NASH en bariatrische heelkunde voor- of nadelen?

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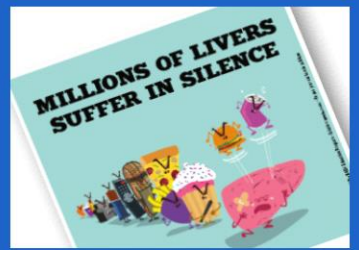
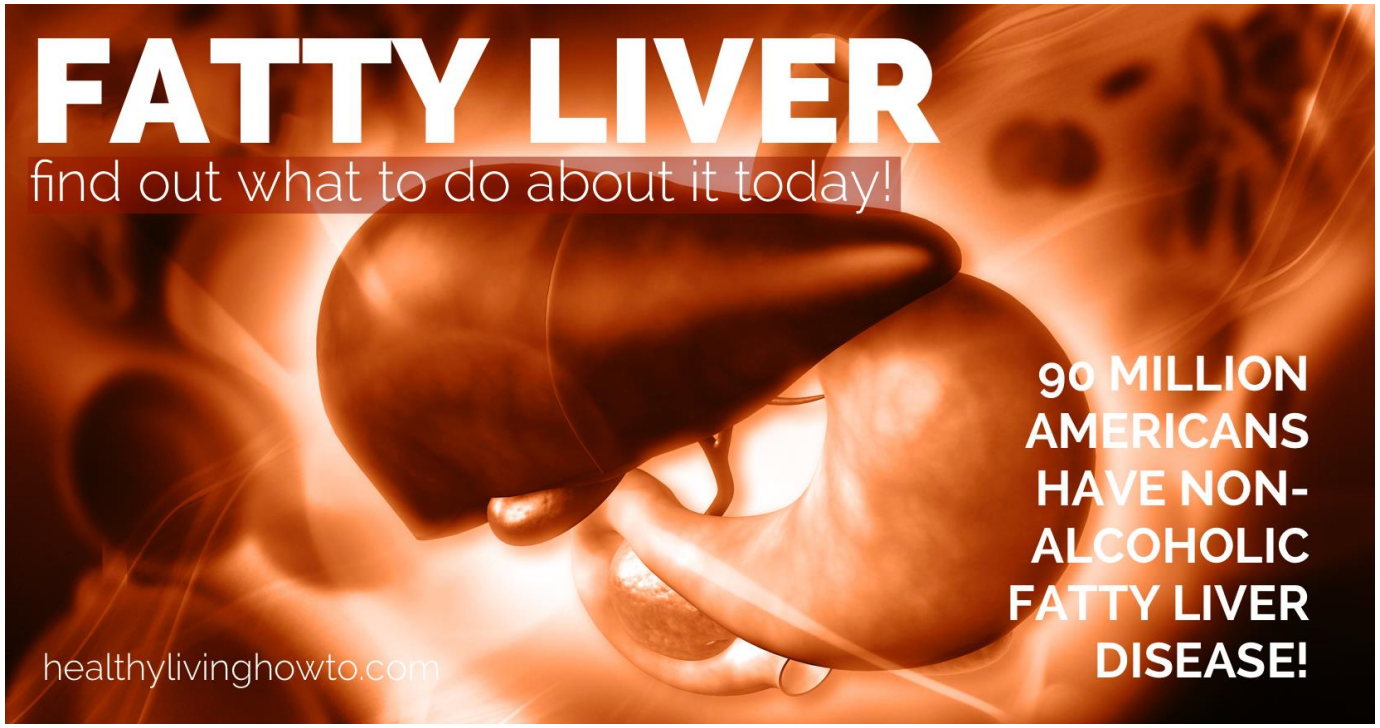
Agenda

- Wat is steatose? NASH?
- Voordelen van bariatrische heelkunde in NAFLD patiënten
- Nadelen van bariatrische heelkunde in NAFLD patiënten

LEVERVERVETTING: EEN DREIGEND GEZONDHEIDSPROBLEEM





Steatose

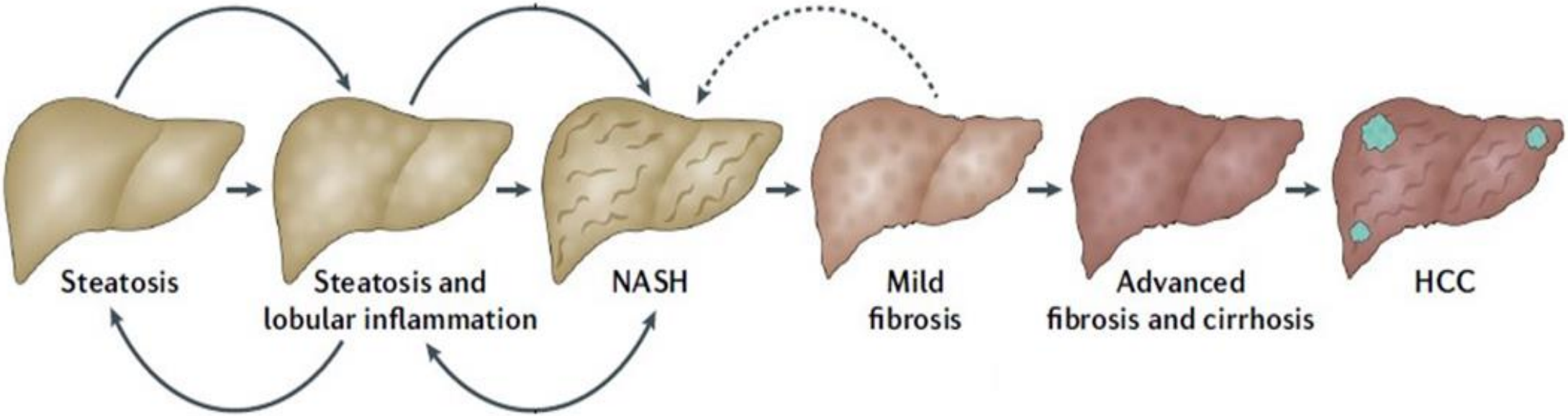
Primair ⟷ Secundair

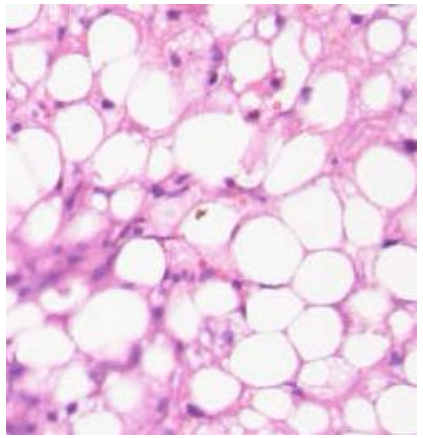
Niet-alcoholische leververvetting

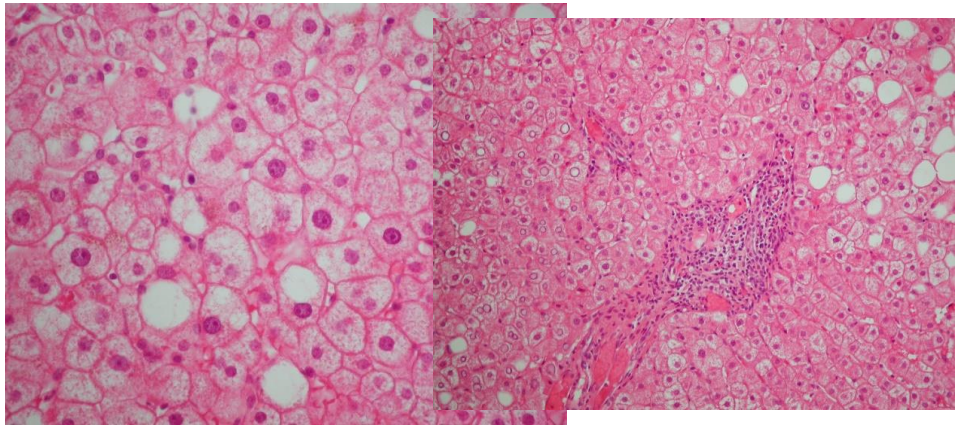
Geassocieerd met obesitas, diabetes, dyslipidemie, metabool syndroom

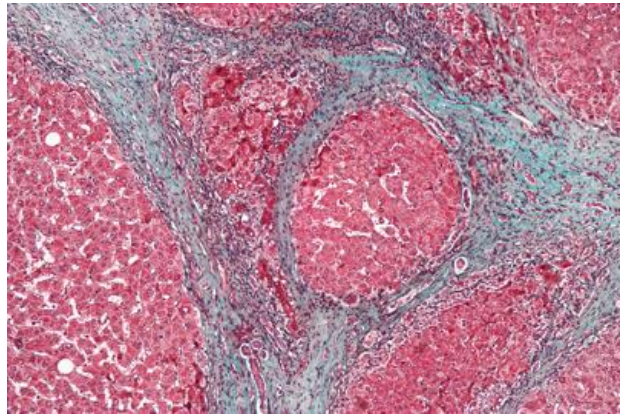
- Alcohol
- Geneesmiddelen
- Hepatitis C
- …

