Dutch Liver week, Leiden 22 juni 2017

Voeding en de lever

Ger H Koek, M.D., PhD

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Geen disclosures

Vraag: wat is de rol van de MDL arts tav metabole aspekten lever?

- geen rol
- rol in diagnostiek en behandeling
- Alleen rol bij gecompliceerd leverlijden
- Centrale rol in lever gerelateerde metabole aandoeningen

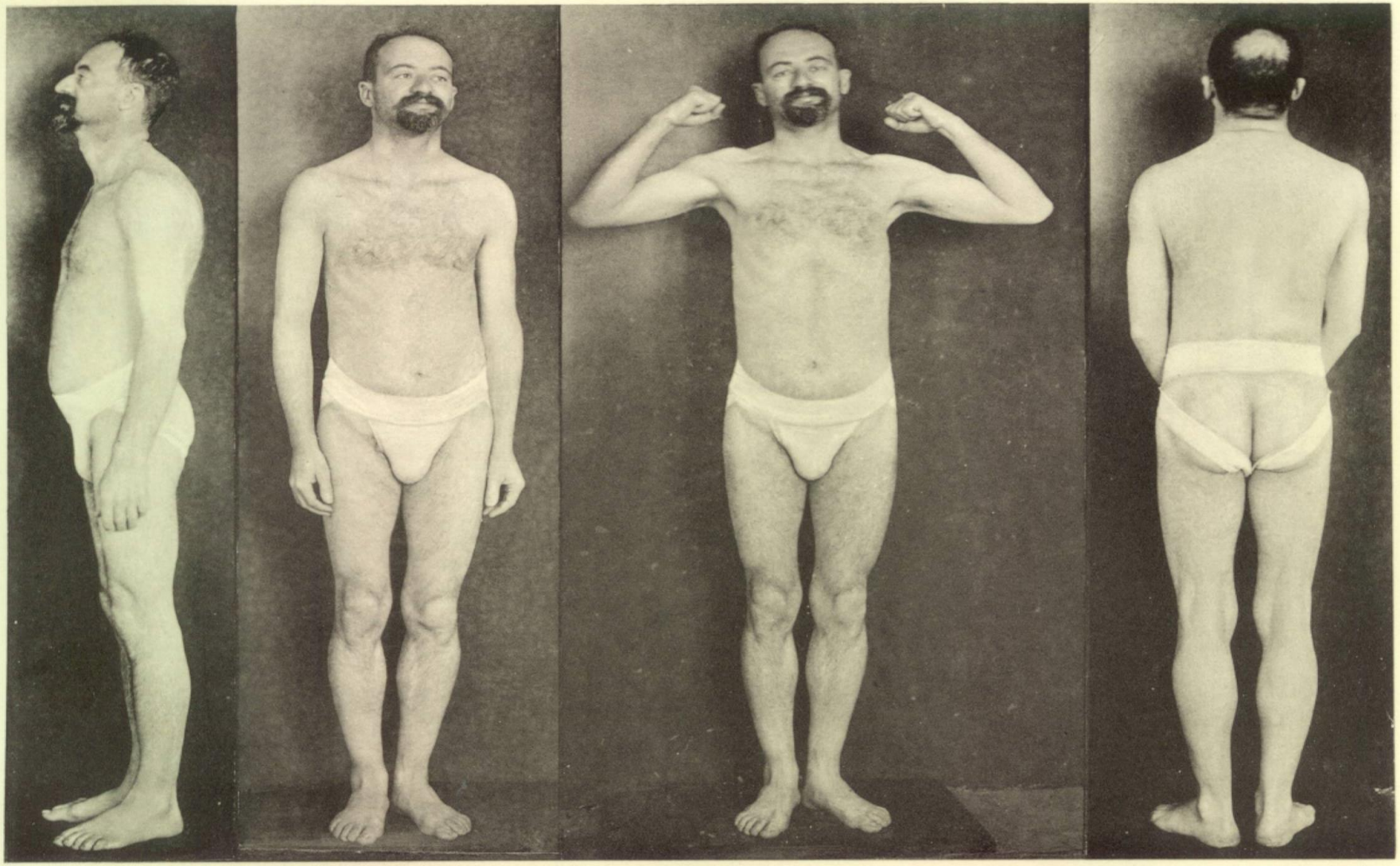
Statement

Lever gerelateerde metabole aandoeningen zijn domein MDLever arts

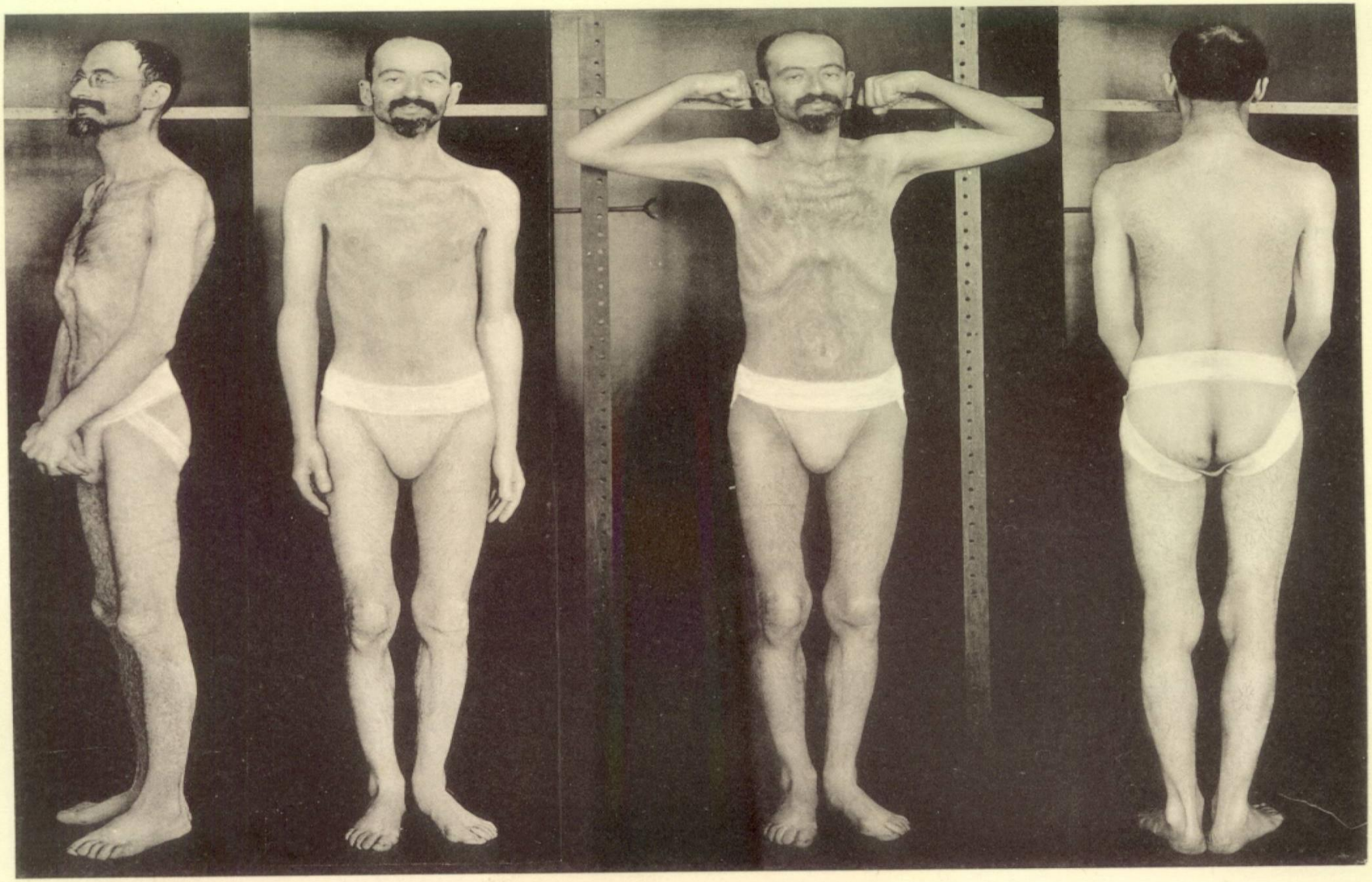
Functie in:

- Diagnostiek en behandeling
- Coördineert interdisciplinaire samenwerking
  - 1e lijn huisarts en huisarts ondersteuning
  - endocrinologie
  - vasculair geneeskundige

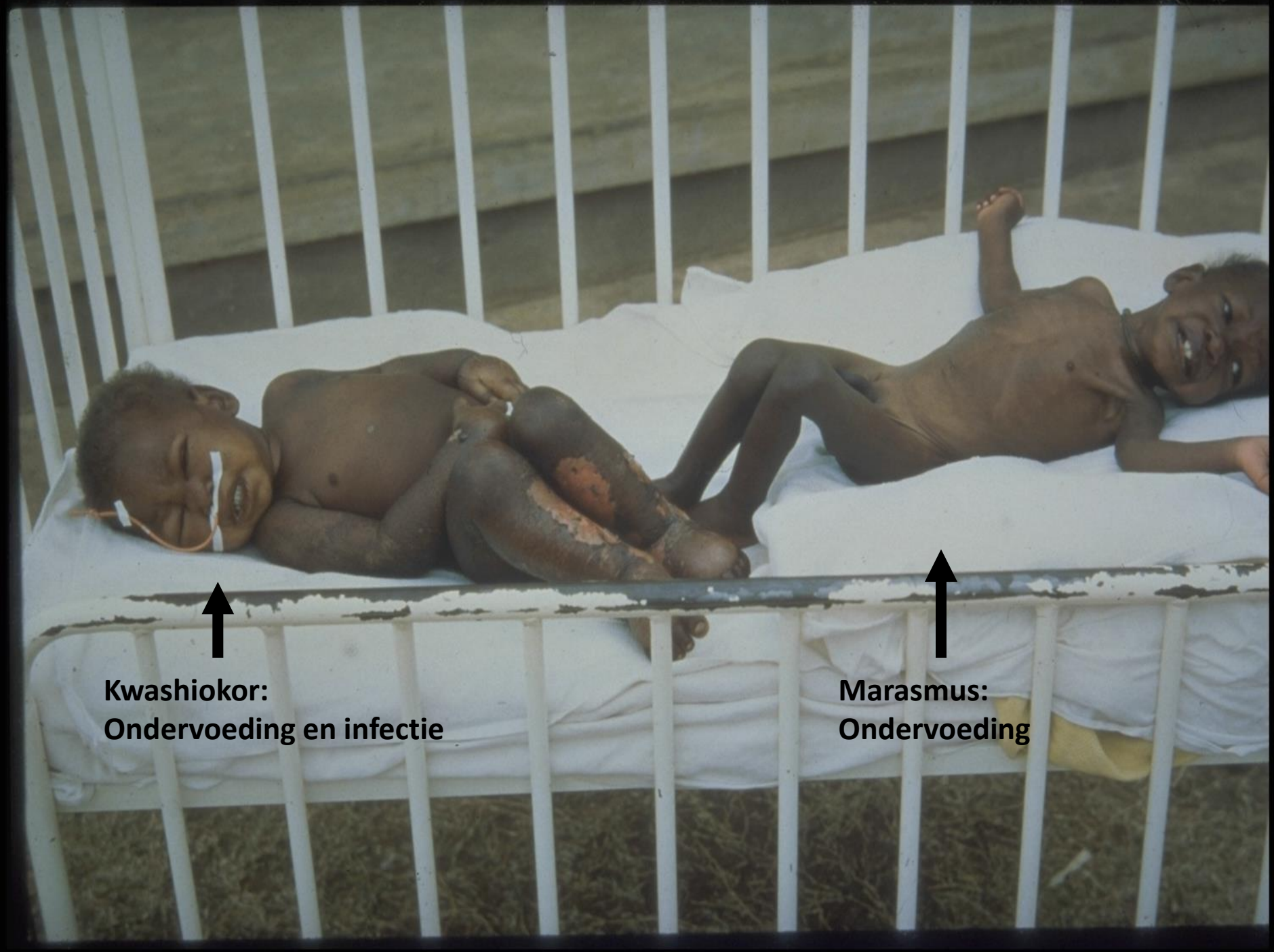
N=1 studie 1912 Heer Levanzin



Views of subject Levanzin on first day of Thirty-one day Fast.



