Bariatric Surgery and Liver Transplantation

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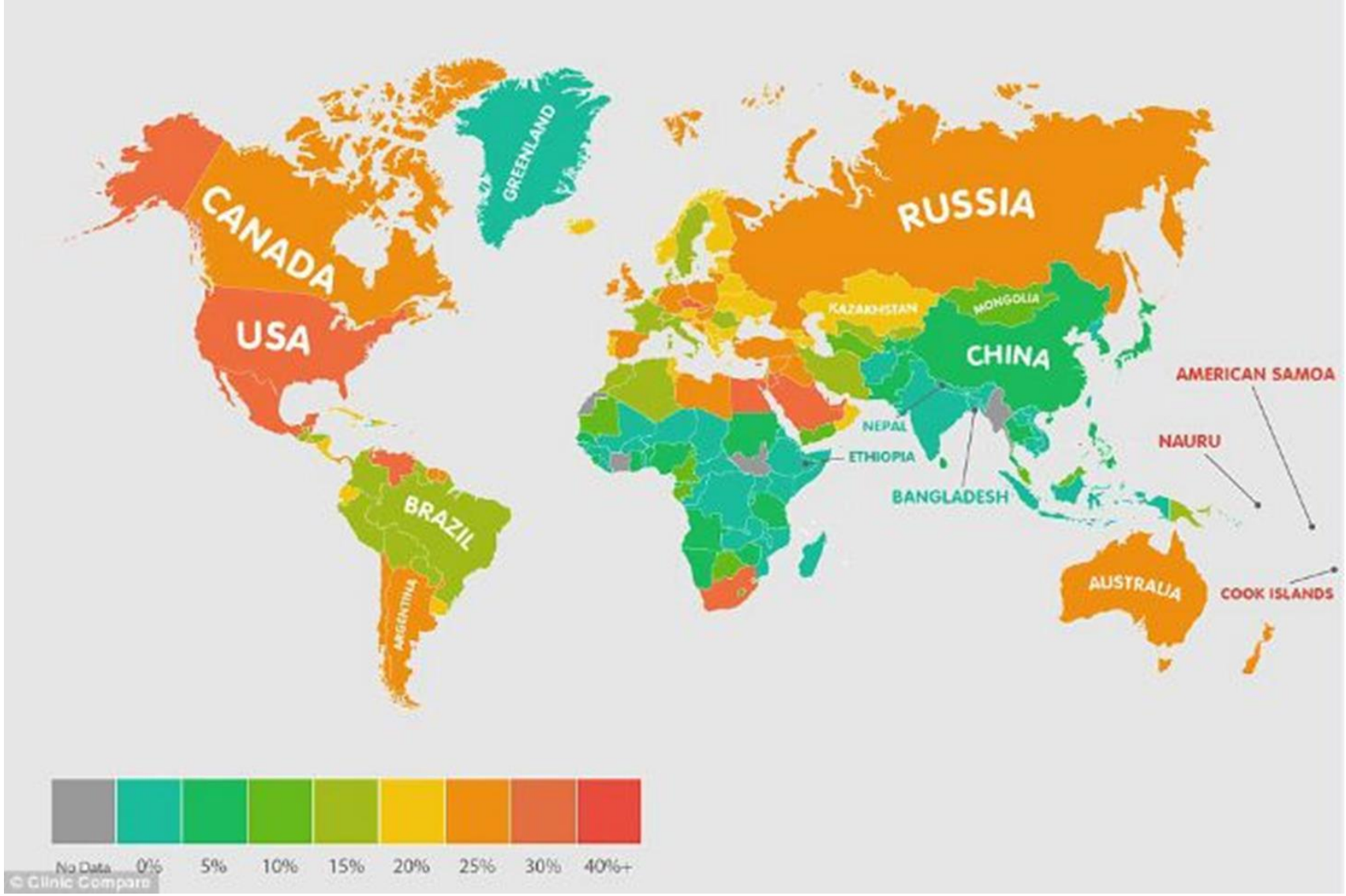
Objectives

- Outline current scope of the obesity epidemic
- Implications of NASH pre and post LT
- Discuss the role of bariatric surgery