Natural history of NAFLD



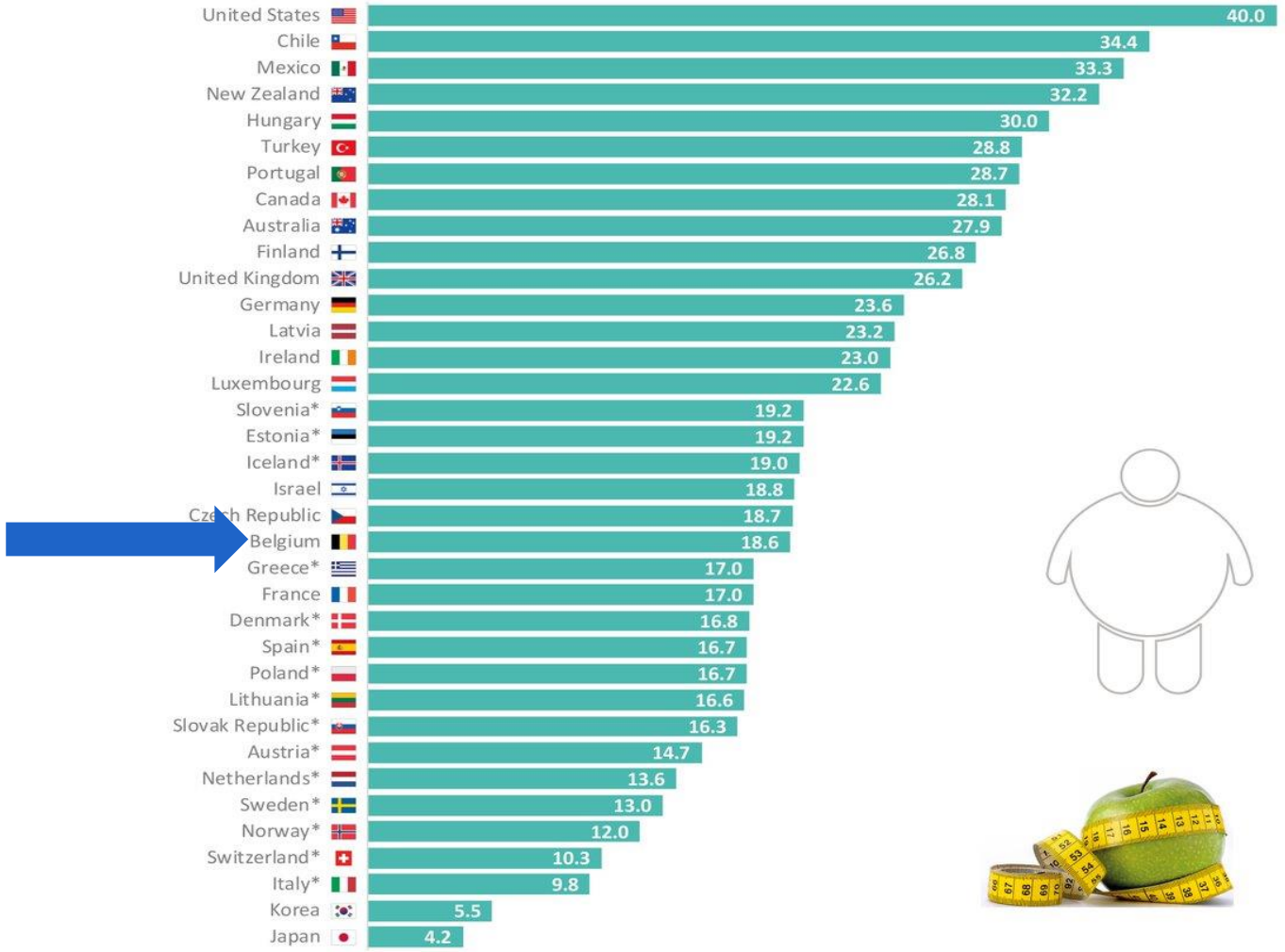






Obesity rates

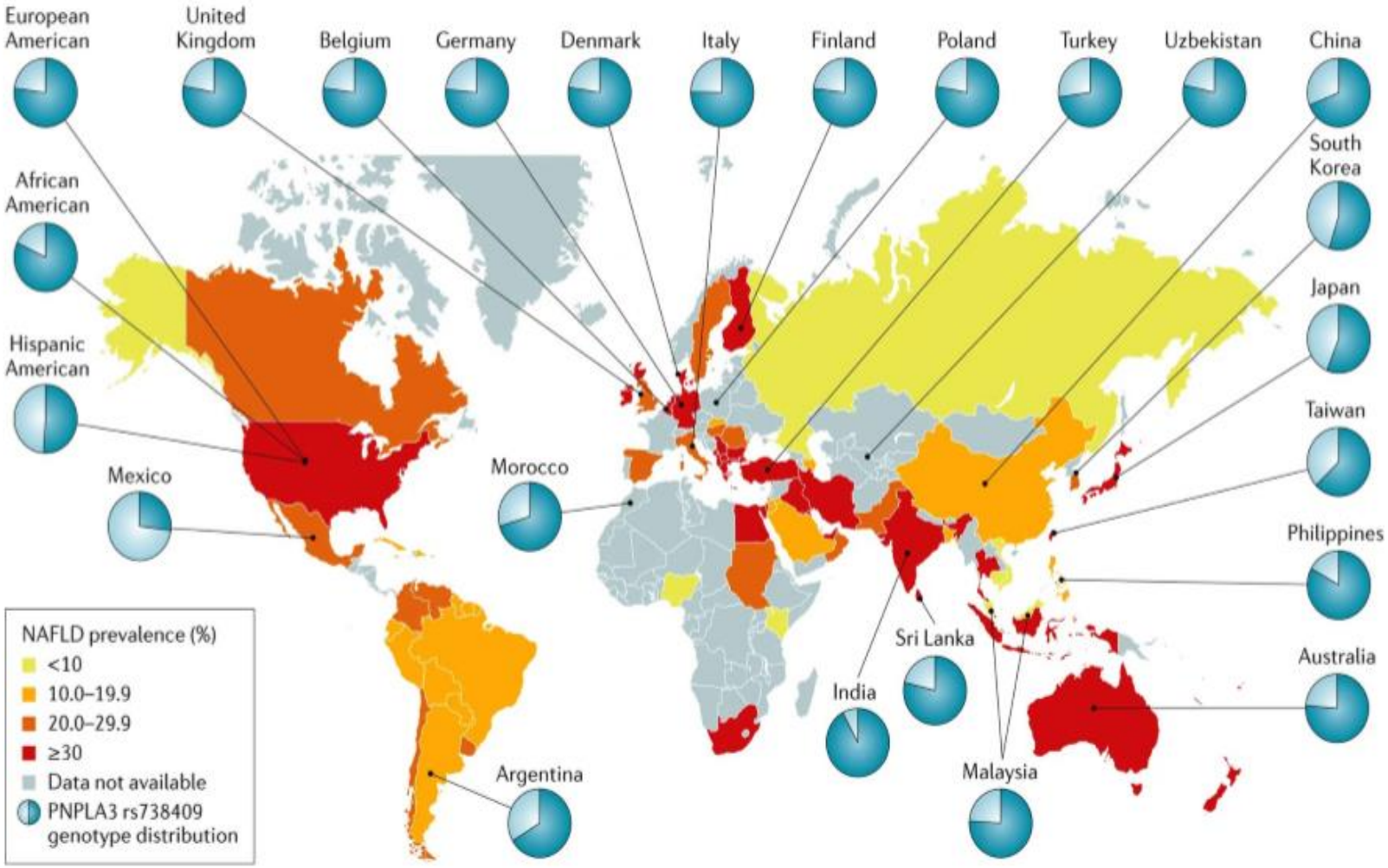
As % of total adult population (aged 15 years and over), 2016 or latest year



Note: * means that self-reported height and weight data are used in these countries, while measured data in other countries.
Source: OECD (2018), OECD Health Statistics 2018
www.oecd.org/health/obesity-update.htm

OECD

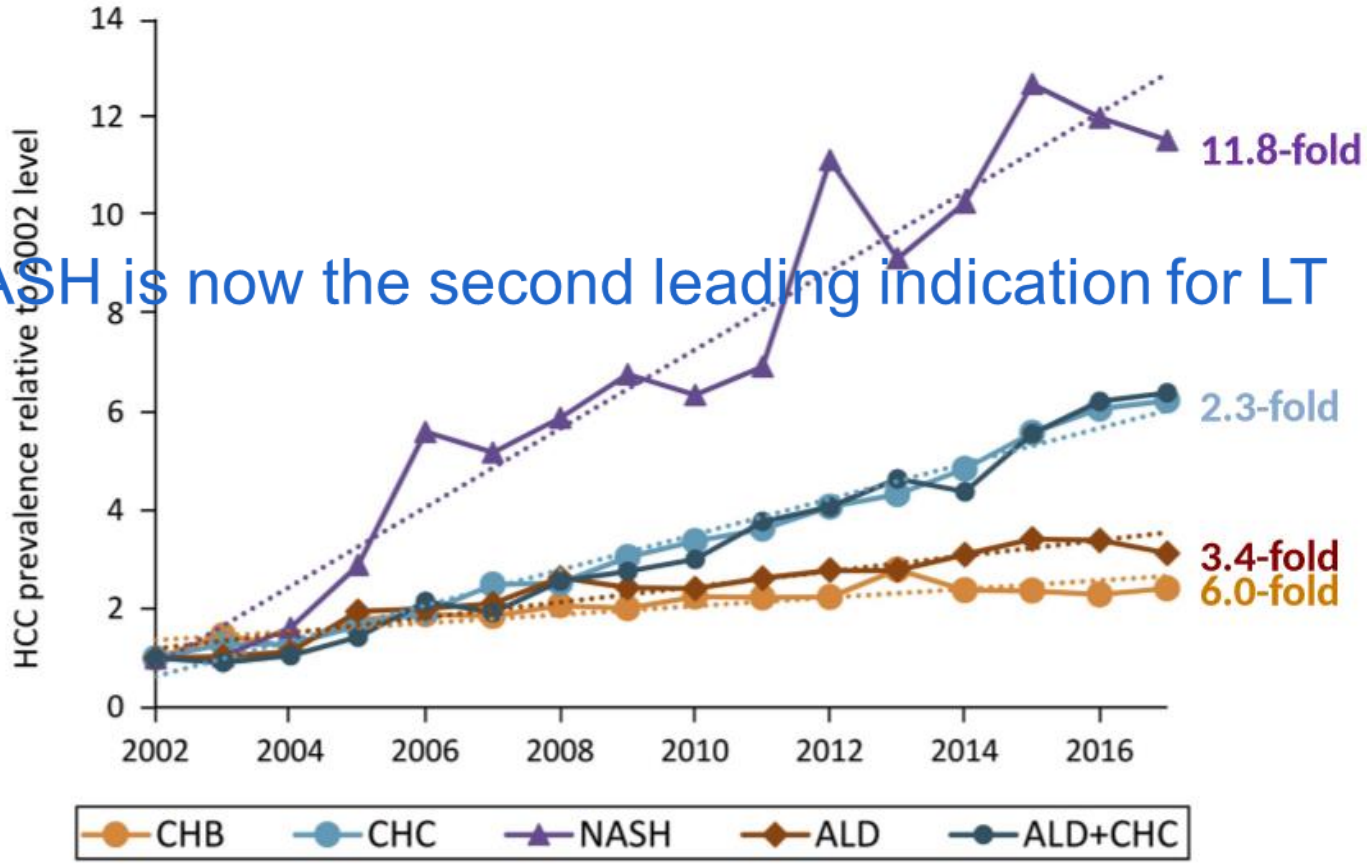
Prevalentie van NAFLD = parallel met de obesitas epidemie