Views of subject Levanzin on last day of Thirty-one day Fast.


Kwashiokor:
Ondervoeding en infectie
Marasmus:
Ondervoeding

—*Nitrogen excreted in urine, per day and per kilogram of body-weight, in experiment with L.*

Date.	Day of fast.	Nitrogen excreted.		Date.	Day of fast.	Nitrogen excreted.	
		Per day.	Per kilogram of body-weight per day.			Per day.	Per kilogram of body-weight per day.
1912.		*gm.*	*gm.*	1912.		*gm.*	*gm.*
Apr. 11–12	.....	15.92	0.264	Apr. 30–May 1	17th...	8.81	0.169
12–13	.....	14.48	.238	May 1–2	18th...	8.27	.160
13–14	.....	11.54	.190	2–3	19th...	8.37	.163
14–15	1st...	7.10	.118	3–4	20th...	7.69	.151
15–16	2d....	8.40	.142	4–5	21st...	7.93	.156
16–17	3d....	11.34	.195	5–6	22d....	7.75	.154
17–18	4th...	11.87	.207	6–7	23d....	7.31	.146
18–19	5th...	10.41	.184	7–8	24th...	8.15	.164
19–20	6th...	10.18	.181	8–9	25th...	7.81	.158
20–21	7th...	9.79	.176	9–10	26th...	7.88	.160
21–22	8th...	10.27	.186	10–11	27th...	8.07	.165
22–23	9th...	10.74	.196	11–12	28th...	7.62	.157
23–24	10th...	10.05	.185	12–13	29th...	7.54	.156
24–25	11th...	10.25	.190	13–14	30th...	7.83	.163
25–26	12th...	10.13	.189	14–15	31st...	6.94	.146
26–27	13th...	10.35	.193	15–16	.....	4.83	.102
27–28	14th...	10.43	.196	16–17	.....	3.81	.081
28–29	15th...	8.46	.160	17–18	.....	[1]2.75	[1].058
29–30	16th...	9.58	.182				

[1]Determined in urine for about 22 hours.

Stress en Katabolie

- 10 – 14 g N (stikstof) /dag
- 10 – 14 x 6.25 = 62 – 87 g eiwit /dag
- 62 – 87 x 4 = 250 – 350 g nat spiergewicht (grotendeels spier, ook huid, bot)

Hoe zit het met voedingstatus van deze obese patient?

Abdominale operatie

Platzbauch

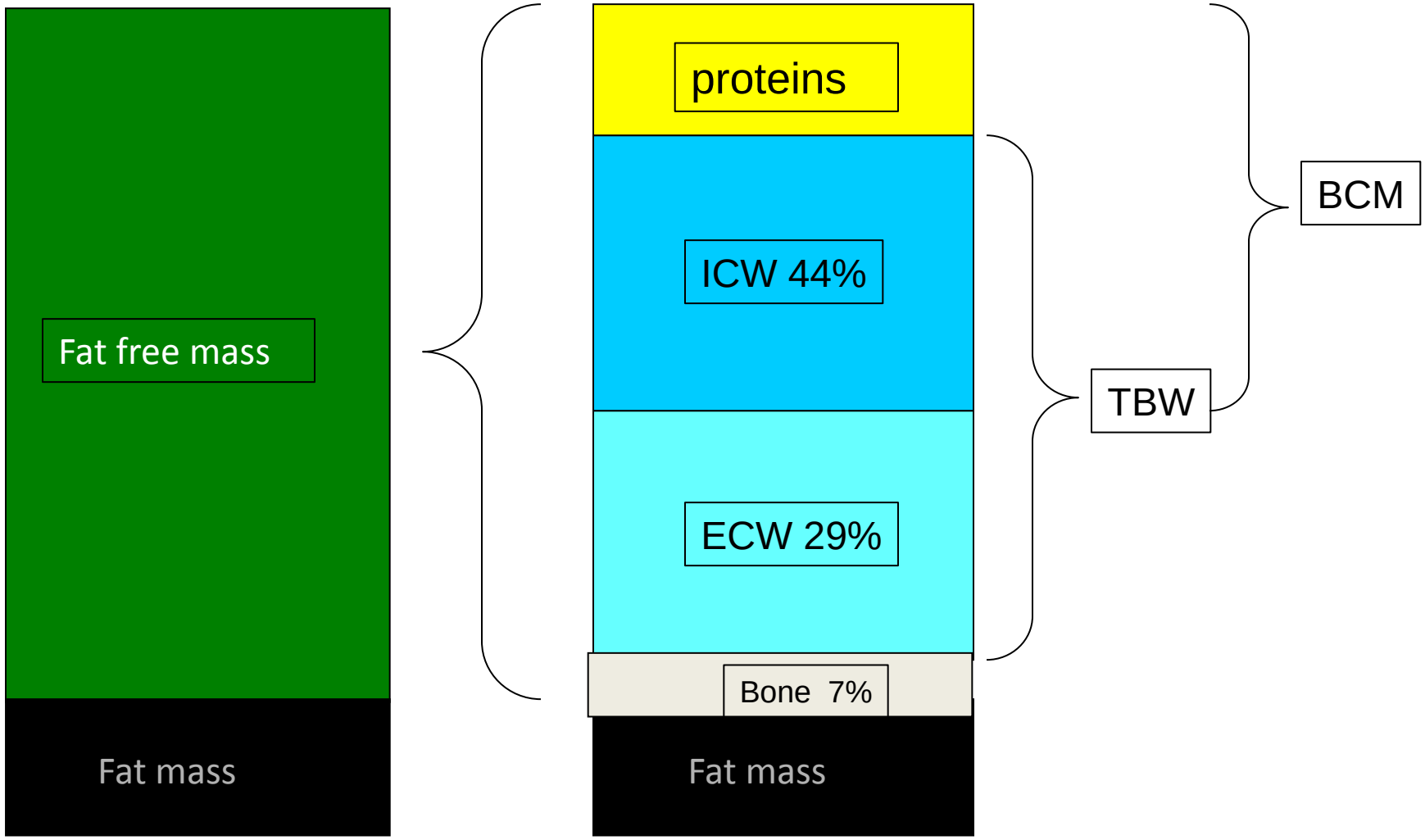
maagretentie

ARDS

Vetmassa en overvulling kunnen verlies van vetvrije massa (body cell mass) maskeren

Body composition

2 compartment model



Body composition

The normal ranges for muscle mass:

Age	Women	Men
20-39	63% - 75.5%	75% - 89%
40-59	62% - 73.5%	73% - 86%
60-79	60% - 72.5%	70% - 84%

The normal ranges for bone mass

Women	Men
2.5% - 4%	3% - 5%

The normal ranges for fat mass

Age	Women	Men
20-39	22% - 33%	8% - 20%
40-59	24% - 34%	11% - 22%
60-79	25% - 36%	13% - 25%

The normal ranges for water mass

Women	Men
45% - 60%	50% - 65%

Fat mass + Bone mass + Muscle mass = 100% of the body composition

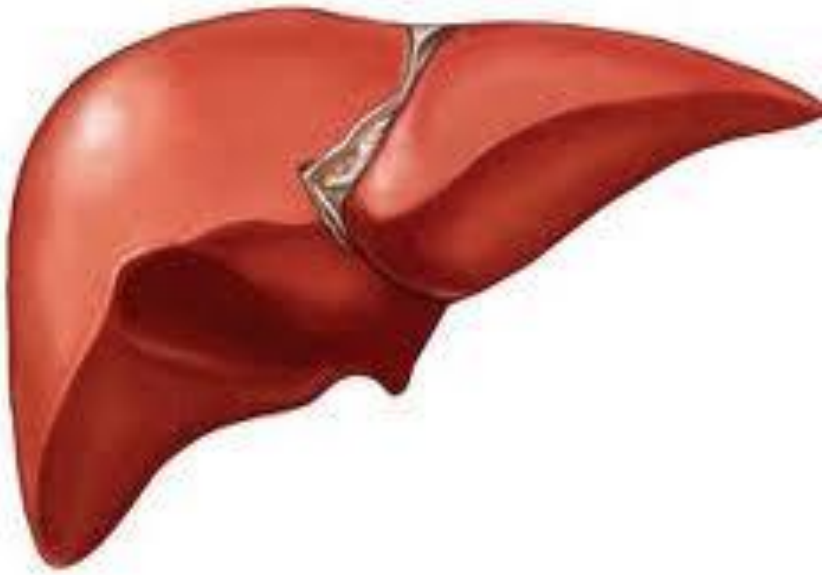
Withings Withings Body Cardio (NEW - 2016) Body Composition

Body changes in progressive chronic liver disease

Tense ascites
hernia umbilicalis

atrophic muscle
skin
haematomas
diminished subcutaneous fat mass

Disturbed liver metabolic function



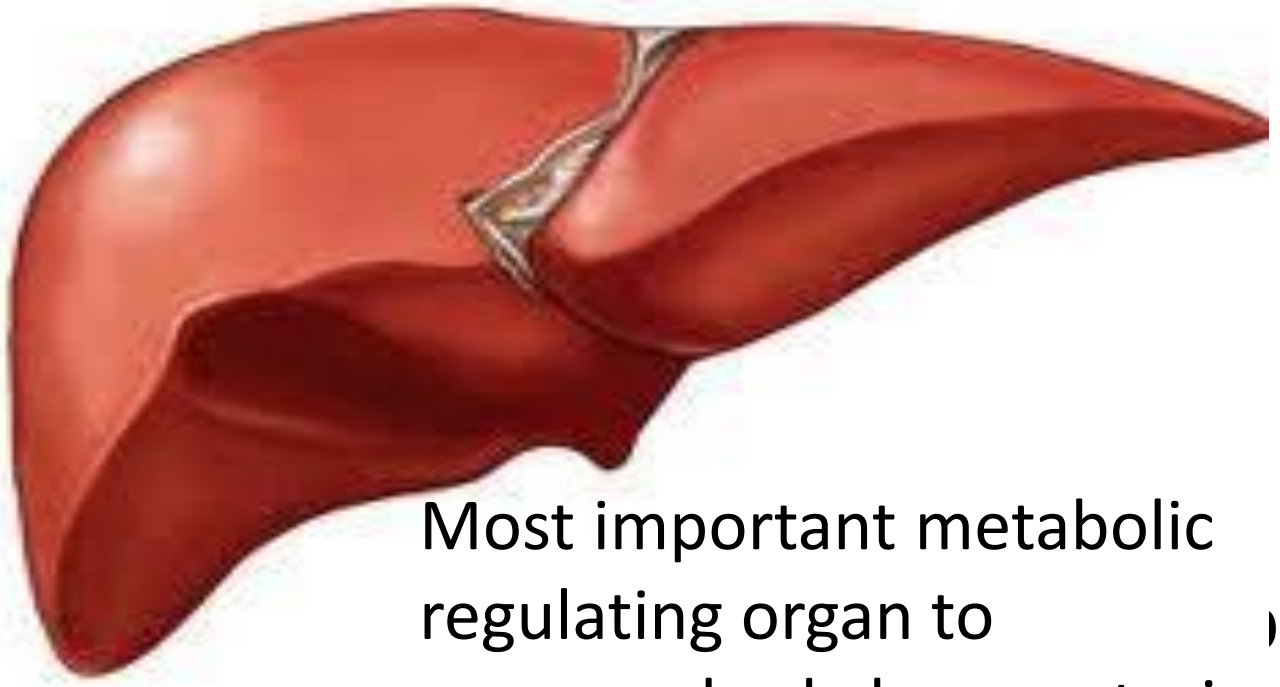
Disturbed nutritional balance

Metabolism
fueling and building blocks

carbohydrates

proteins

lipids



protein

Most important metabolic regulating organ to preserve body homeostasis

lids

Energy

- Sources: carbohydrates, lipids and proteins
- Triacylglycerols more efficient energy storage compared to glycogen
- ATP yield Triacylglycerols: glycogen= 2.5:1
- Triacylglycerols stored without water
- Glycogen binds twice its weight of water

Hoeveel energie in glycogeen opgeslagen bij persoon van 70 kg?

