. Cognitive functioning was assessed by neuropsycological examination (n=192) or, when unavailable, by Mini Mental State Examination (cut off <24). Logistic regression analyses were performed to associate MNA categories to severe WHMs (Fazekas scale > 1), severe GCA (>2) and severe MTA (>2). All analyses were adjusted for age, sex, education, comorbidities and life style factors and MNA scores were additionally adjusted for micronutrient levels. In addition, micronutrient levels (per SD decrease as well as absolute deficiency) were associated with severe brain alterations, again adjusted for possible confounders. Mean age of the cohort was 80 (SD 7) years and 34% was male. According to MNA, 13% were malnourished, 55% at risk of malnutrition and 32% well-nourished. Absolute vitamin deficiencies were observed in 5% (B1), 1.7% (B6), 8.1% (B12), 64.6% (D) and 1.9% (folic acid). MNA 17-23.5 and MNA < 17 were associated with severe WHMs (adjusted OR 2.15, 95% CI 1.10 – 4.22 and OR 2.98, 95% CI 1.25-7.09), but not with CGA and MTA. Stratification for cognitive status showed no differences between cognitively healthy and cognitively unhealthy patients. Also lower vit B1 levels and vit B12 levels were associated with increased risk of WMHs (adjusted OR per SD decrease in vit B1 1.49, 95% CI 1.08-2.08, adjusted OR for absolute vit B12 deficiency 2.55, 95% CI 1.04-626). An absolute vit D deficiency (<50 nmol/L) was associated with increased risk of severe GCA (adjusted OR 2.21, 95% CI 1.02-4.75).

Conclusion: this study shows an association between both malnutrition and vit B1 and B12 deficiencies and severe WMHs, independent of each other and independent of cognitive status. Also, an association was observed between vit D deficiency and severe GCA. Underlying mechanisms need to be further clarified and it also needs to be studied whether these findings are modifiable by nutritional interventions.

Undernutrition in nursing home rehabilitation patients

J.I. van Zwienen-Pot[1,2], M. Kuipers[3], M.F.A. Grimmerink[4], M.Visser[1,5], D.Z.B. van Asselt[1,6], H.M Kruizenga[1,7], [1]Dutch Malnutrition Steering Group, Amsterdam, [2]Zorgpartners Midden-Holland, Gouda, [3]Heliomare, Wijk aan Zee, [4]Amstelring, Amsterdam, [6]Dept of Health Sciences, Faculty of Earth and Life Sciences, VU University, Amsterdam, [7]Geriatric Medicine, Medical Centre Leeuwarden, [5]Dept of Nutrition and Dietetics, Internal Medicine, VU University Medical Center, Amsterdam, The Netherlands

In recent years, more attention is given to undernutrition in Dutch healthcare settings. However, the prevalence of undernutrition in patients admitted to rehabilitation wards of nursing homes has received less attention. This study investigated the prevalence of undernutrition in older patients admitted to nursing home rehabilitation wards, dietetic treatment and self-perception of nutritional status. In this cross sectional study we included 190 patients (all ≥65 y) admitted to seven nursing home rehabilitation wards between December 2012 - February 2014. Admission reasons were categorized as: trauma, elective orthopaedics, stroke and other. Nutritional status within the first week of admission, was characterized as: severely undernourished (>10% unintentional weight loss in the past six months and/or >5% unintentional weight loss in the past month and/or BMI ≤ 20 kg/m2), moderately undernourished (5-10% unintentional weight loss in the past 6 months and/or BMI 20.01-22), well-nourished (<5% unintentional weight loss in the past 6 months, BMI 22.01-28) and overweight (BMI>28). Patients' perception on nutritional status and dietetic treatment were also assessed. Mean age was 81.4 y (SD 7.8) and 70% women. A total of 50 patients (28%) were found to be severely undernourished, 27 patients (15%) were moderately undernourished and 41 patients (23%) were overweight. Undernutrition did not differ by age or gender. Elective orthopaedics patients were the least likely to suffer from undernutrition (19%).There were no further significant associations for reason for admission and nutritional status (other 51%, stroke 46% and trauma 48%). Of all patients, 43% were under treatment by a dietitian. This percentage was higher in undernourished patients compared to well-nourished patients (65% vs 28%, p<0.001). Only fourteen patients (18%) out of 77 undernourished patients considered themselves undernourished.

Conclusion: More than one in four older patients in Dutch nursing home rehabilitation wards appeared to be moderately or severely malnourished. The majority did not consider themselves undernourished and about one-third of these patient were not treated by a dietitian. More attention to undernutrition in nursing home rehabilitation patients seems warranted.