Younossi et al. Nat Rev Gastroenterol Hepatol 2017;15:11-20

NASH is the fastest growing cause of HCC in liver transplant candidates

(US SRTR, n = 26,121 HCC in 158,347 adult LT candidates, 2002-2016)



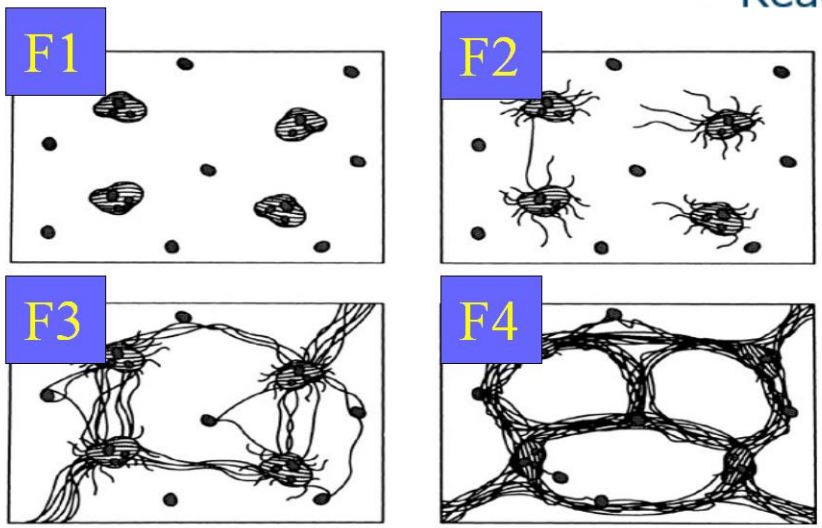
NASH is now the second leading indication for LT

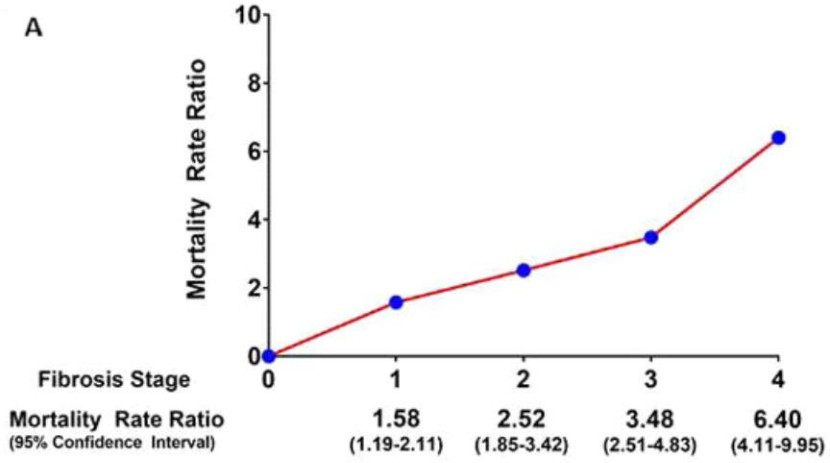
Cotter and Charlton Liver Transpl 2020:26;141-159
Younossi Z et al Clin Gastroenterol Hepatol 2019;17:745-755

PROGNOSE

Fibrosis is the strongest predictor of outcome

- Overall mortality and liver-related mortality
- Read-out of long-standing active disease





RISICOGROEPEN

- Geen of lage fibrose graad (0-1)
- Gevorderde fibrose graad >2

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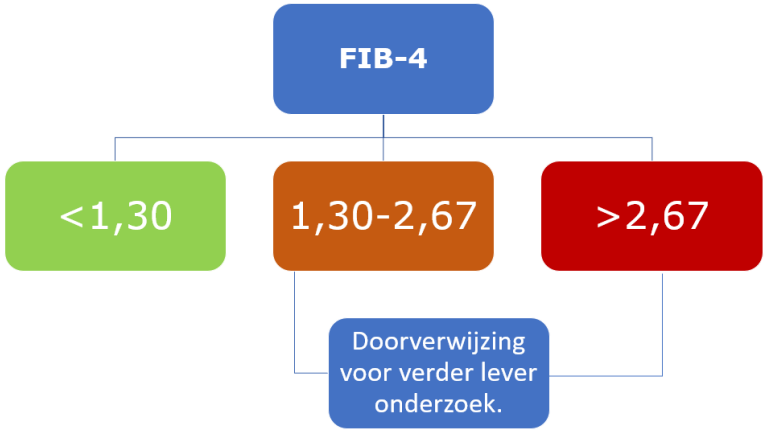
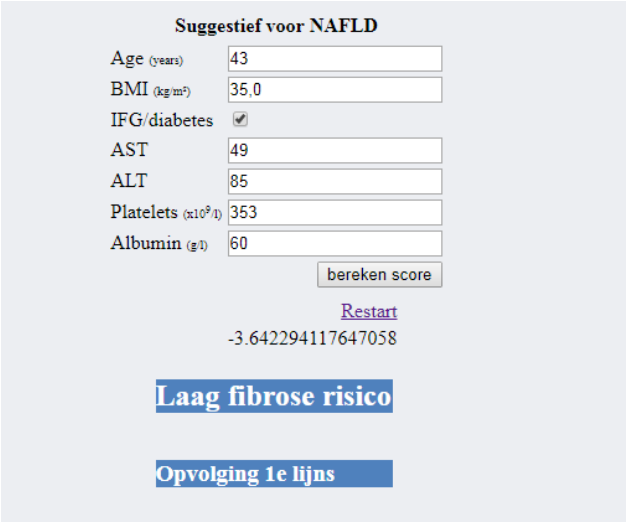
Dulai P. Hepatology 2017

Niet-invasieve biochemische bepalingen voor fibrose



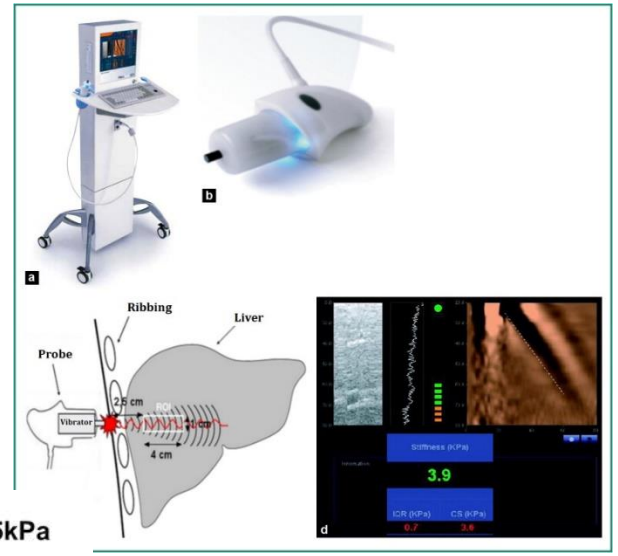
$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count } (10^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}}$$

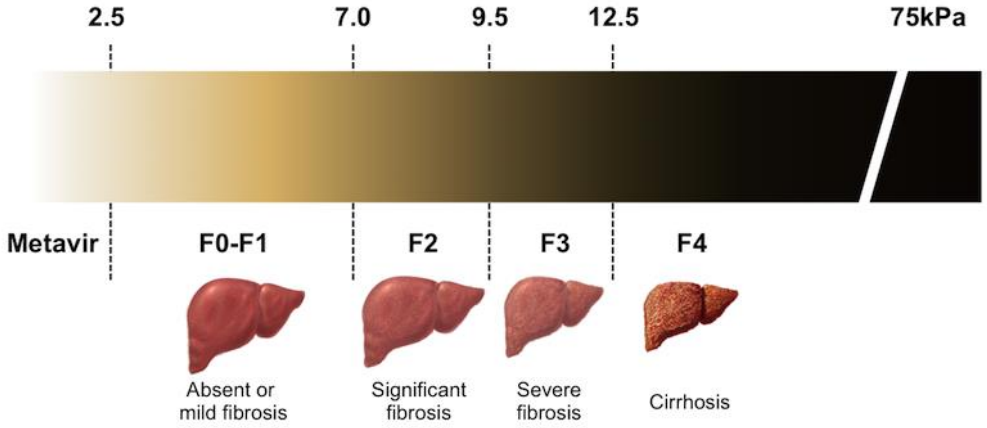
NAFLD fibrose score



uzgent-nafld.be/nafld

Niet-invasieve fibrose bepaling via beeldvorming





LEVERSTEATOSE polikliniek
http://www.uzgent.be/leversteatose

Waarom screenen?