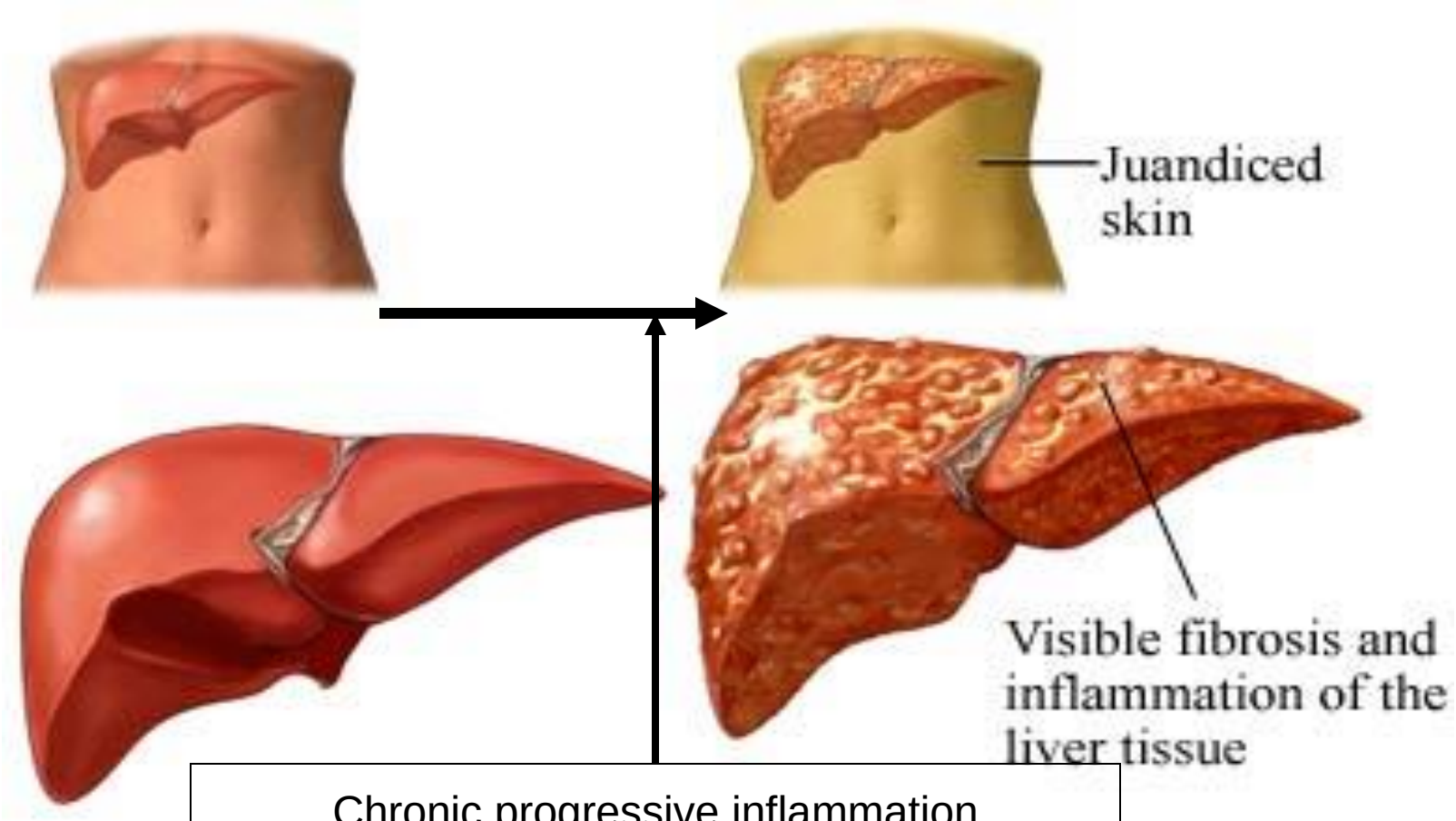
a. 125g 500 kcal
b. 250g 1000 kcal
c. 375g 1500 kcal
d. 500g 2000 kcal

Energy stores in healthy condition

70 Kg human

- 250g glycogen in liver and muscle
- Represents 1000 kcal energy
- 16 kg Triacylglycerol energy sufficient to survive several weeks of starvation
- Triacylglycerol pool easy to expand
  - Adipose tissue
- Protein pool

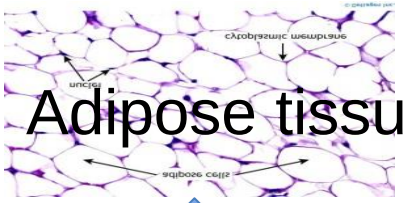
Disturbed nutritional balance in progressive liver disease



Chronic progressive inflammation

Toxicity

Liver organ interactions



Adipose tissue

Brain

Endocrine system
Exo / endocriene
pancreas

Liver

Kidney

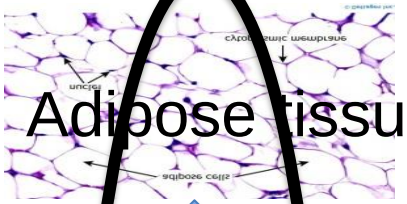
Gut liver axis

Intestine

cardiovascular system

Muscle

Liver organ interactions



Adipose tissue

Brain

Endocrine system
Exo / endocriene
pancreas

Liver

Kidney

Gut liver axis

Intestine

cardiovascular system

Muscle

Disturbed nutritional status in progressive chronic liver disease (CLD)

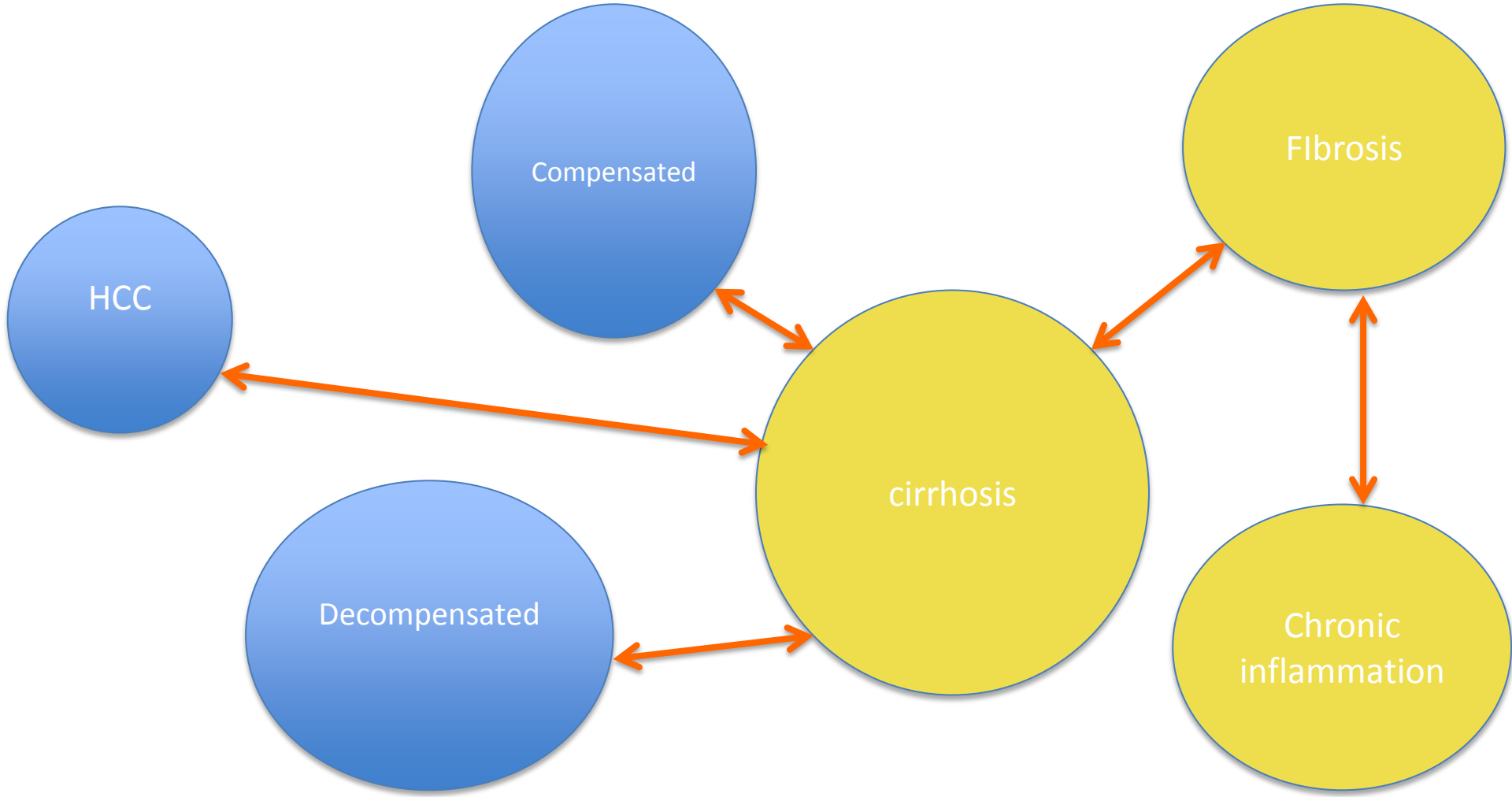
- Malnutrition

  2 or > characteristics

  – Insufficient energy intake
  – Weight loss
  – Loss of muscle mass
  – Loss of subcutaneous fat
  – Localized or generalized fluid accumulation that may sometimes mask weight loss
  – Diminished functional status as measured by handgrip strength

- Sarcopenia
  – Condition characterized by loss of muscle mass and strength
- Cachexia
  – Multifactorial syndrome characterized by increased protein catabolism due to underlying disease