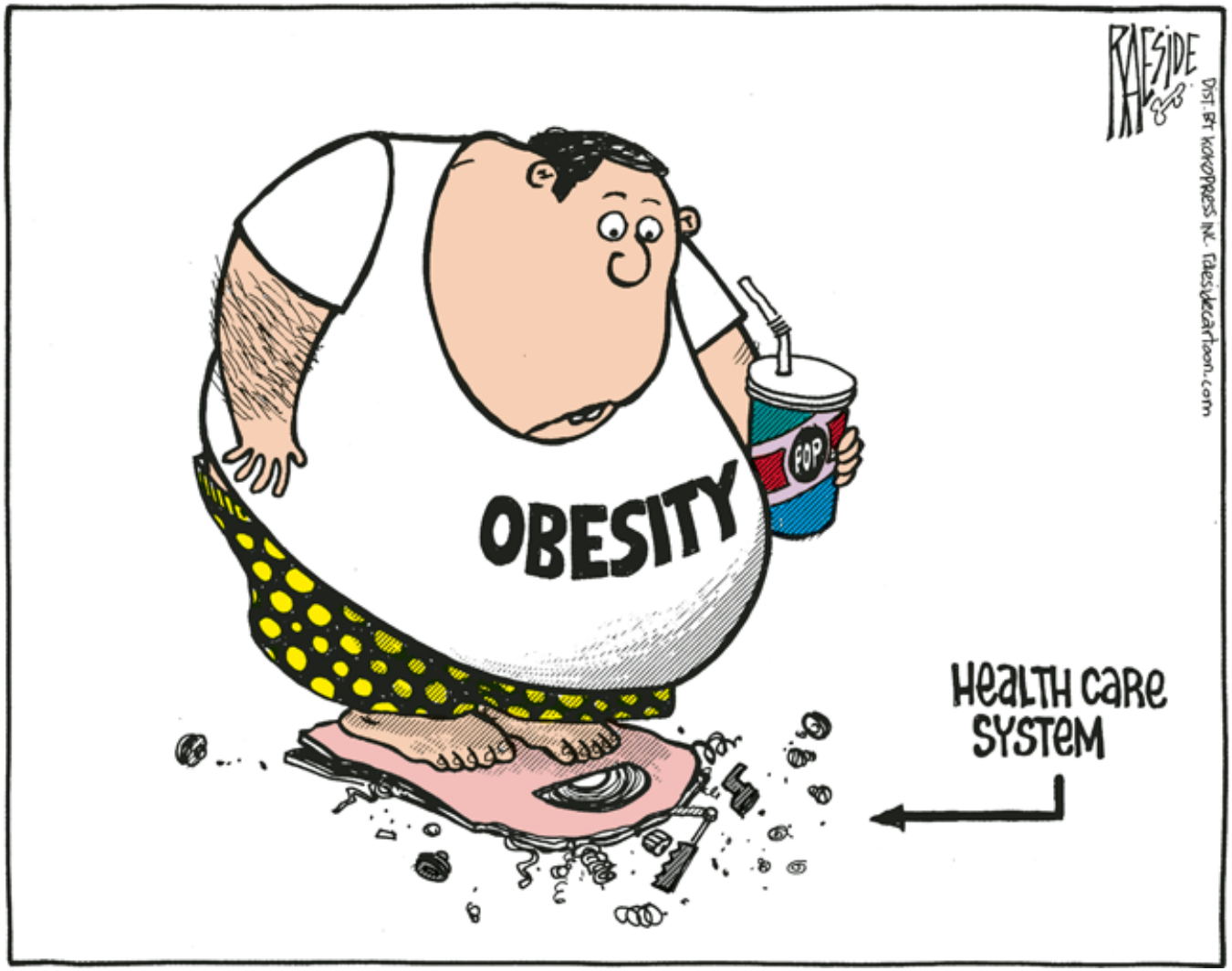
How can we best care for the obese liver transplant candidate?