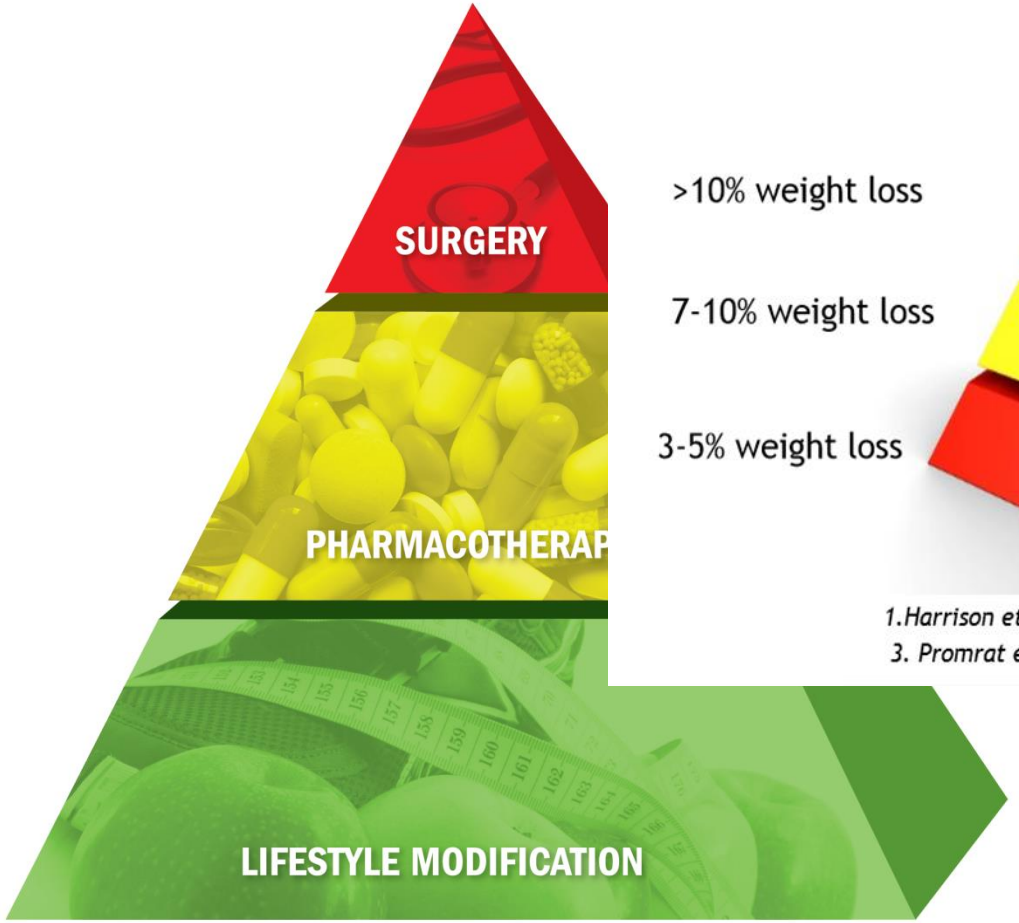
- Evolutieve “stille” leverziekte
- Hoge prevalentie > mortaliteit/morbiditeit > hoofdindicatie voor leverTx > impact op kosten
- NAFLD correlatie met DM en CV factoren
- Detectie van gevorderde fibrose (hoog risicogroepen: > 50y, DM, MetS)
- Gevorderde fibrose/cirrose: screening naar HCC
- Therapie?

Wie screenen?

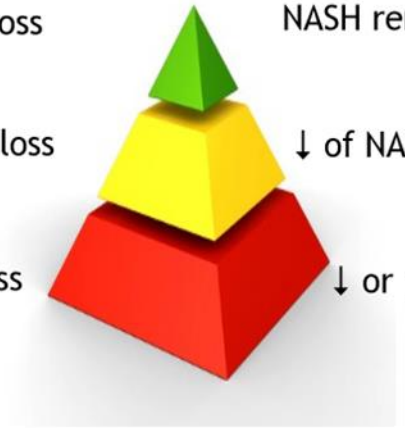
- Alle patiënten met hoog risico op NAFLD
- metabool syndroom
- Obesitas
- DM type 2
- Ischemisch CVD

- persisterend gestoorde leverset
- Toevallige vondst echografisch van steatose

Gewichtsverlies: “the cornerstone” in behandeling van NAFLD



>10% weight loss	NASH remission (90%) and fibrosis (45%)[4]
7-10% weight loss	↓ of NASH score parameters (72%)[1,3]
3-5% weight loss	↓ or remission of steatosis (64%)[1,2]



1.Harrison et al. Hepatology 2009; 2. Wong et al. JHepatol. 2013
3. Promrat et al. Hepatology 2010; 4. Vilar-Gomez et al. Gastroenterology 2015

Life-style modification works well… but hard to achieve..

Current NAFLD/NASH Pipeline with Targeted Pathways

Target Pathway

Fibrotic · Inflammatory · Metabolic · Metabolic/Inflammatory · Metabolic/Fibrotic · Fibrotic/Inflammatory · Metabolic/Fibrotic/Inflammatory

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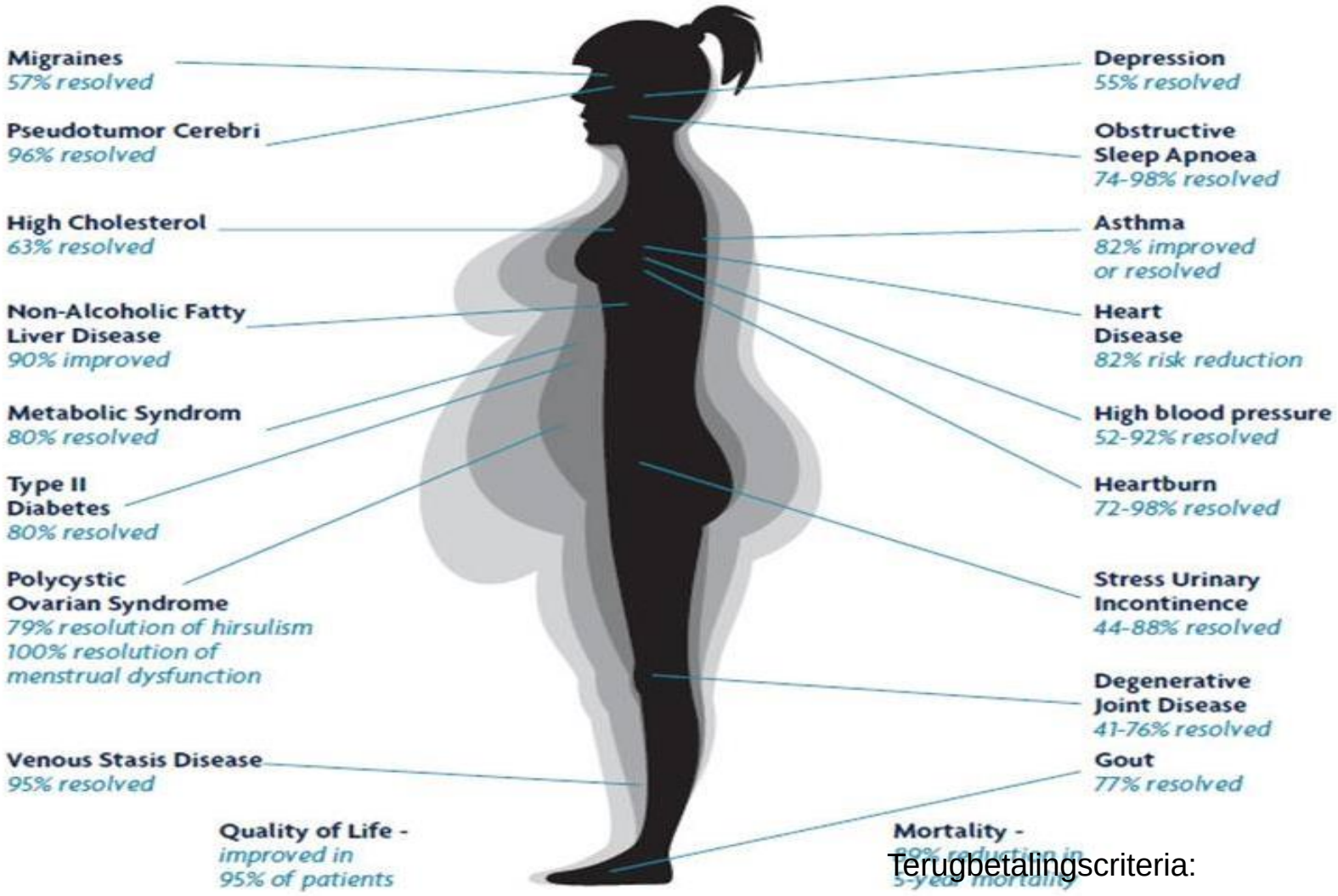
BARIATRISCHE PROCEDURES IN BELGIË



Terugbetalingscriteria:

Leeftijd>18y

BMI>40

BMI>35 met DM, severe AHT or sleep apnea

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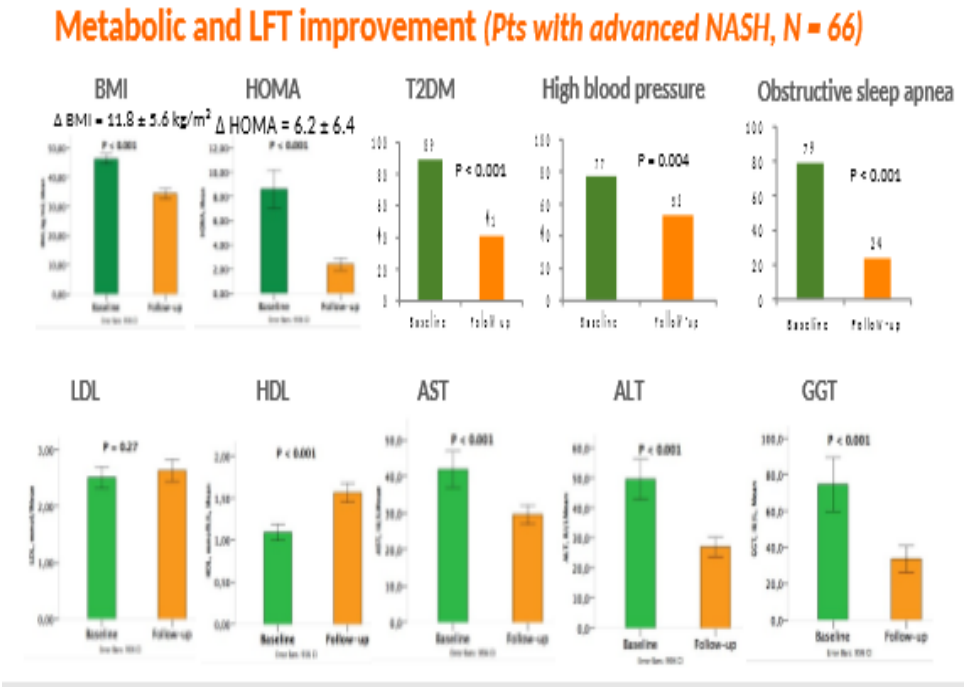
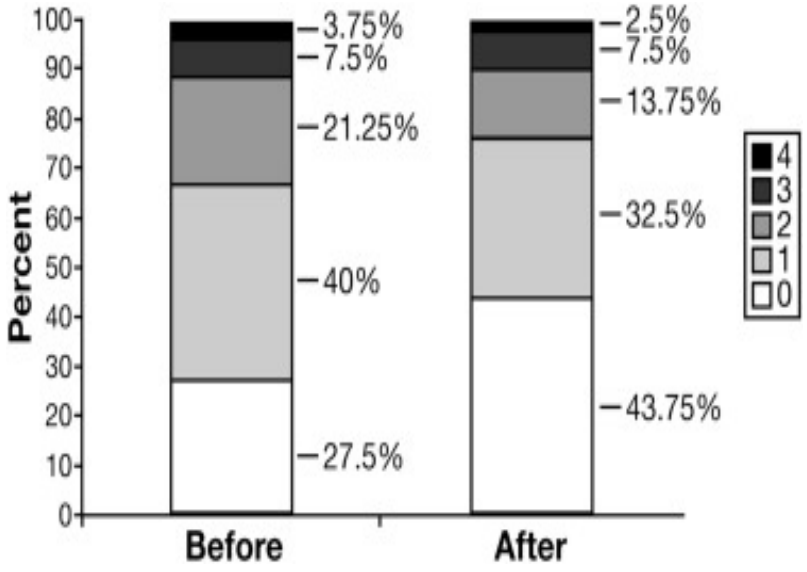
Bariatrische heelkunde in NAFLD patiënten

EFFECT van bariatrische heelkunde in NASH korte termijn

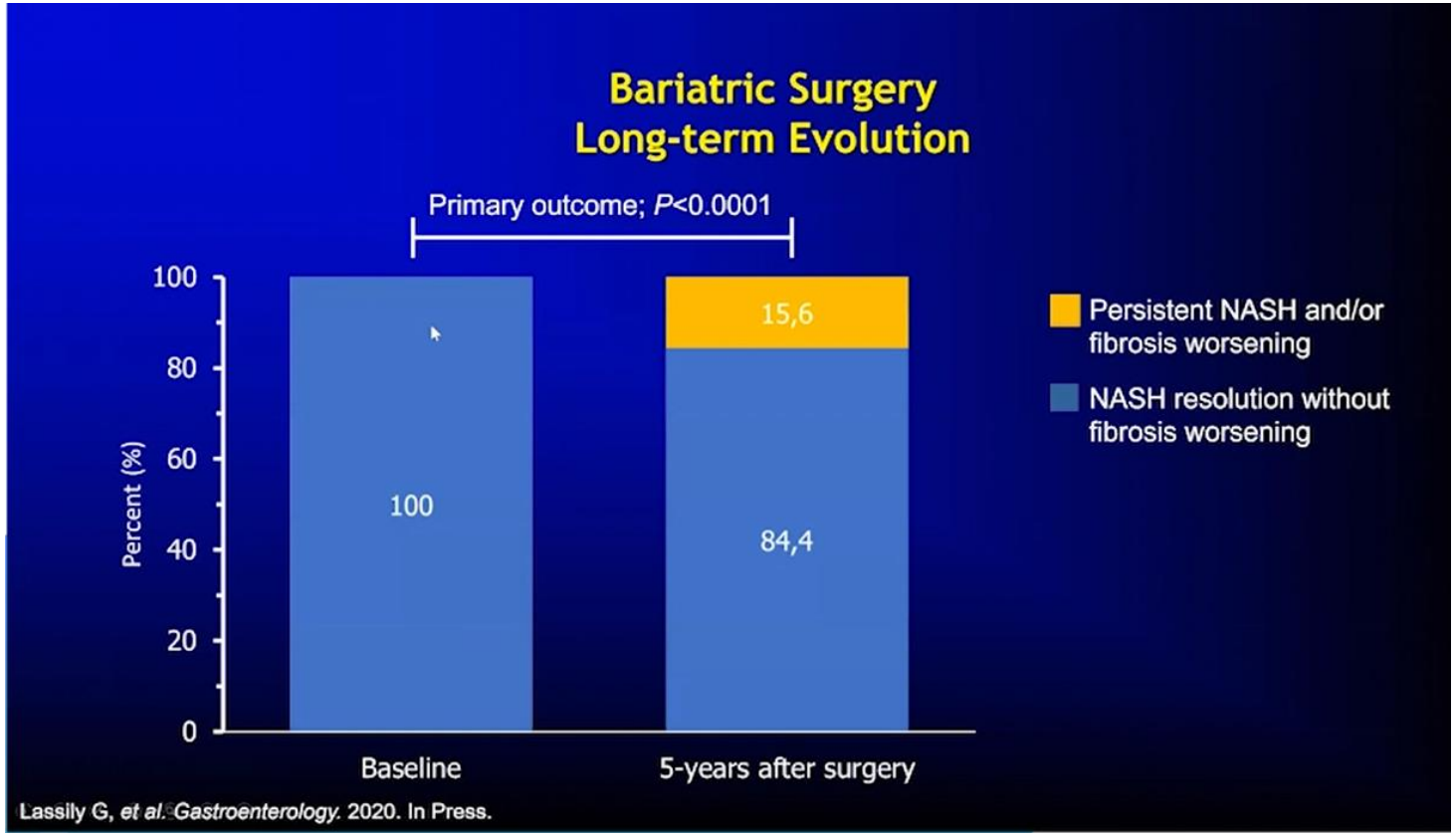




Improvement of fibrosis after one year surgery

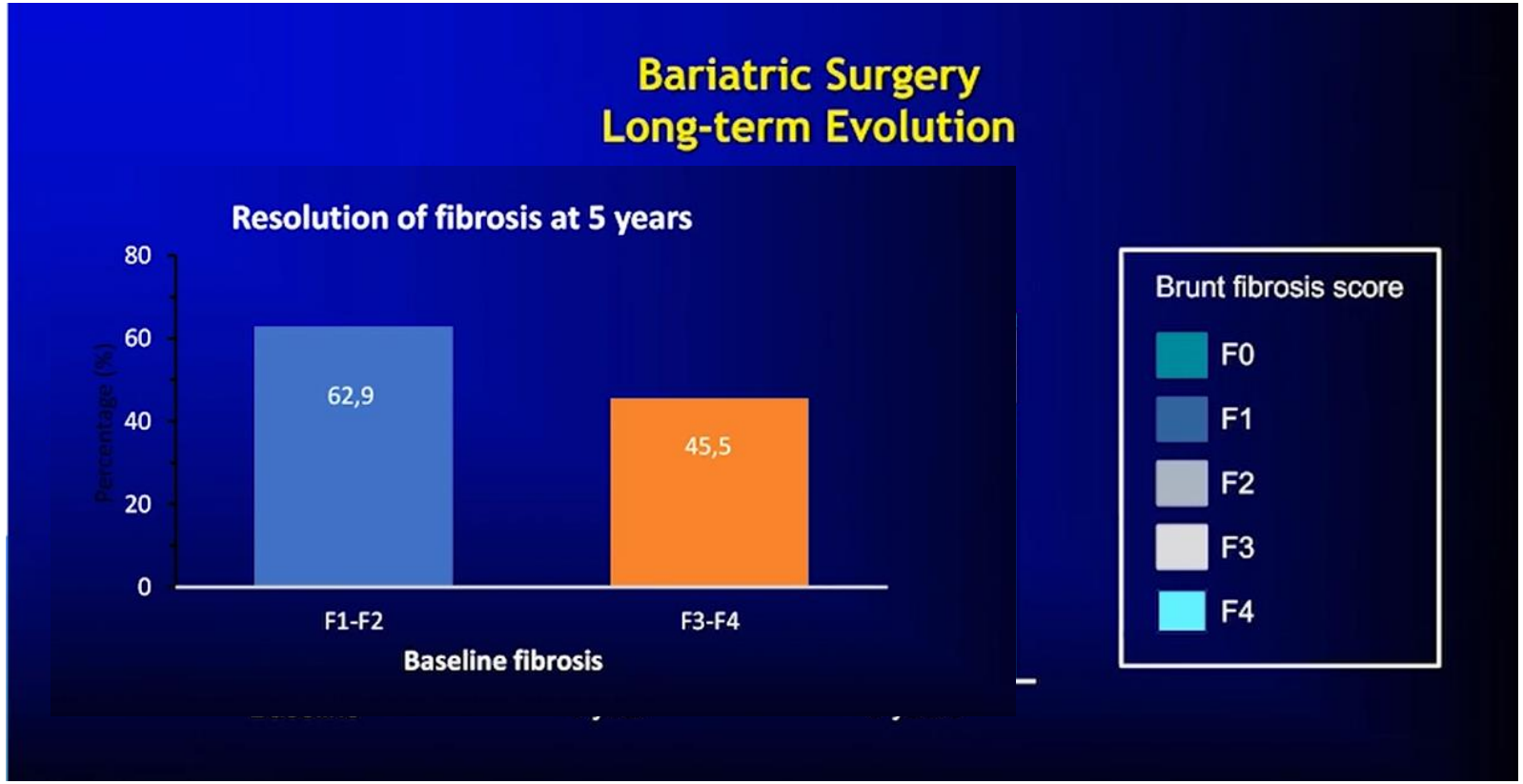
Lassailly et al. Gastroenterology 2015
Pais, AASLD 2019