Differentiating CLD



Questions

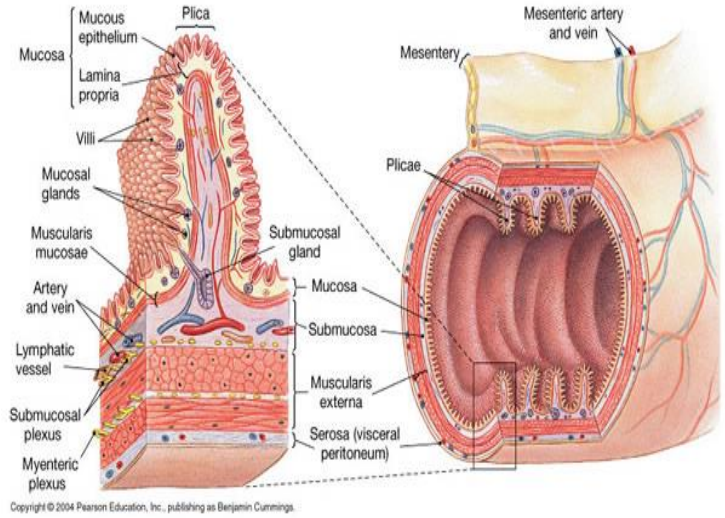
- Nutritional status chronic liver disease (CLD) patients
  - Malnutrition
  - Sarcopenia
  - Cachexia
- etiology
- How to diagnose
- How to treat

Pathophysiological aspects in metabolic status of CLD

- Liver related
- Portosystemic shunting
- Inflammatory status
- Muscle wasting

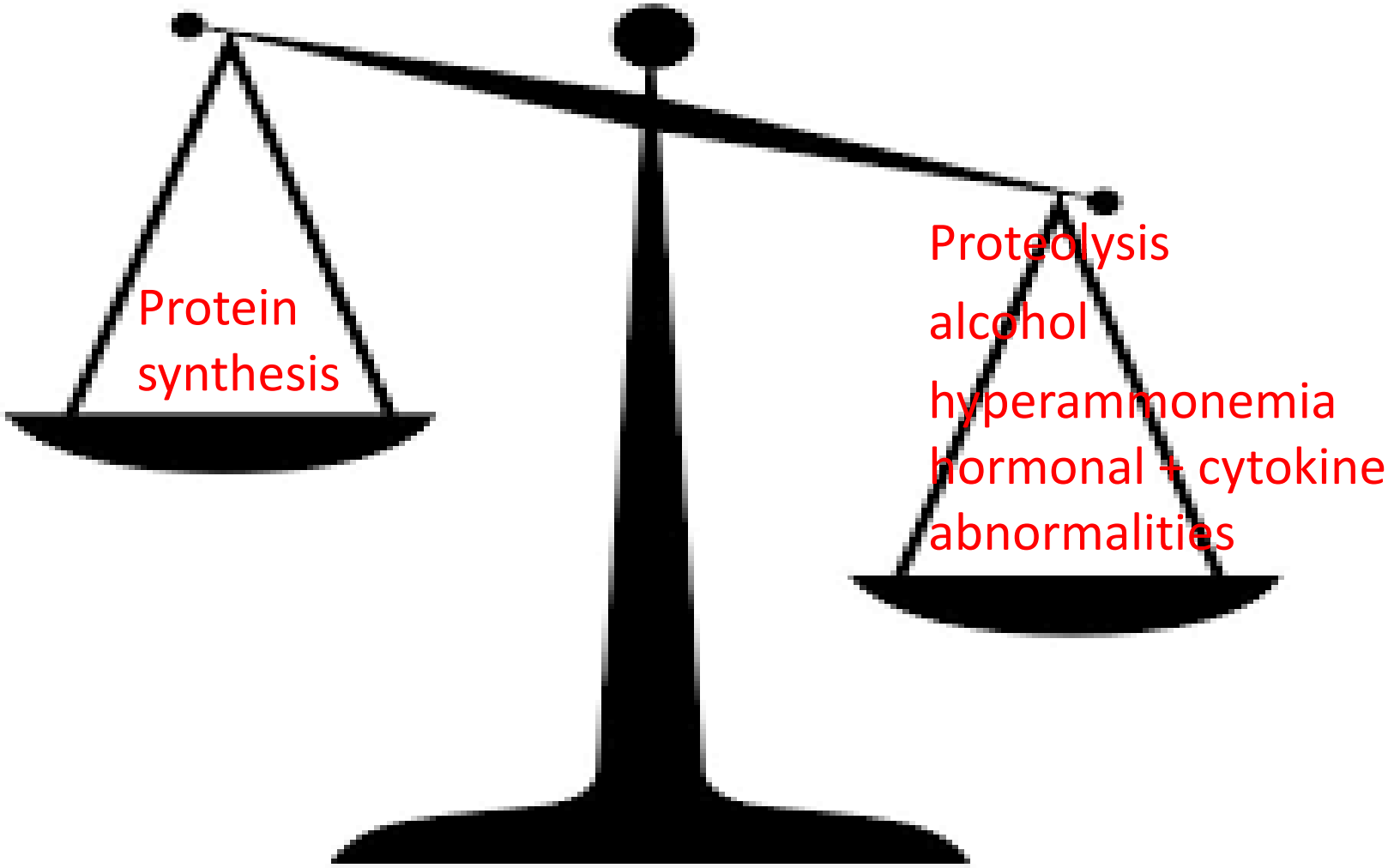
Portal hypertension

- Portal hypertension and portosystemic shunting
- Congestion GI tract
  - Diminished absorption
  - Diminished lymph transport
  - Diminished first pass effect



- Compromising metabolism; malabsorption
- Bacterial overgrowth small intestine
- Change in bacterial population colon

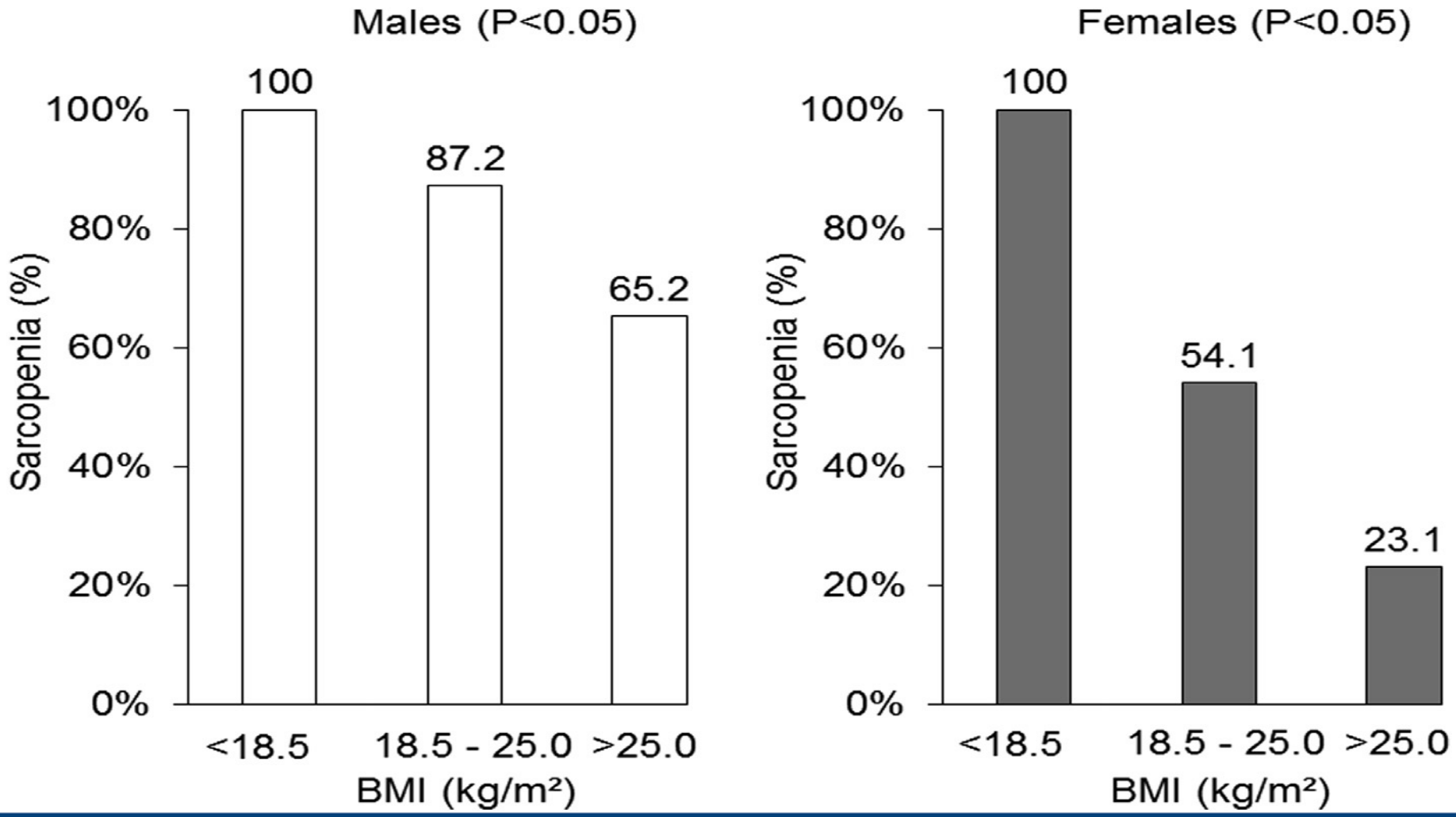
Muscle mass


Protein synthesis
Proteolysis
alcohol
hyperammonemia
hormonal + cytokine abnormalities

How often?

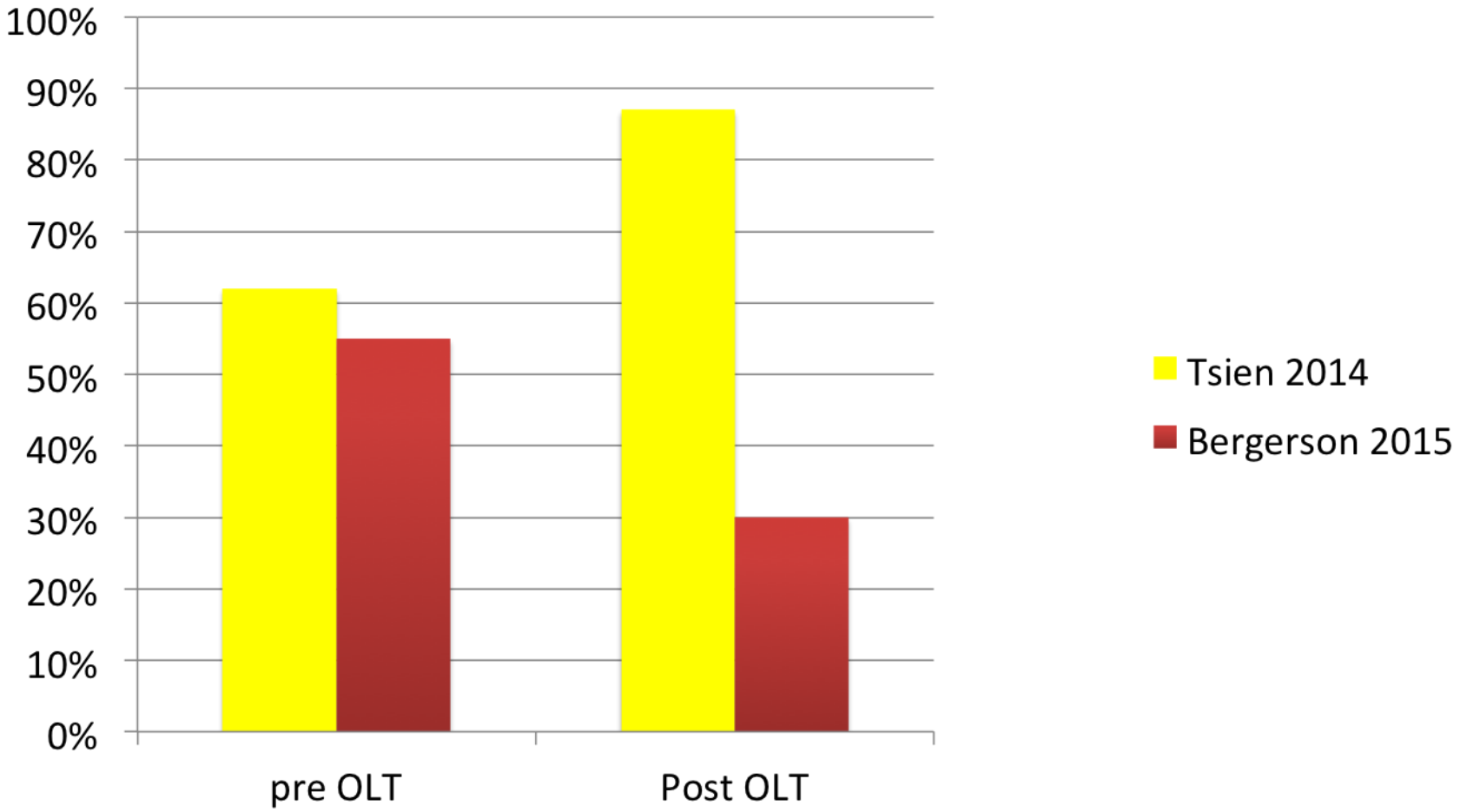
- prevalence of malnutrition in advanced cirrhosis 65–90 % (Merli etal. 2010).
- CT N3 Study in 338 patients before OLT showed cachexie in 68% (Di Martini 2013).
- Low proteine intake (<1g/kg/d) cause decline in muscle and fat tissue responsible for higher mortality after OLT (Ney 2015).