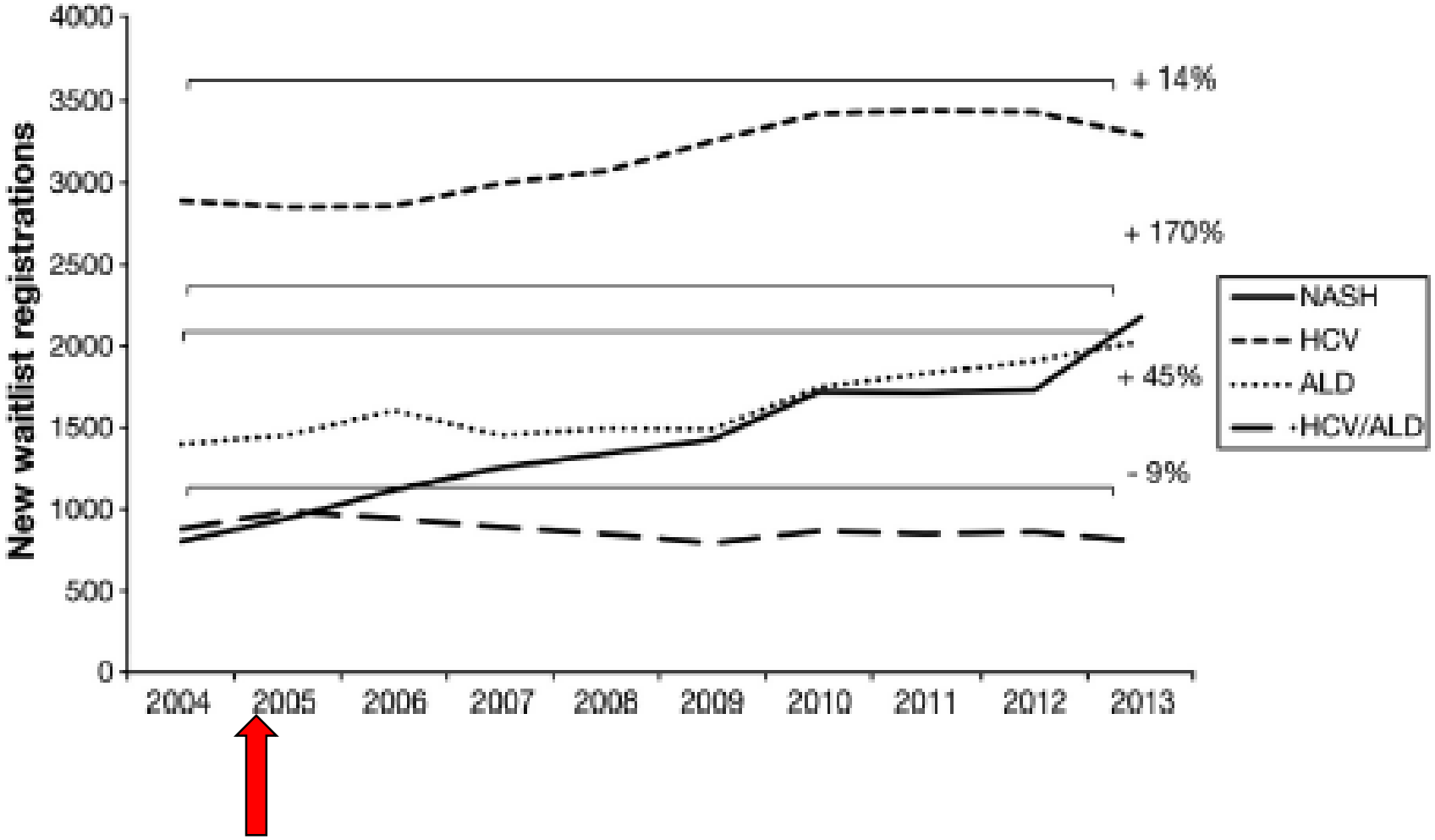
- World wide, obesity has doubled since 1980
- Currently, 600 million obese adults in the world

Why?