EFFECT van bariatrische heelkunde in NASH lange termijn



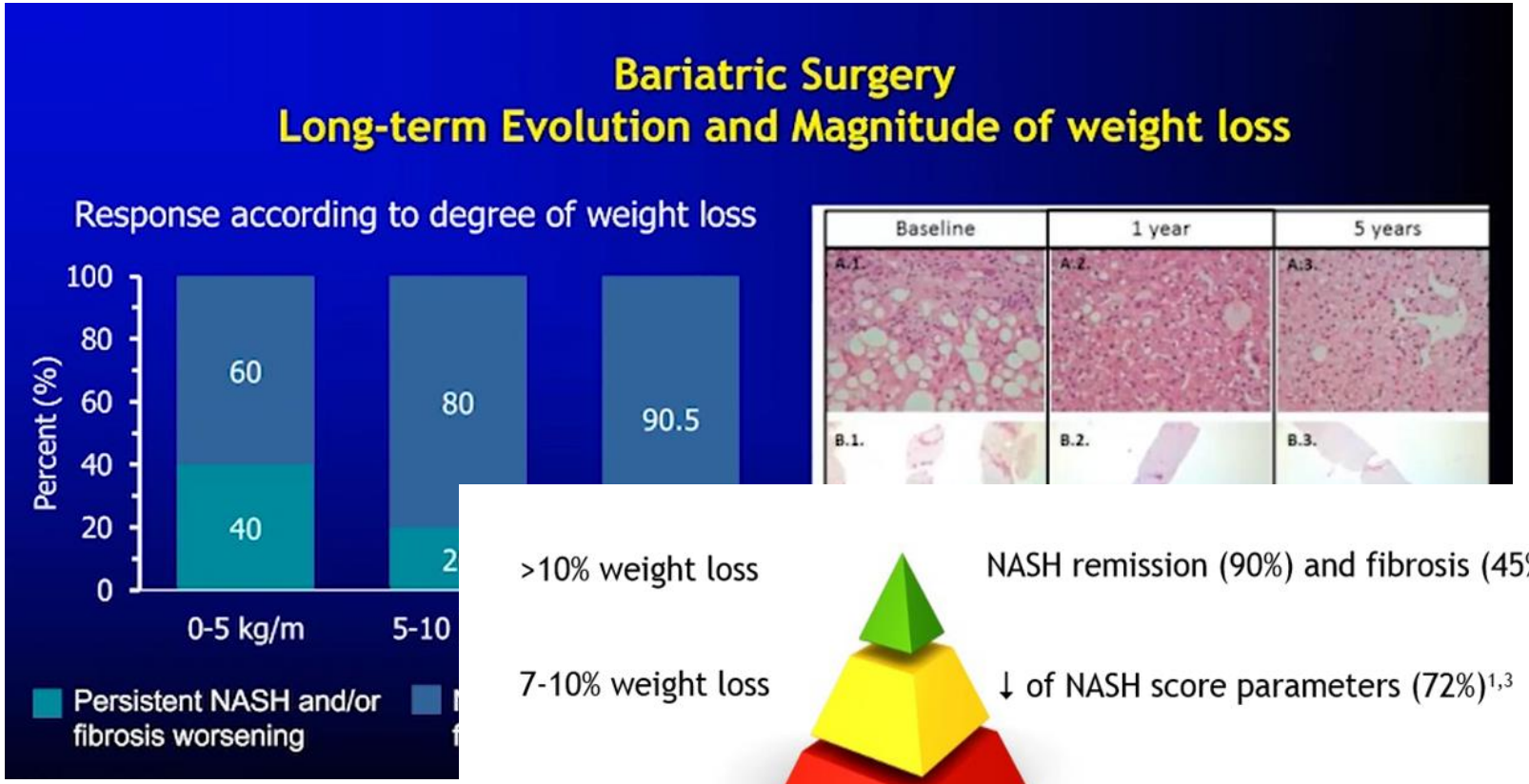
Lassailly et al. Gastroenterology 2020

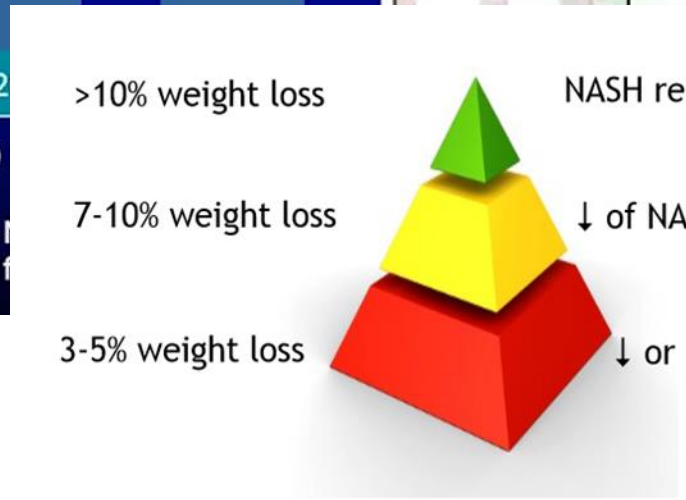
EFFECT van bariatrische heelkunde in NASH lange termijn



Lassailly et al. Gastroenterology 2020

EFFECT van bariatrische heelkunde in NASH lange termijn





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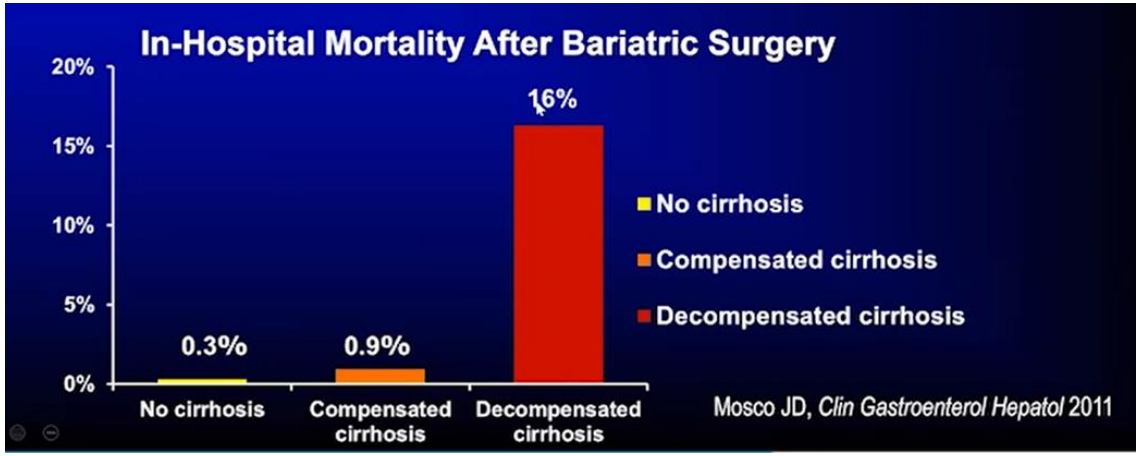
Bariatrische heelkunde in NAFLD patiënten

- Is bariatrische heelkunde een optie in het behandeling plan van NASH patiënten?
- Bariatrische heelkunde reduceert NASH activiteit
- Bariatrische heelkunde reduceert graad van fibrose

Bariatrische heelkunde in patiënten met cirrose

Bariatric surgery safe in cirrotic patients?

- Case reports/retrospective data
- Incidental findings of cirrhosis at time of BS, ranging from 0.14% - 0.4% -1.5 %



- Complication rates: up tot 34% have been reported with a leak rate up to 12,5%

Younus et al. Obesity Surg 2019

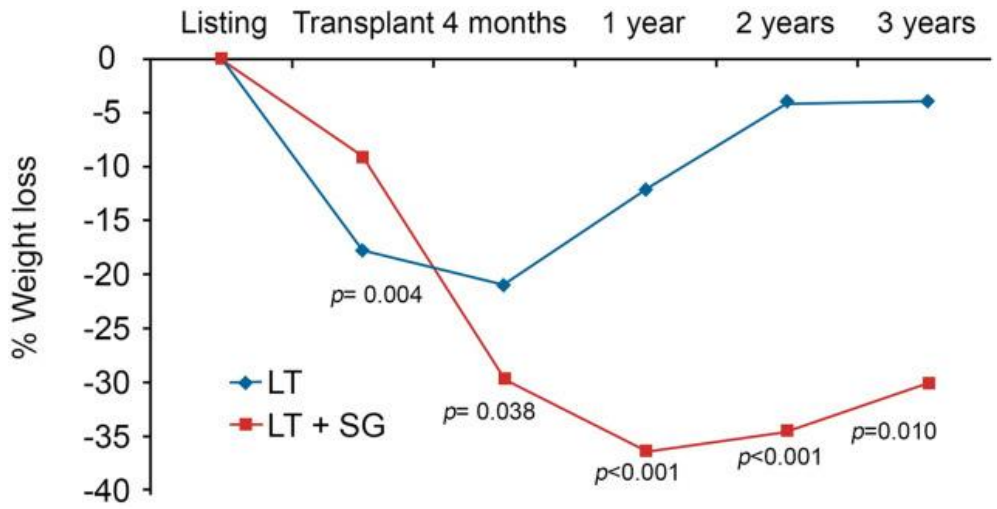
Spengler E et al Transplantation 2017

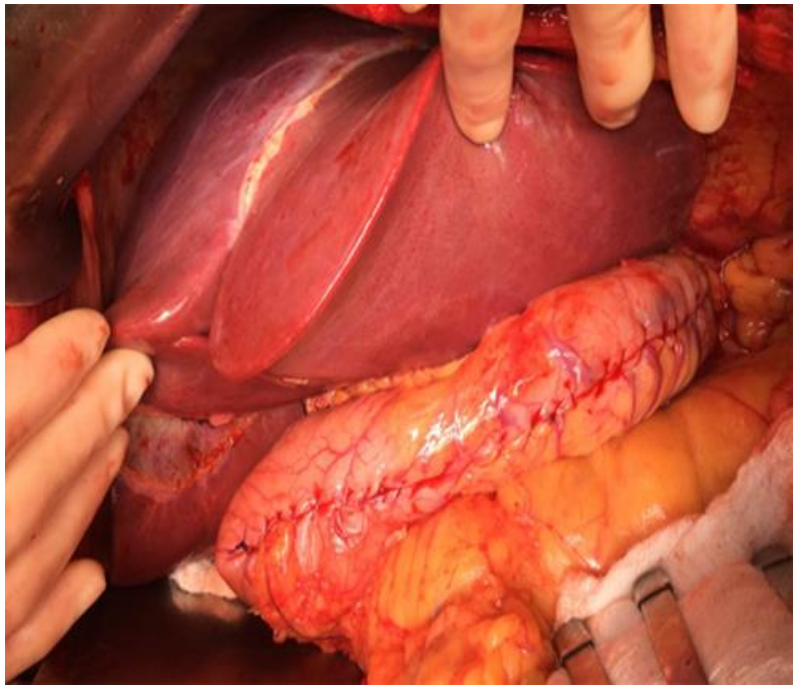
Approach to bariatric surgery in patients with cirrhosis