BMI and sarcopenia

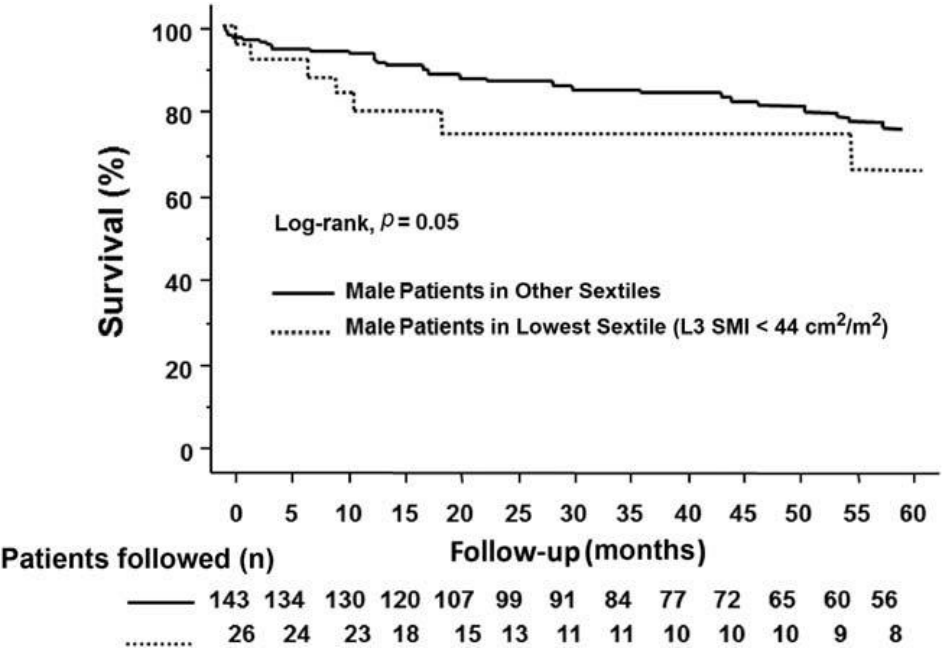


Hanai T et al. Nutrition. 2015

Sarcopenia and OLT



Survical post OLT

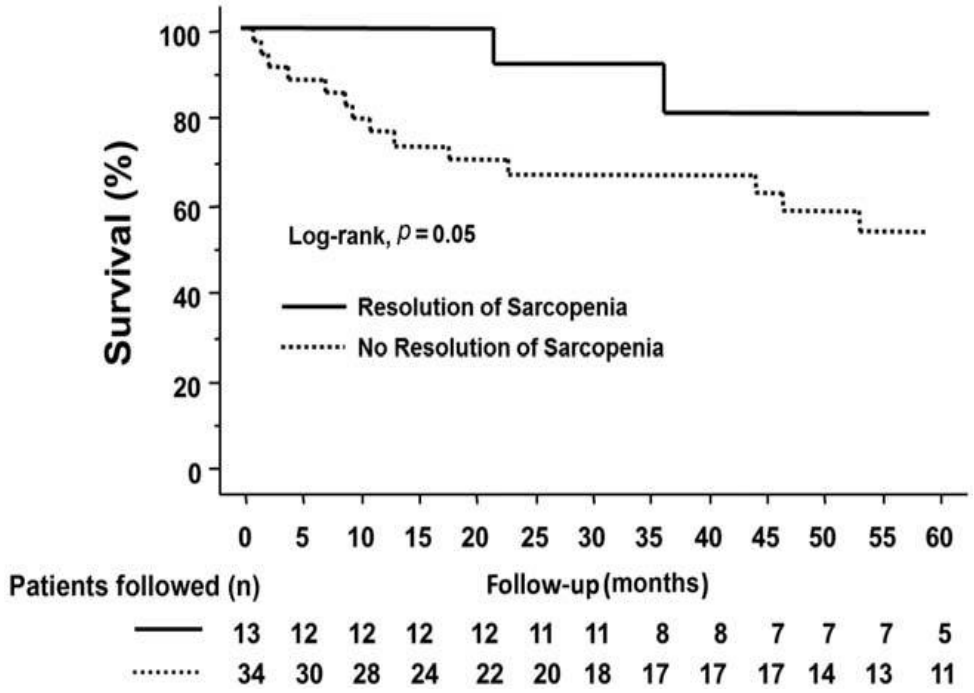


45% sarcopenia male patients (N=112)
Survival after OLT
1yr 81% vs 93%
5yr 67% vs 76%

Low BMI associated with mortality post OLT
Impaired immunity

MONTANO-LOZA ET AL. LIVER TRANSPLANTATION 2014

Survical post OLT

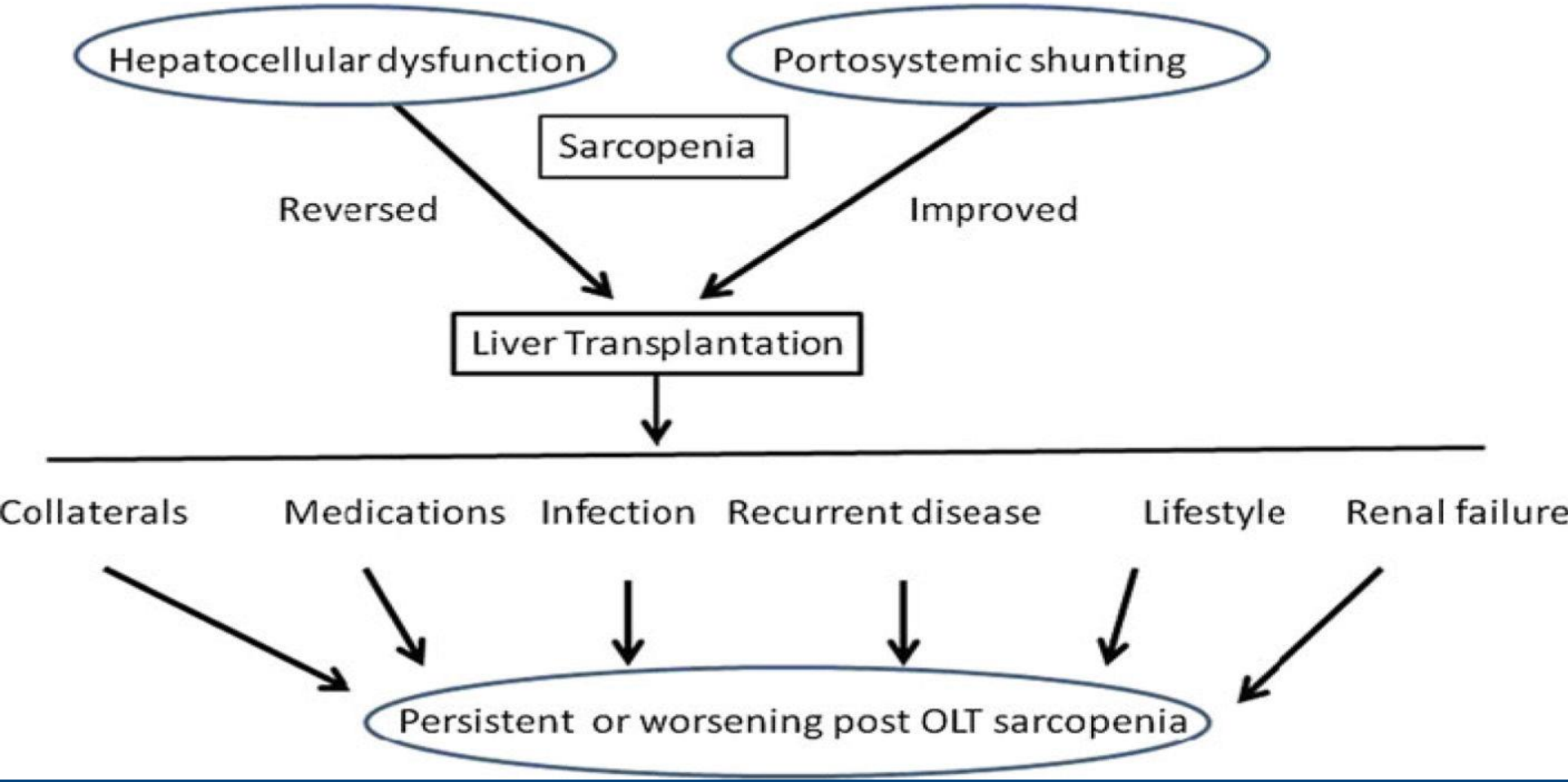


45% sarcopenia (112)
No resolution of sarcopenia
1yr 77% vs 92%
5yr 54% vs 82%

Longer recovery after OLT
Higher rates of bac infections
Impaired immunity

MONTANO-LOZA ET AL. LIVER TRANSPLANTATION 2014

Persistent post OLT sarcopenia complicating factors



Dasarathy S Dig Dis Sci. 2013

Diagnostic approach

1. Liver related
   - Liver disease: MELD, CP
2. nutritional assessment
3. body composition measurements

Orientation

- One question
- One test

Orientation

- One question: how much weight did You lost in the last 6 month?
- One test: give me a hand as firm as possible

Diagnostic nutritional status

http://www.nutritionalassessment.azm.nl/algoritme+na/onderzoek/energiegebruik/berekenen.htm

Weight loss could be either >10% of habitual weight indefinite of time, or >5% over 3 months

Diagnostic criteria for malnutrition - An ESPEN Consensus Statement. Cederholm et al. Clin Nutr. 2015.