Lijst van standhouders, voorjaarscongres NVGE, 19-20 maart 2015 te Veldhoven

G = Genderzaal, D = Diezezaal, K = Kempenhal	*Standnummer*
AbbVie B.V.	K1
Alvleesklliervereniging	D7
Aquilant Nederland B.V.	D3
Boston Scientific Nederland B.V.	G11
Bristol Myers Squibb	D1
Cablon Medical b.v.	G2
Campro Scientific GMBH	D11
Cobra Medical B.V.	D5
Cook Nederland B.V.	K5
Covidien	K16
Crohn en Colitis Ulcerosa Ver. Nederland	G14
Dr. Falk Pharma Benelux B.V.	G1
Endotechniek	K9
Erbe Nederland B.V.	K10
Ferring B.V.	K8
FMH Medical B.V.	K7
Fresenius Kabi Nederland B.V.	G8
GE Healthcare B.V.	D4
Gilead Sciences Netherlands B.V.	K4
Hitachi Medical Systems B.V.	G4
Hospira Benelux	D12
Ikproductions	G13
Janssen-Cilag B.V.	G3
Lamepro B.V.	K12
Maag Lever Darm Stichting	G12
Medify	D16
Medical Measurements Systems B.V.	D14
Merck Sharp & Dohme B.V. Afd CME en Travel	K3
Mermaid Medical	G10
Mundipharma Pharmaceuticals BV	D2
Norgine B.V.	D13
Olympus Nederland B.V.	K2
Pentax Medical	G5
RMS Medical Devices	G15
Roche Nederland B.V.	D15
RVC B.V.	K6
Selinion Medical	K13
Shire International Licensing B.V.	K11
Skills Meducation BV	G6
Stichting Opsporing Erfelijke Tumoren	D10
Stöpler Instrumenten & Apparaten B.V.	G18
Synageva BioPharma	K14
Takeda Nederland BV	G7
Tramedico B.V.	D6
V&VN MDL	D9
Vereniging Ziekte van Hirschsprung	D8
Vifor Pharma	G16
Winclove Probiotics	G9
W.L. Gore	G17
Zambon Nederland B.V.	K15

plattegrond expositie, in te voegen door drukkerij.

plattegrond Koningshof (zelfde als in boekje najaar 2014, in te voegen door drukkerij)

Nederlandse Vereniging voor Gastroenterologie

Aanmeldingsformulier lidmaatschap *(doorhalen wat niet van toepassing is)*

naam en voorletters		m / v
voornaam		geb. datum:
titel		
specialisme / functie		
doctoraal examen	neen / ja d.d.	zo ja, studierichting:
arts examen	n.v.t. / ja d.d.	
assistent i.o. voor		einde opleiding:
inschrijving MSRC	neen / ja d.d.	BIG registratie nr.
huisadres		
postcode en plaats		
telefoonnummer		
werkinstelling		
afdeling		
adres		
postcode en plaats		
telefoonnummer		
e-mail adres		
Toezending verenigingspost aan huis- / werkadres		

Tevens wil ondergetekende zich aansluiten bij:

□ Sectie Gastrointestinale Endoscopie
□ Netherlands Society of Parenteral and Enteral Nutrition
□ Sectie Neurogastroenterologie en Motiliteit
□ Sectie Experimentele Gastroenterologie
□ Sectie Kindergastroenterologie
□ Sectie Inflammatoire Darmziekten
□ Sectie Gastrointestinale Oncologie

n.b. Aanvullende lidmaatschappen van secties zijn kosteloos

□ Hierbij machtig ik de penningmeester van de Nederlandse Vereniging voor Gastroenterologie om de verschuldigde contributie tot wederopzegging automatisch van mijn bank-/girorekening af te laten schrijven. Betaling geschiedt nadat u door de eerstvolgende ledenvergadering als lid bent aangenomen. Indien u geen machtiging tot incasso geeft ontvangt u automatisch een factuur. Voor verzending van facturen worden vanaf volgend jaar administratiekosten in rekening gebracht.

IBAN:

BIC:

Datum en handtekening:

_____

Dit ondertekende formulier per post of fax (023 – 5513087) sturen naar: Secretariaat NVGE, Postbus 657, 2003 RR Haarlem

Aanvullende informatie: De contributie van de Nederlandse Vereniging voor Gastroenterologie bedraagt € 50,00 per jaar.

NEDERLANDSE VERENIGING VOOR HEPATOLOGIE

Aanmeldingsformulier lidmaatschap

naam en voorletters		m / v
voornaam		geb. datum:
titel		
specialisme / functie		
doctoraal examen	neen / ja d.d.	zo ja, studierichting:
arts examen	n.v.t. / ja d.d.	
assistent i.o. voor		einde opleiding:
inschrijving MSRC	neen / ja d.d.	BIG registratie nr.
huisadres		
postcode en plaats		
telefoonnummer		
werkinstelling		
afdeling		
adres		
postcode en plaats		
telefoonnummer		
e-mail adres		
* Toezending verenigingspost aan huis- / werkadres		

** Doorhalen wat niet van toepassing is.*

☐ Hierbij machtig ik de penningmeester van de Nederlandse Vereniging voor Hepatologie om de verschuldigde contriutie tot wederopzegging automatisch van mijn bank-/girorekening af te laten schrijven. Betaling geschiedt nadat u door de eerst-volgende ledenvergadering als lid bent aangenomen. Indien u geen machtiging tot incasso geeft ontvangt u automatisch een factuur. Voor verzending van facturen worden vanaf volgend jaar administratiekosten in rekening gebracht.

IBAN:

BIC:

Datum en handtekening:

_____

Dit ondertekende formulier per post of fax (023 – 5513087) sturen naar:
Secretariaat NVH, Postbus 657, 2003 RR Haarlem

Aanvullende informatie: De contributie van de Nederlandse Vereniging voor Hepatologie bedraagt € 35,00 per jaar.
Na toetreding als lid ontvangt u een factuur (conform de regels is volledige contributie verschuldigd in het jaar van toetreding).