- Carefully select patients
- ***recognise and diagnose cirrhosis pre-op***
- Compensated cirrhosis Child A
- Estimate liver function – presence of PHT (HVPG < 10 mmHg)
- Less invasive laparoscopic approach
- Sleeve gastrectomy has been advocated as the bariatric modality of choice (technical ease/ preservation of GI tract/ endoscopic access to distal stomach and duodenum)

Lazzari et al. Obes Surg 2015;25:134-142

Bariatric surgery simultaneously with liver transplant





Zamora-Valdes D et al Hepatology 2018;68:485-495

Bariatrische heelkunde na levertransplantatie

Cotter et al Liver Transplantation 2020 26;141-159

Recurrent and de novo NAFLD

- Recurrent NAFLD after LT is very common

  NAFLD 10-100% or NASH 4-28%

  Risk factors: older age, higher BMI, presence of DM pre-Tx, dyslipidemia

- De novo NAFLD

  78% NAFLD and 3,8 % NASH of 2378 recipients at 5 year

  Risk factors: obesity (>10% increase in BW), dyslipidemia, DM, AHT

! **Faster progression of fibrosis**: rate of cirrhosis of 14% at 5 years after Tx

increase of 1 stage of fibrosis every 2.5 years

Galvin et al Liver transplantation 2019;25:56-67
Dumortier et al Am J Gastroenterol 2010
Narayanan et al Transplantation 2019
Saeed et al Transplantation 2019

Bariatrische heelkunde post transplant

- Benefits
  - > Loss of excepted weight and BMI
  - > Improvement in obesity-associated comorbidities
- This strategy leaves the critical perioperative period of LT unaffected
- Optimal timing need to be defined

  delaying too long can place fibrosis
  reduce patient survival !
- Sleeve gastrectomy most performed (80%)
  - > lack of malabsorption
  - > Immuunsuppression

- No difference in mortality with general population
- Although higher morbidity (reoperation rate of 12-33%)

Ayloo S et al Transplantation Proceedings, 52; 276-283 (2020)


CAUTION

Bariatrische heelkunde en lever falen

The Multicenter Belgian Survey on Liver Transplantation for Hepatocellular Failure after Bariatric Surgery

A. Geerts, T. Darius, T. Chapelle, G. Roeyen, S. Francque, L. Libbrecht, F. Nevens, J. Pirenne, and R. Troisi

Refractory subacute steatohepatitis after biliopancreatic diversion.

Lefere S[1], Hoorens A[2], Raevens S[1], Troisi R[3], Verhelst X[1], Van Vlierberghe H[1], Geerts A[1].

Year of BPD	2000	2003	1998	2003	1997	2001	1999	1987	1994
Initial BMI	65	48	40	41	55	40	45	40	47
Post-BPD BMI	41	23	20	20	29	24	25	22	25
Maximum weight loss (kg)	88	88	60	47	55	40	45	53	50
Onset of LF after BPD (mo)	13	27	84	62	11	18	20	21	14
Time of OLT after BPD (mo)	22	85	listed	65	11	18	21	Died on list	Died on list
Waiting time on list (mo)	3	9	listed	3	2	2d	1	Died on list	Died on list
Time of BPD reversal	OLT	OLT	—	8 wk after OLT	OLT	OLT	OLT	—	—

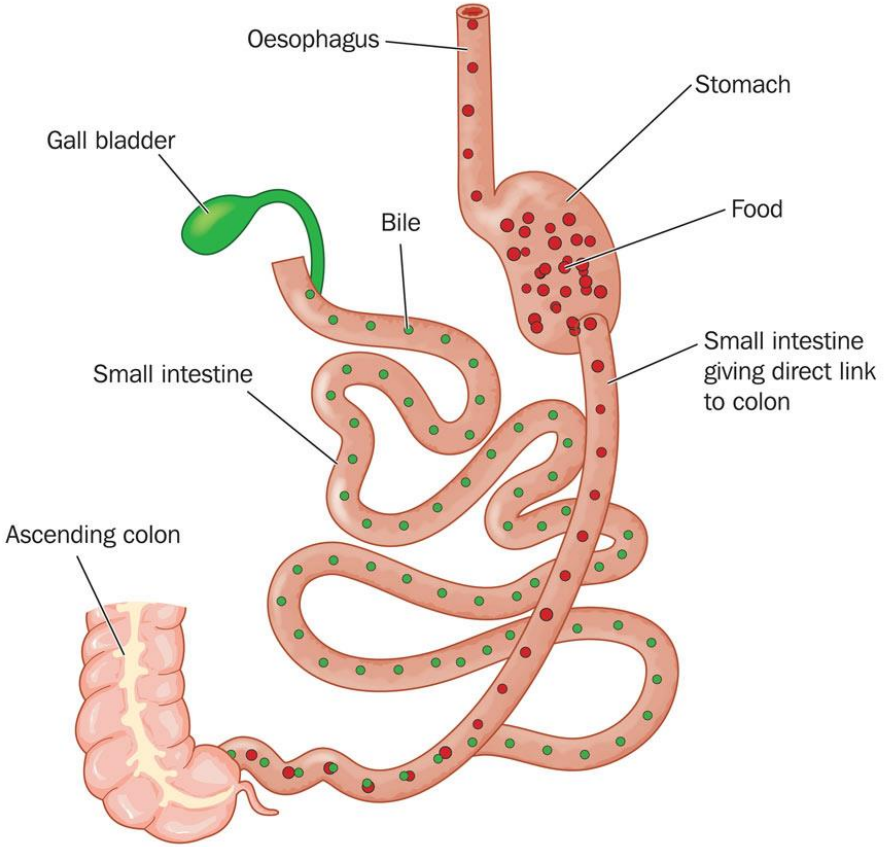
Abbreviations: BPD, biliopancreatic diversion; BMI, body-mass index (kg/m^2); LF, liver failure; OLT, orthotopic liver transplantation.

Transplantation Proceedings, 42, 4395–4398 (2010)

Biliopancreatic diversion (Scopinaro)

- Gastric pouch
- Long excluded intestinal loop

-> Macro- and micronutrient malabsorption



Lefere S et al. Hepatology

Pathophysiology

- Malnutrition
- Rapid weight loss and delivery of fat to the liver
- Small intestinal bacterial overgrowth

  - Long excluded limb
  - Dysmotility
  - Decreased gastric acidity
  - Protein deficiency – malnutrition
  - Undigested food reaching the colon

  -> mucosal injury, increased gut permeability -> endotoxin absorption

Lefere S et al. Hepatology

Bariatrische heelkunde en leverfalen: Rol van alcohol

Prevalence of Alcohol Use Disorders Before and After Bariatric Surgery FREE

Wendy C. King, PhD; Jia-Yuh Chen, MS; James E. Mitchell, MD; Melissa A. Kalarchian, PhD; Kristine J. Steffen, PharmD, PhD; Scott G. Engel, PhD; Anita P. Courcoulas, MD, MPH; Walter J. Pories, MD; Susan Z. Yanovski, MD