Nutrional Assessment

=

Risk Assessment

=

individualizing therapy

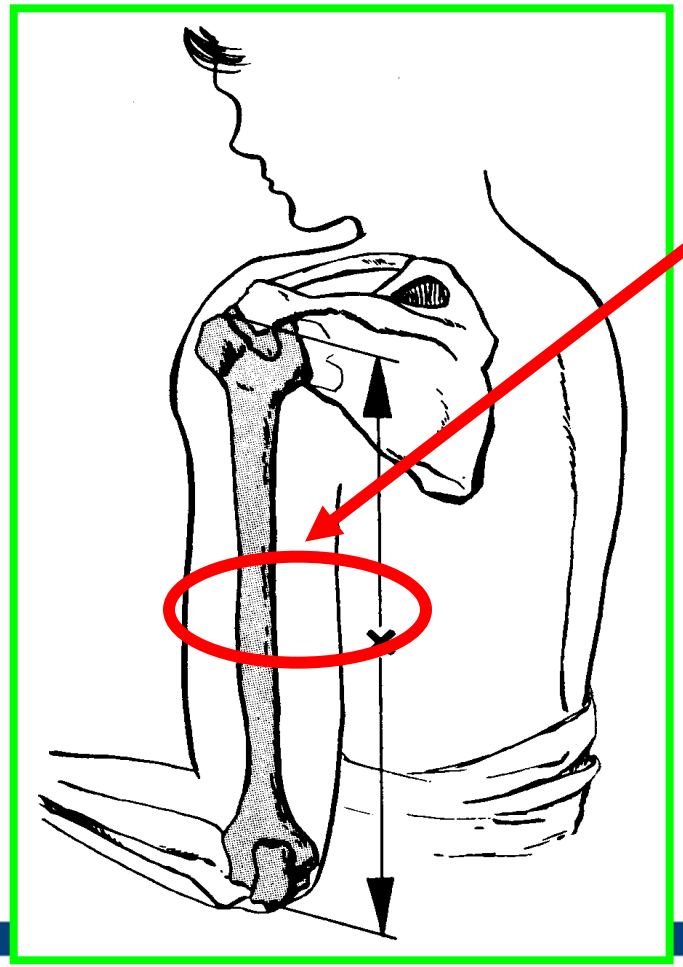
Nutritional Assessment

ESPEN
THE EUROPEAN SOCIETY FOR CLINICAL NUTRITION AND METABOLISM

Steps to be taken:

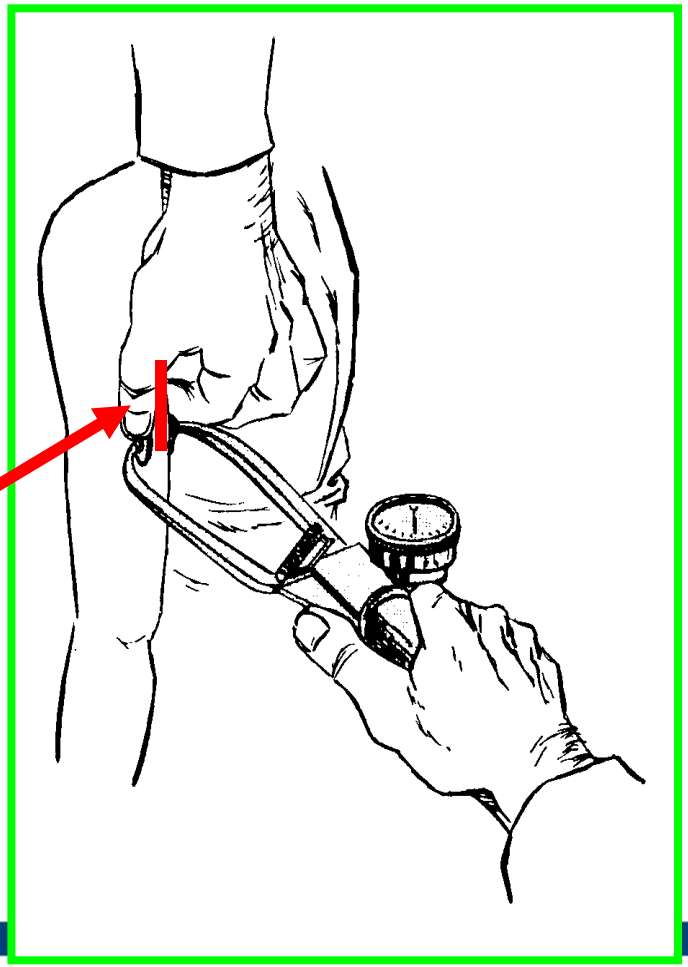
- Analyze previous dietary intake
- Measure body composition
- Measure/evaluate inflammatory activity/disease activity
- Measure function:
  - Muscle strength
  - Cognitive function (mood, concentration, memory etc)
  - Immune function

Anthropometry



Muscle mass

Fat mass



Muscle strength

Handgrip strength

- peak expiratory flow rate
  - Squeeze three times
  - Highest value is used
  - Dominant hand

- diagnosis of decreased muscle strength
- HGS <5th percentile according to standard values for the general population matched for age and sex

Hornby et al, Clin Nutr 2005 109:179 – 187, Hillman TE Clin Nutr 2005; 24:224-228.

Nutritional assessment

Evaluate grip strength

- predictor of complications
- relation with arm muscle area
- function changes before mass
- decreases with age
- Not to use during:
  - sedation
  - coma patients
  - muscular of neurological disease

Compare measured value with age and gender specific reference values.

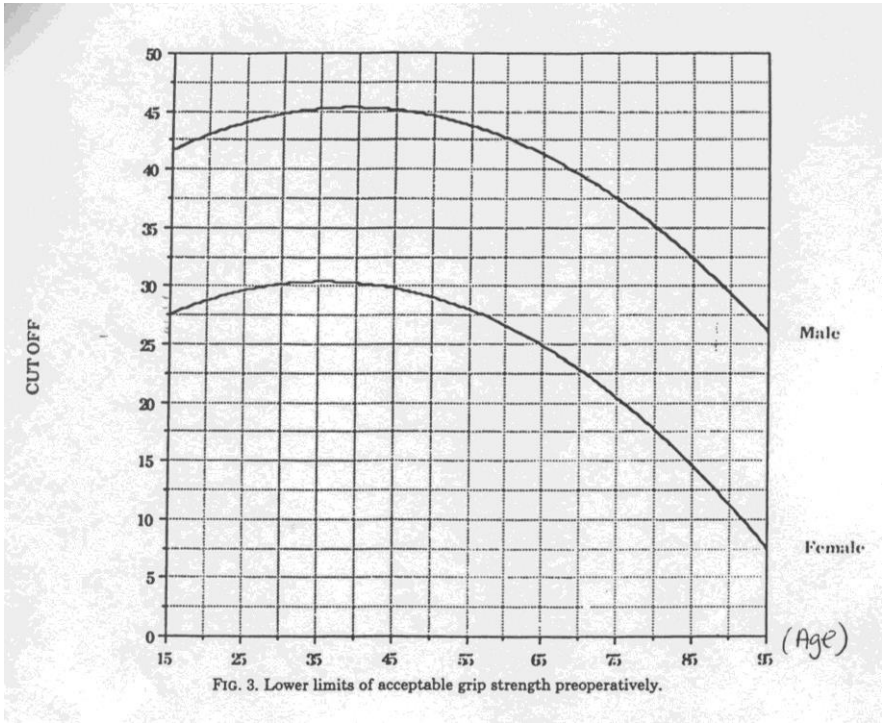


FIG. 3. Lower limits of acceptable grip strength preoperatively.

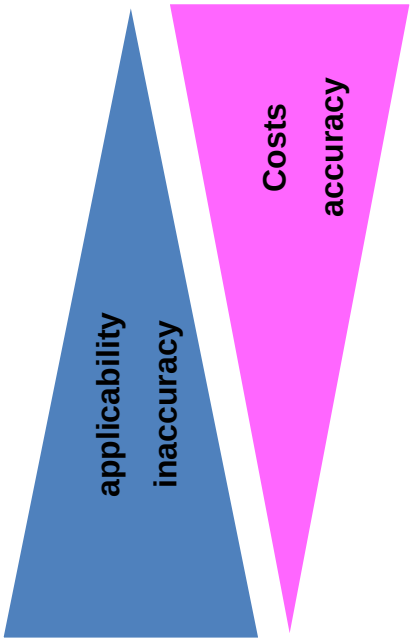
Recente referentiewaarden Spaanse populatie:
Luna-Heredia E et al. Clin Nutr 2005; 24:250-258

Bioelectrical impedance analysis (BIA)

- Longitudinal follow-up of body composition by BIA is possible between BMI of 16-34 kg/m2 without abnormal hydration
- Cheap and easy to preform
- Reproducible
- Not suitale in decompensated cirrhotic patients

ESPEN-Guideline BIA I, Clin Nutr, 2004, ESPEN-Guideline, BIA II, Clin Nutr, 2004

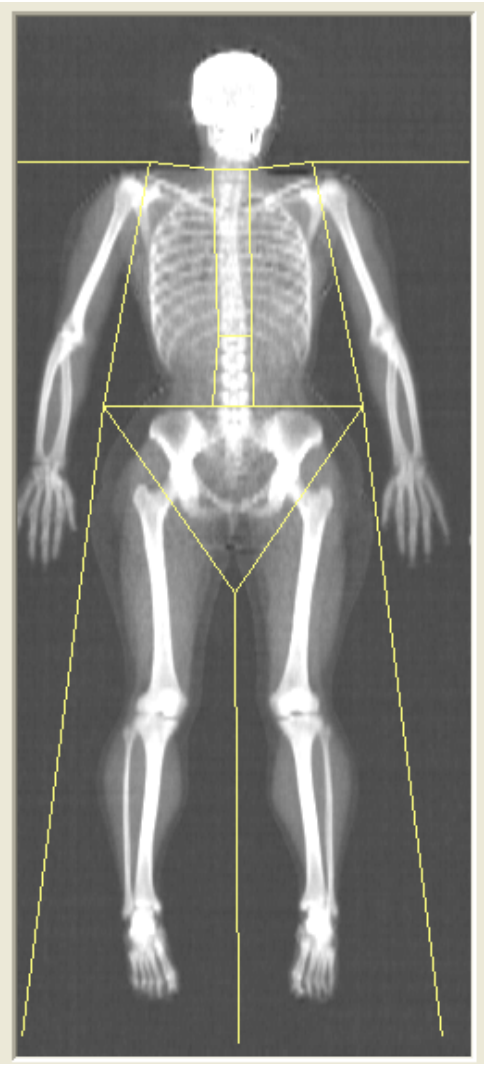
Techniques for measuring body composition