- **Clinical need for a different approach**



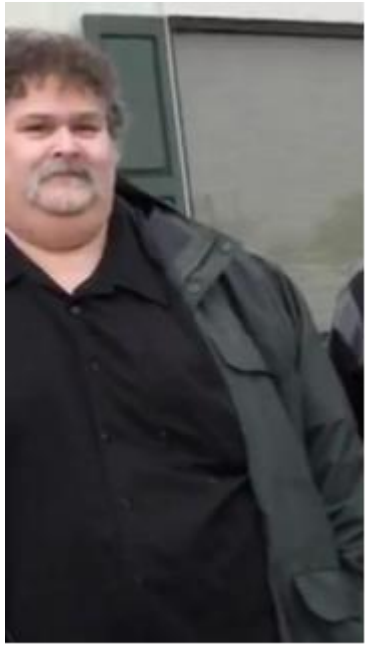
NASH as an indication for listing for liver transplantation in US



Wong et al Gastro 2015; 148: 547-55.

Why?

- 57 year old male, BMI 52, MELD 30, referred to hospice by his local transplant center
- LT+SG (MELD =40), current BMI=34 stable 3 years post LT
- "One day I am dying, the next week I am not," he said. "That just doesn't happen."



Why?

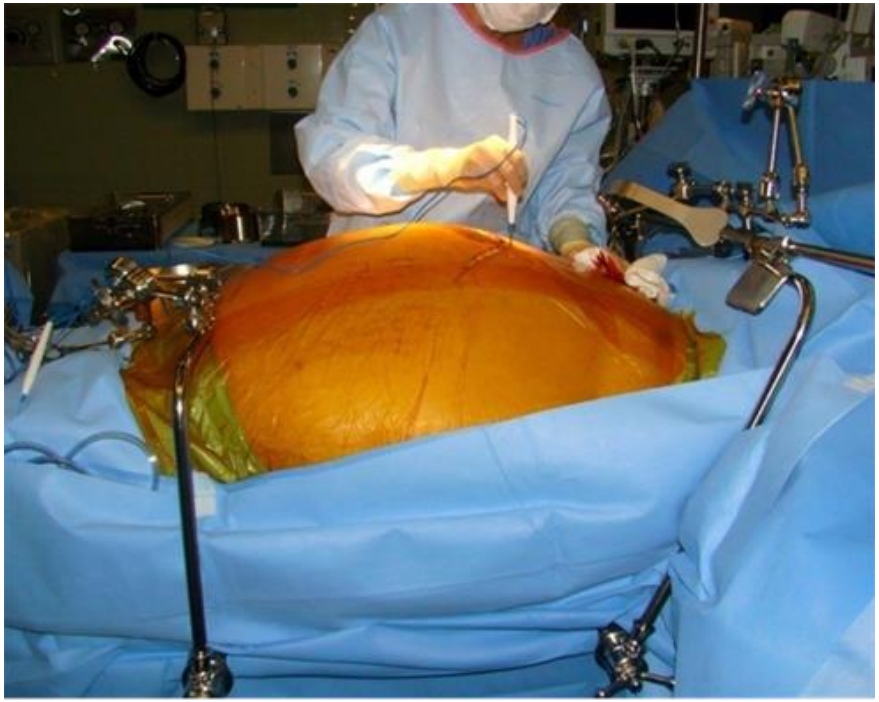
- Structured approach to the problem
- Allows patients to return to full function– as transformative as transplant
- Reduces the long-term complications of obesity

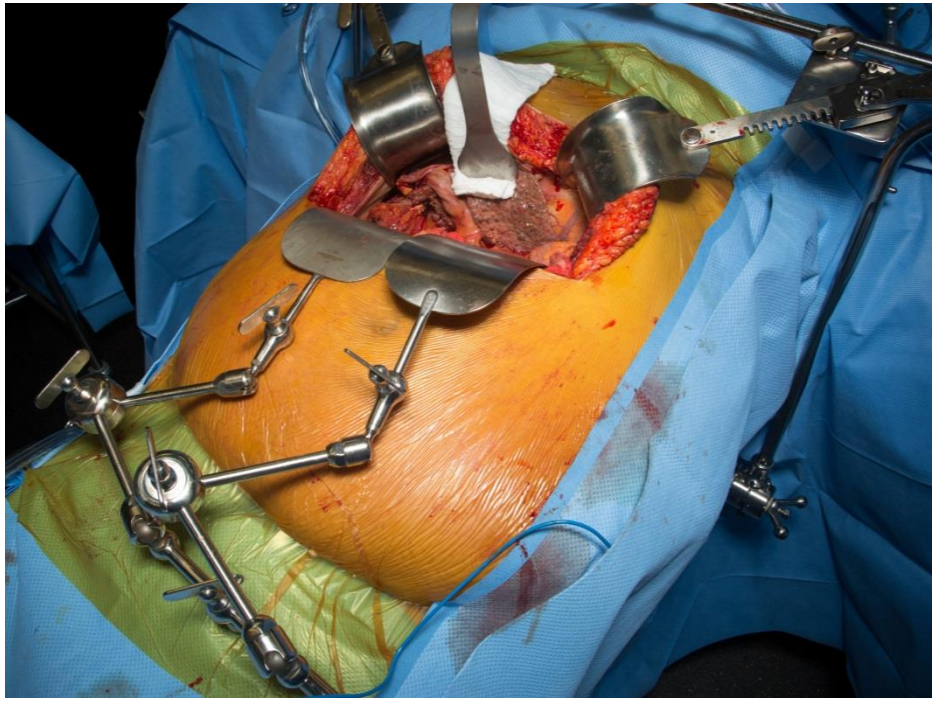
Impact of obesity on pre-transplant patient selection