Obesity Surgery
https://doi.org/10.1007/s11695-020-04806-8

IFSO

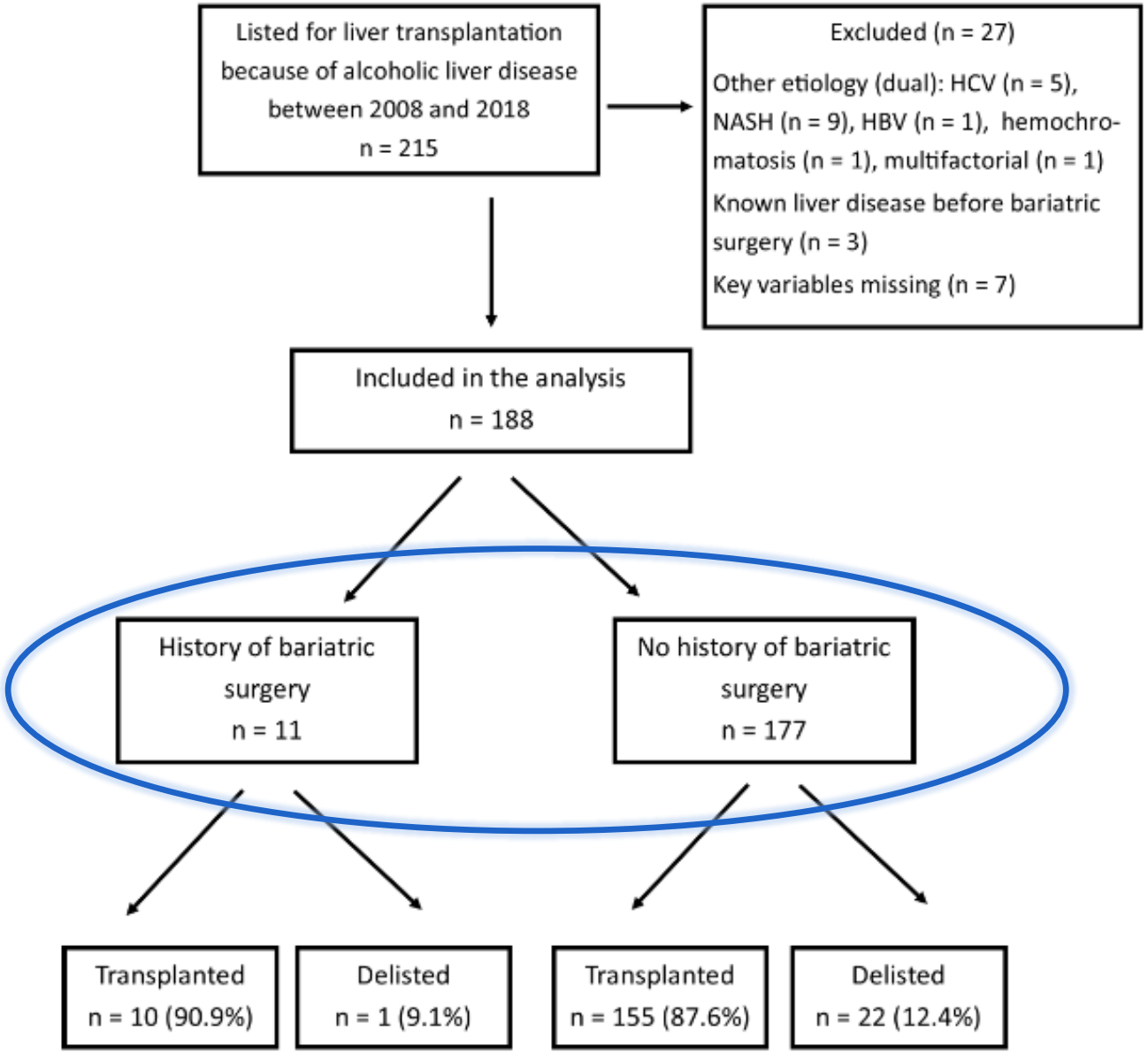
BRIEF COMMUNICATION

Check for updates

Bariatric Surgery Patients Are at Risk for Alcoholic Liver Disease with Need for Liver Transplantation

Sander Lefere[1] · Lenka Stroobant[1] · Xavier Verhelst[1] · Aude Vanlander[2] · Frederik Berrevoet[2] · Roberto Ivan Troisi[2,3] · Yves Van Nieuwenhove[4] · Xavier Rogiers[2] · Hans Van Vlierberghe[1] · Anja Geerts[1]

METHODOLOGY



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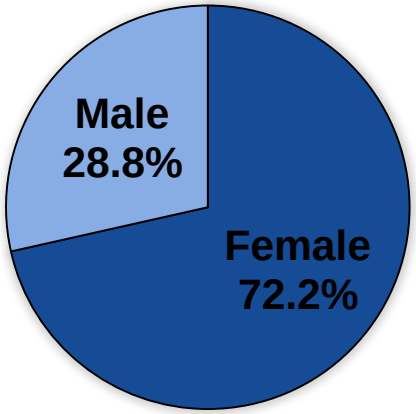
Lefere S et al. Obesity Surgery 2020

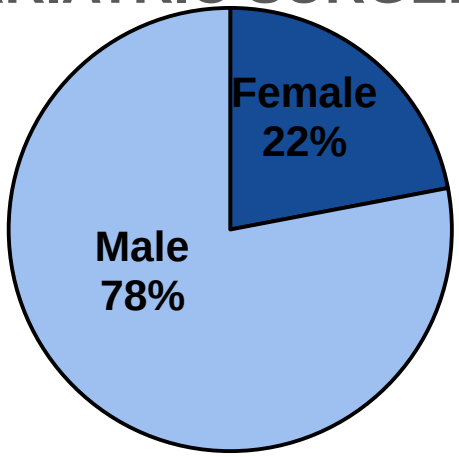
RESULTS

GENDER

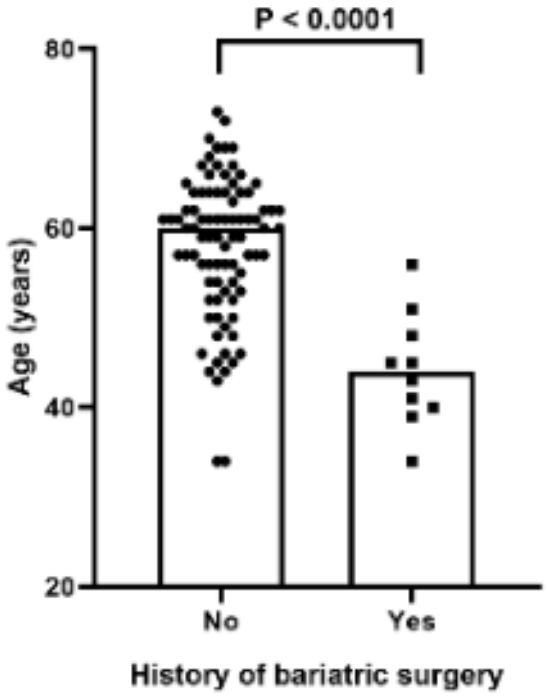
HISTORY OF BARIATRIC SURGERY



NO HISTORY OF BARIATRIC SURGERY



AGE



BS: 45 years
No BS: 60 years

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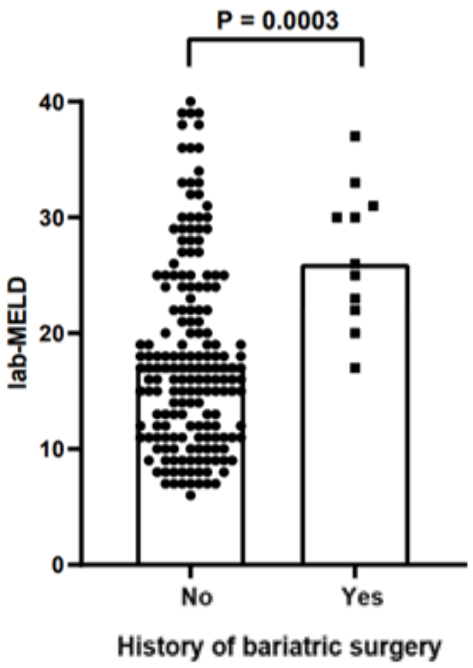
SEVERITY OF LIVER DEASE

Lab values

	BS	No BS	
INR *(0.9-1.1)*	2,30	1,51	↑↑
Albumin *(35-54 g/L)*	28	33	↓↓
Total bilirubin *(0.3-1.2 mg/dL)*	4,90	2,48	↑↑

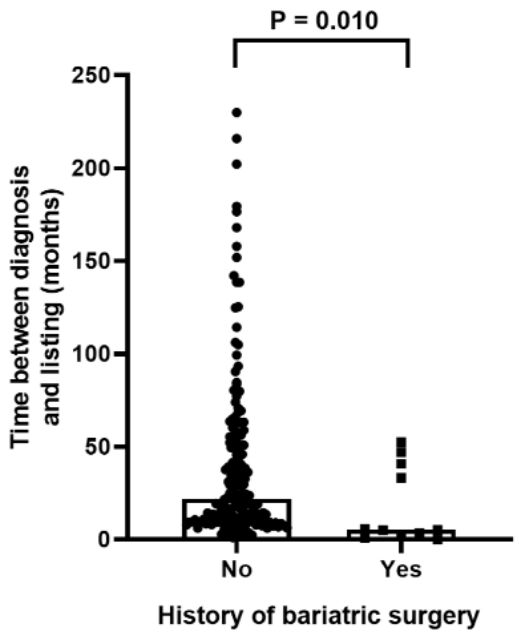
Lab-MELD-score



BS: 26

No BS: 17

Time between diagnosis and listing



BS: 5 months

No BS: 22 months

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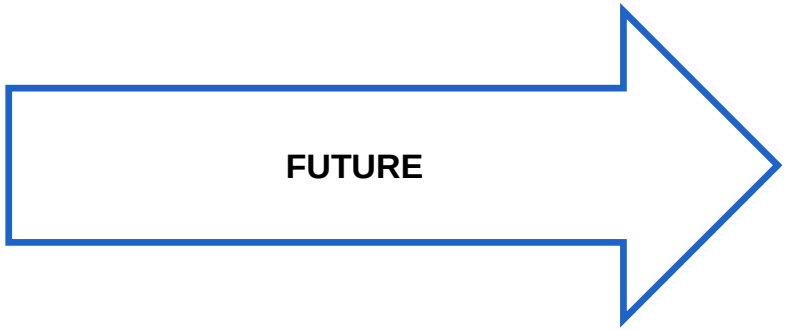
Bariatric population and alcoholic liver failure:

- Younger and female
- More severe form of liver disaese
- Less chronic complications of cirrhosis



- Reasons?
- Risk factors?

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Conclusies

- Bariatrische heelkunde : behandelingsoptie voor NAFLD/NASH patiënten
- 85% disappearance of NASH and 60% reductie van fibrose in patiënten met niet-gevorderde NASH 5 jaar na heelkunde

- “Feasible and safe” in patiënten met cirrose
  - voorkeur type heelkunde ; sleeve gastrectomie
  - belang van diagnose cirrose voor de heelkunde

- Leverfalen na bariatrische heelkunde vooral in ernstige malabsorptieve procedures
- Alcohol gebruik na bariatrische heelkunde kan leiden tot een snelle ontwikkeling van leverfalen

NASH en bariatrische heelkunde voor- en nadelen?

Dank voor Uw aandacht

Prof Dr Anja Geerts
Department of Gastroenterology & Hepatology
University Hospital Ghent

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