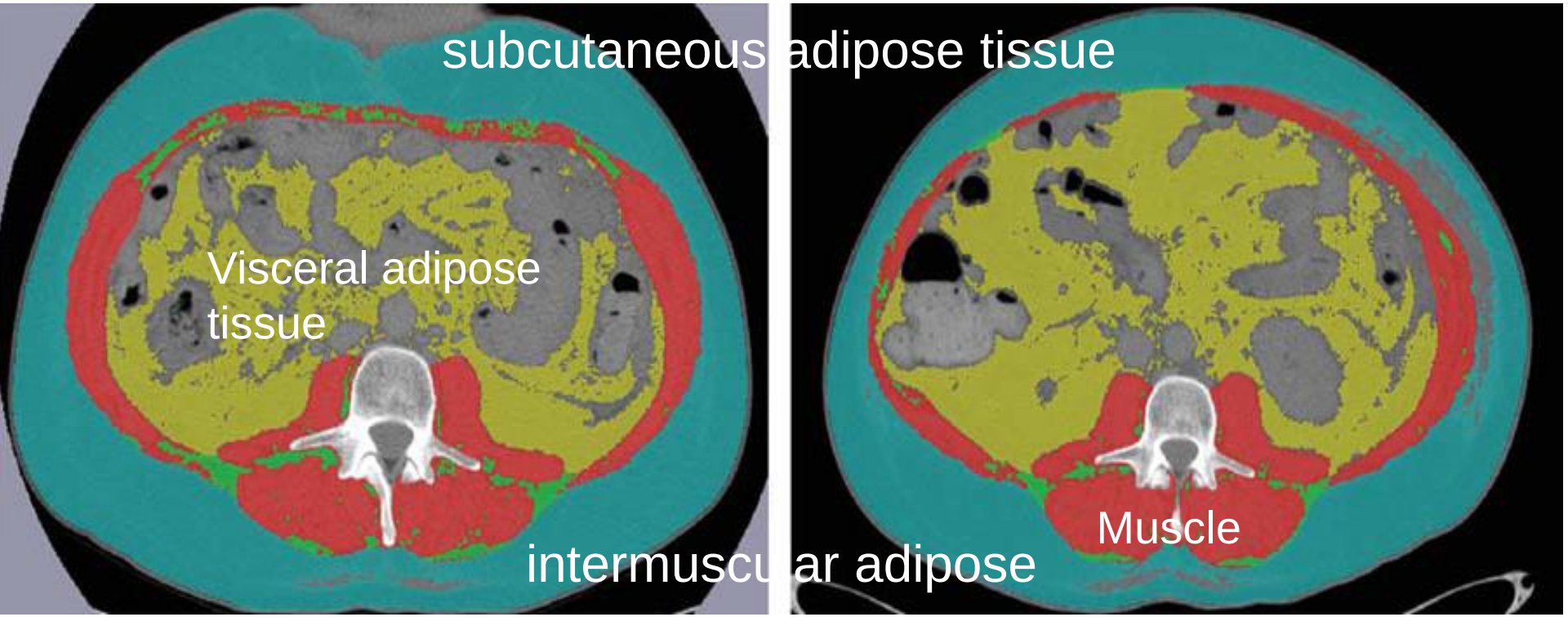
- CT scan, MRI, Total N, total K.
- Volume measurements (under water weighing, in air (BodPod))
- DEXA scan (VVM, VM, Bone density)
- Indicator dilution methods (TBW, ECW)
- bio-electrical impedance analysis
- Skin fold thickness (VM, VVM)

Total body dual-energy X-ray absorptiometry (DEXA) scan

- Skeletal muscle mass (Fat-free mass)
  - Fat-free mass index (kg/m²) (FFMI)
- Fat mass
  - Fat mass index (kg/m²) (FMI)
- Fat distribution
  - Visceral fat in cm²



CT Lumbar 3
psoas muscle thickness



Montano-Loza AJ, et al, Clin Gastroenterol Hepatol. 2012; Durand, J Hepatol. 2014

Skeletal muscle index (SMI) sectional CT L3

- Measurement single abdominal image of the third lumbar vertebra (L3).
- normalize muscle area to patient height ($cm^2/m^{2)}$
- Sarcopenie definition in ESLD awaiting LT
  - Men SMI < 50 cm^2/m^2
  - Women < 39 cm^2/m^2

Shen W et al. J Appl Physiol 2004; Carey, Liver Transplantation 2017

Liver Kurort

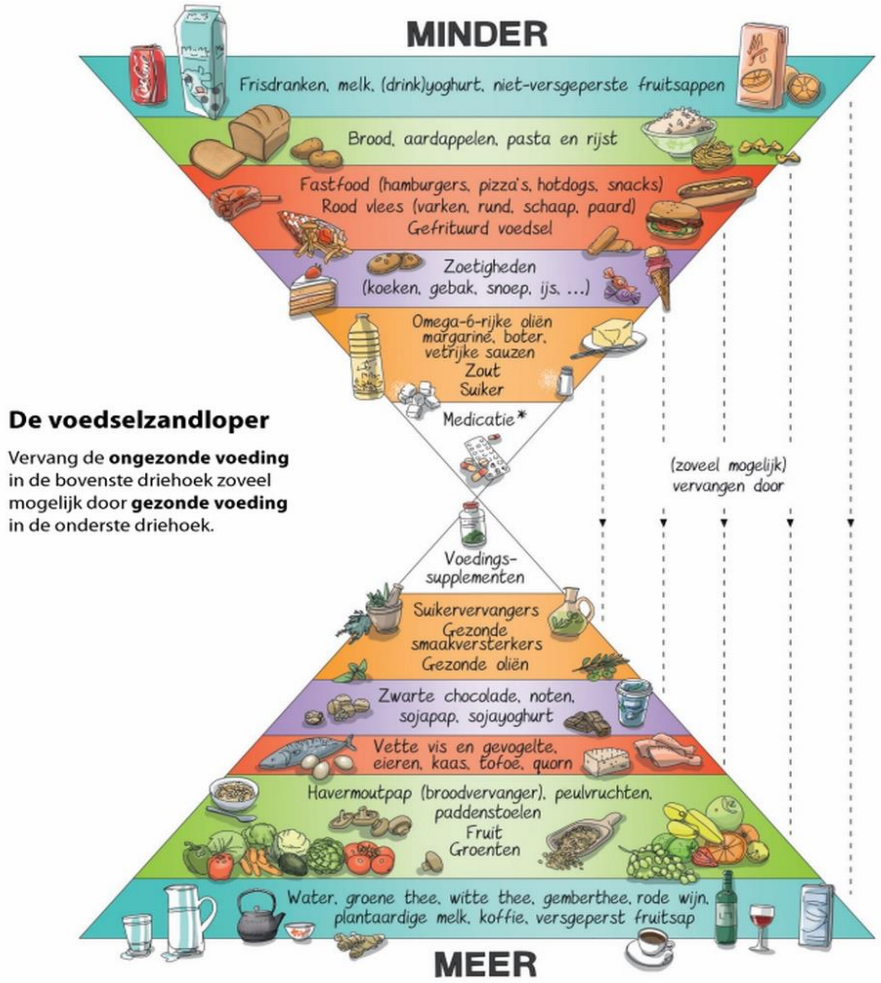
Aim nutritional physical management

- Preservation of skeletal muscle mass and function
- Improve (mal)nutrition/cachexia status (Fueling)
- Improve general health and functioning

Therapeutic interventions

- Treat liver disease
- Treat systemic inflammation
- Adequate balanced nutrition
- Improve muscle function

Recommendations 2016



dietary advise consensus ESPEN

- Energy intake 30-35 Kcal/KgBw/d
- Protein 1.2-1.5 g/KgBw/d
- BCAA if GE bleeding and HE grad III/IV
- Fat as source of energy ratio n6:n3 = 2:1
- Enteral duodenal
- Parenteral feeding if no enteral is possible
- Supplements micronutriënten:

  vitamine A, D, E, K, B12, B1 and C, calcium, magnesium, zink, folic acid, selenium, natrium, fibers.

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What is the goal?

How to treat?

- Branched chain Amino acids
- 20 g before sleep
- Bad taste

Testosteron measurement

- Who does this?

Treatement with androgen

- Treatment with Testim gel?
- Control testosteron

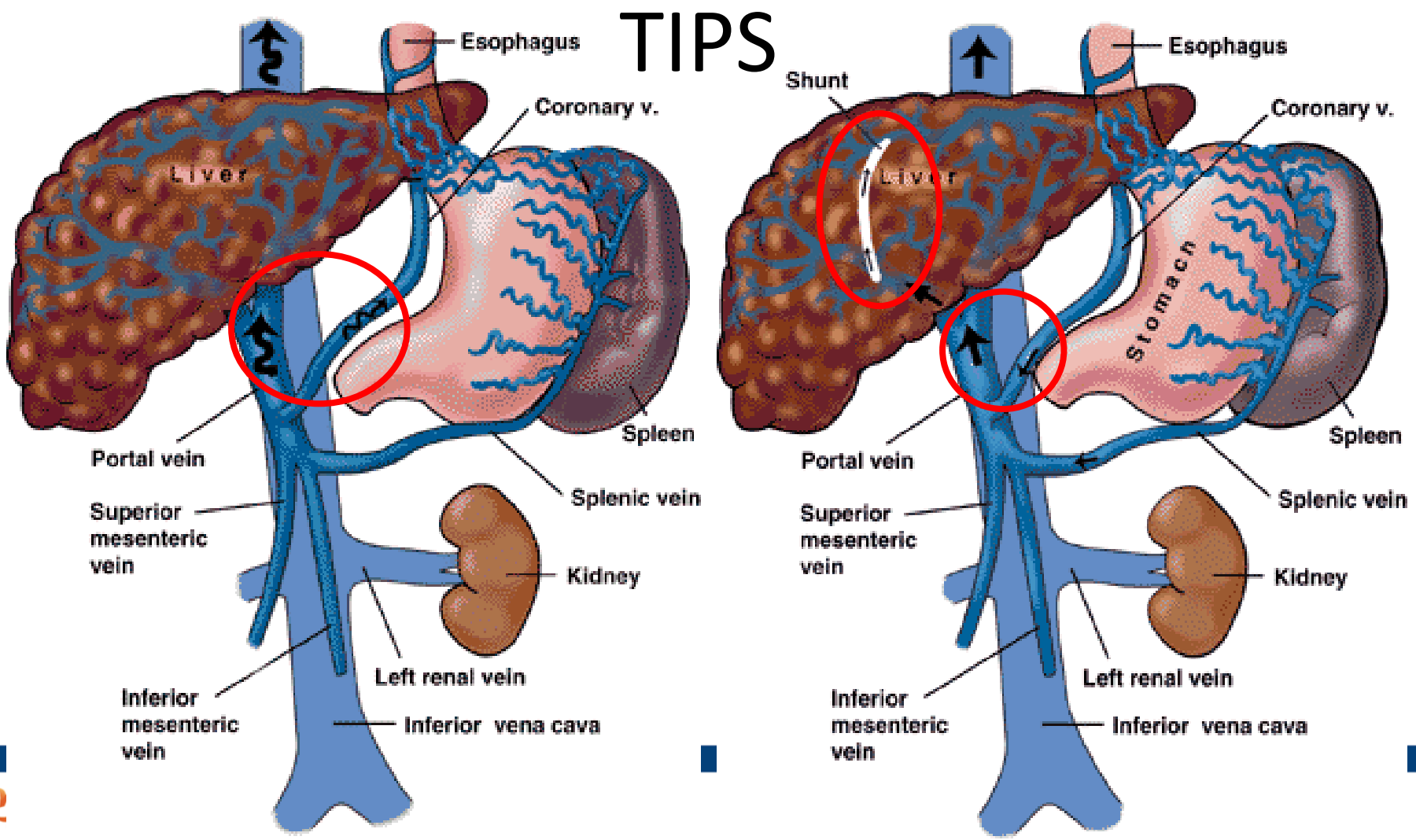
Sinclair, World J Gastroenterol. 2014

Androgenen therapy in cirrhosis

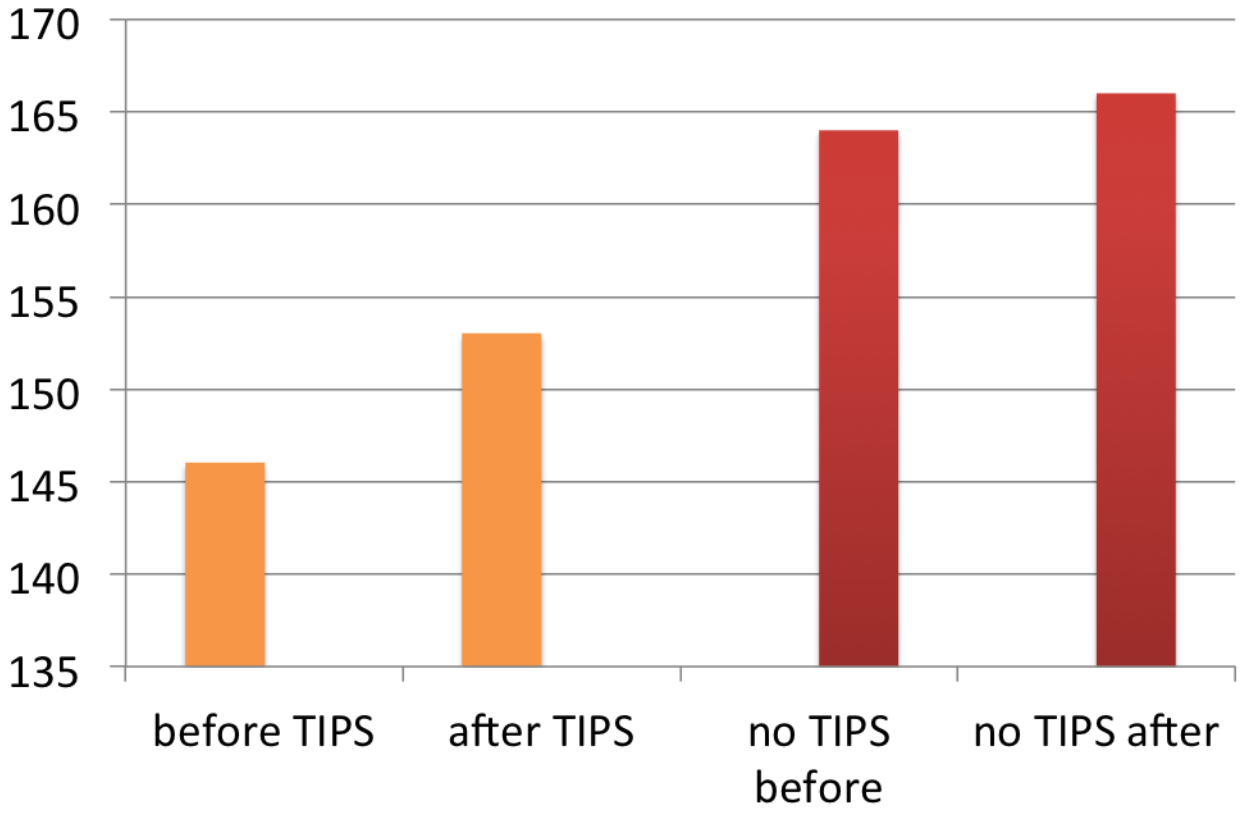
- 90% testosterone reduced
- Important anabolic hormone
- sarcopenia, osteoporosis, gynecomastia, low libido.
- Small studies
- Benificial effect not clear yet
- Androgenen therapy debated side effects?
- Therapy for women?

Orr R et al. drugs 2004, Sinclair M et al. J Gastroenterol Hepatol. 2015

TIPS as metabolic therapy?



TIPS as treatment



Total muscle area cm^2

TIPS group 57
Time interval 10 month

No TIPS group 32
Time interval 13 month

- TIPS reverses sarcopenia in cirrhotic patients

Tsien C et al. Eur J Gastroenterol Hepatol. 2013

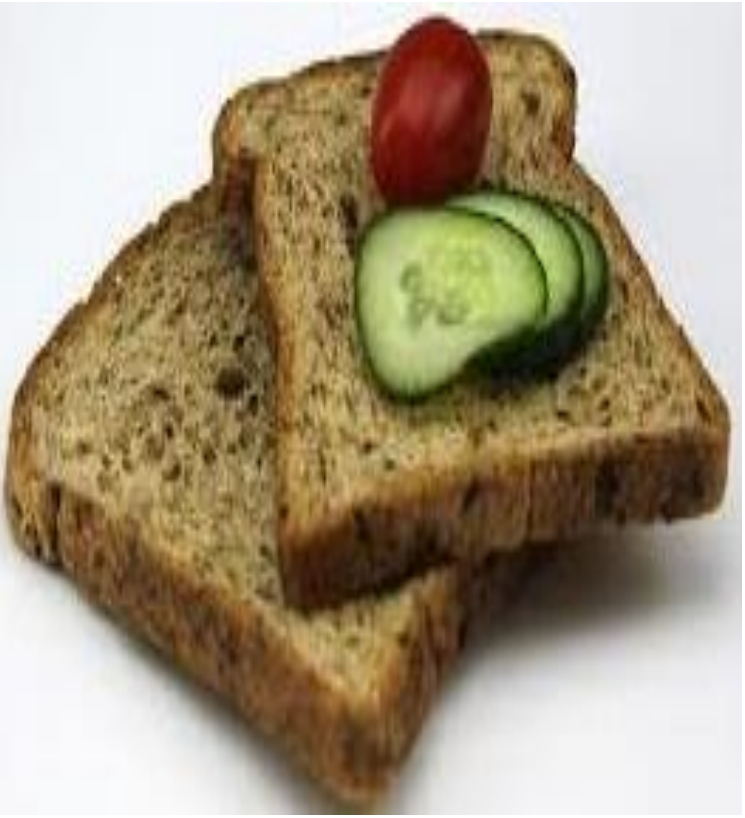
Physio therapist individualized program

- Intake
- Advise
  - Resistance
  - aerobic
- Control
  - Check the results by reporting

Physical activity compensated cirrhotic patients

- walking 5000 or more steps per day
- maintaining a total energy intake of 30 kcal/IBW

Hayashi F, Hepatol Res. 2013

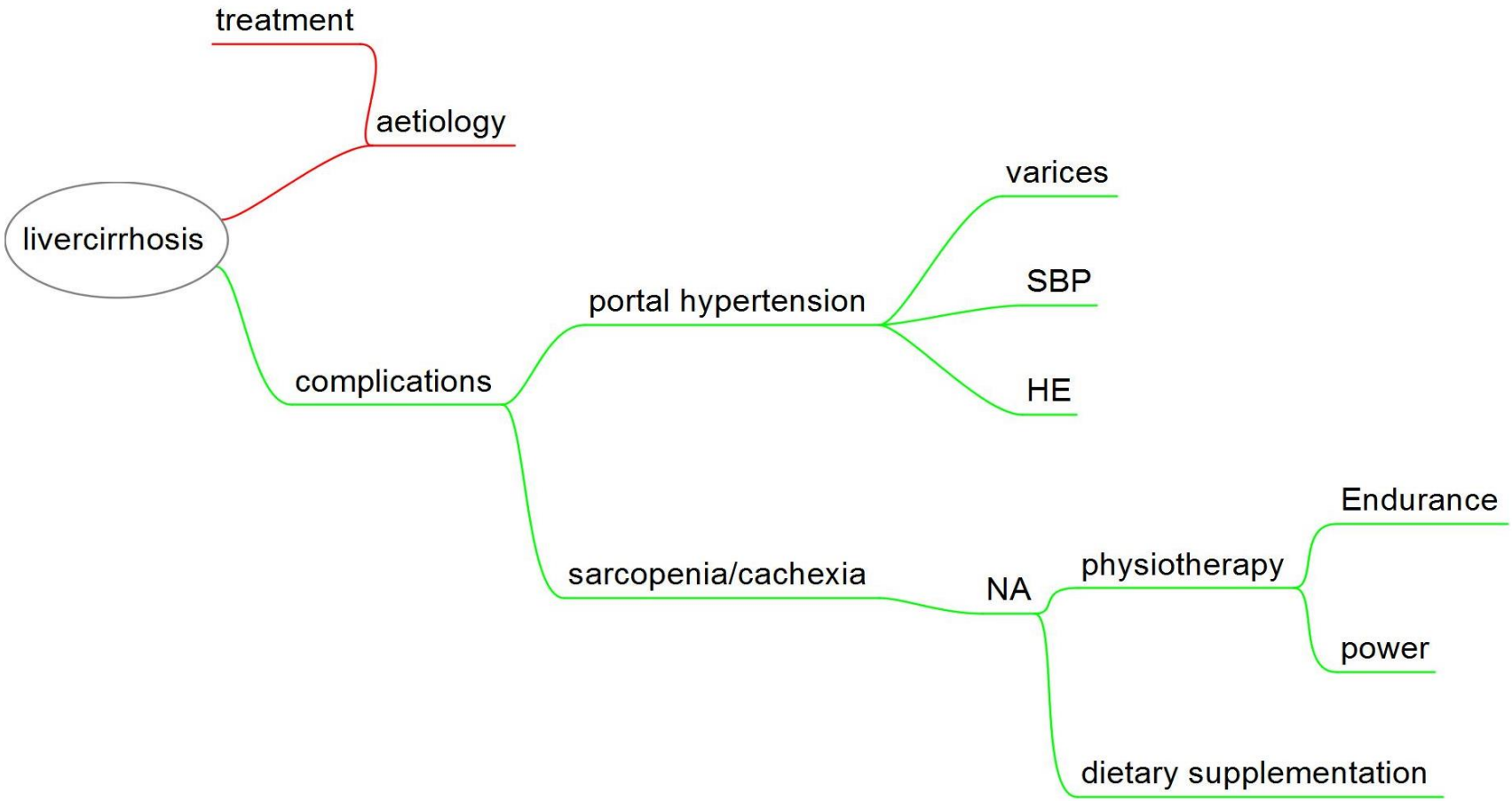


Late evening snack

analysis of 107 published reports suggests that LES is a beneficial nutriceutical intervention in patients with cirrhosis, especially early in the course of the disease.
Rationale:
1. increase in skeletal muscle protein synthesis
2. reduction in proteolysis

Tsien CD et al. J Gastroenterol Hepatol. 2012

Risk management summary



Conclusions

- Sarcopenia, malnutrition and cachexia: serious complications in cirrhosis
- Negatively associated with survival and complication's
- Early detection is warranted
- Active muscle mass improvement or stabilization
- Improve dietary intake

Future….
not today!

Risk profile

- MELD score
- Nutritional
- Functional status (muscularity)

Uitnodiging

2nd European Fatty Liver Conference in Maastricht (NL)

Organizing committee

Ronit Shiri-Sverdlov
Ger Koek
Sven Francque
Frank Tacke
Leo Köhler
Yvonne Oligschläger

Interested?
For updates on registration, please send an e-mail to f.defauwes@maastrichtuniversity.nl

Save the date: February 28 - March 2, 2018

Nonalcoholic steatohepatitis: *Clinical* problems, *basic* ideas, great *solutions*

Scientific mission

* Foster knowledge exchange between junior and senior scientists and clinicians working on NASH

* Create awareness of the opportunities and challenges in translational NASH research: from clinic to bench & back

Thematic highlights

* From NAFLD to NASH: *clinical* and *fundamental* insights in disease progression and mechanism, diagnosis & treatment

* Systemic complications of NASH

* From a NASH patient's point of view

Detail schilderij Hans Keuls