- **Most common cause of death for patients with NAFLD is a cardiovascular event.**
- **Patients who undergo LT for NASH may be at an increased risk for perioperative/post-op cardiac events**
- **Sarcopenia is associated with worse outcomes, including patients with sarcopenic obesity**

Ekstadt et al Hepatology 2006:4;865-73. Vanwagner et al Hepatology. 2012 Nov;56(5):1741-50
Choudary et al Clin Transplant 2015: 29: 211–215.

perioperative concerns:





Impact of obesity on outcome:

- SRTR data **1987-2007**
- 68,172 BMI 18.5-40, 1827 <18.5, and 1,447>40.
- Outcome worse high and low BMI patients (similar to previous report Nair et al 2002)
- No correction for ascites, small number of patients in each of the "extreme" groups

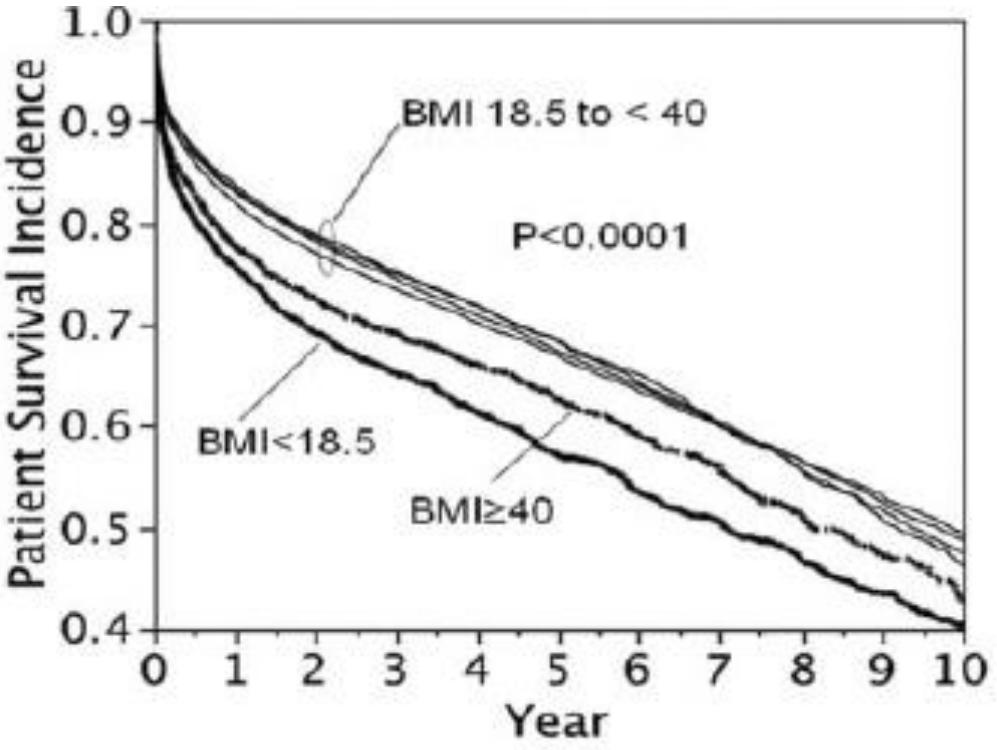
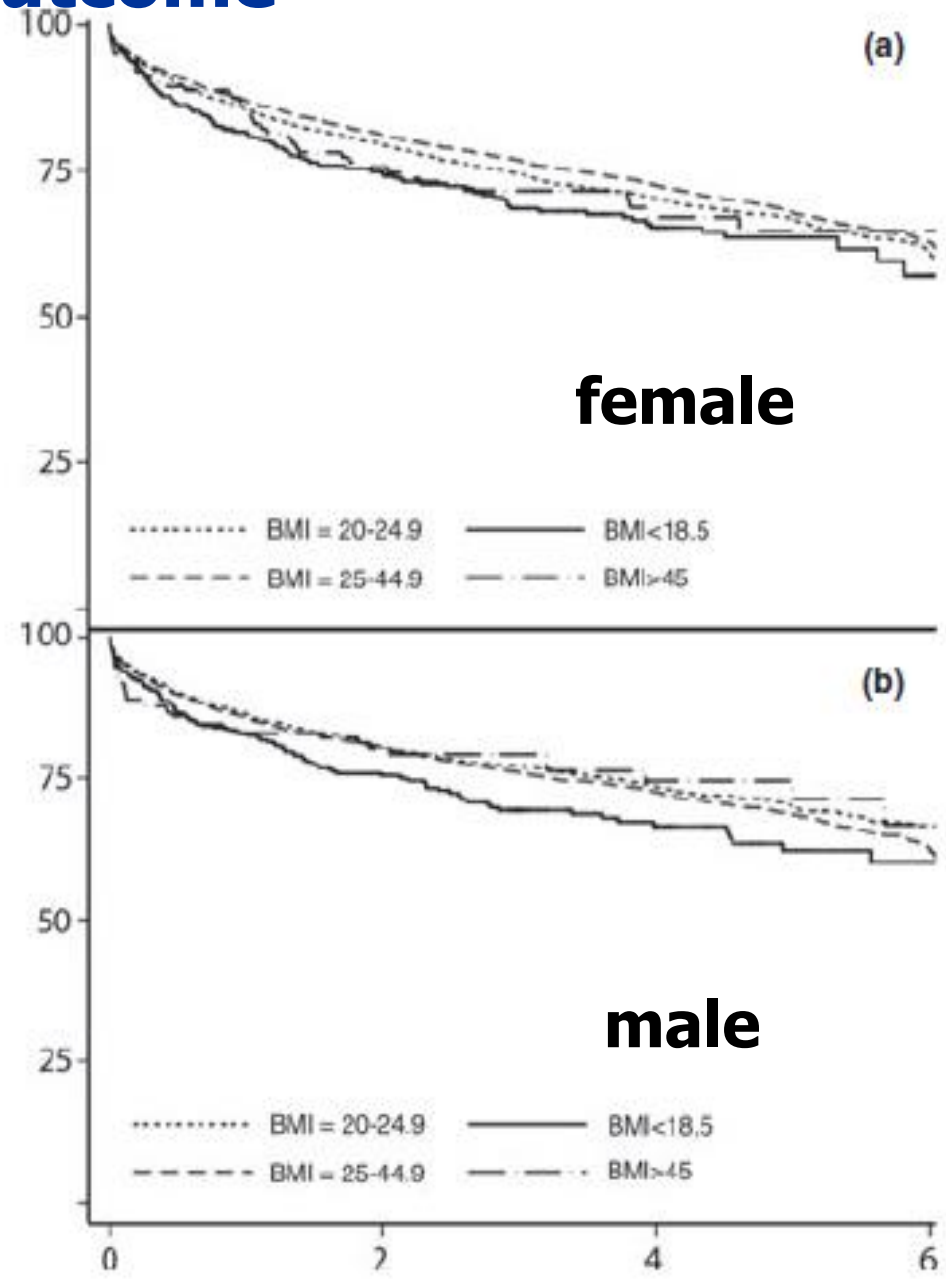


Figure 1. Patient survival according to the body mass index (BMI) groups.

Dick, Liver Transpl. 2009:15;968-77.

Impact of obesity on outcome

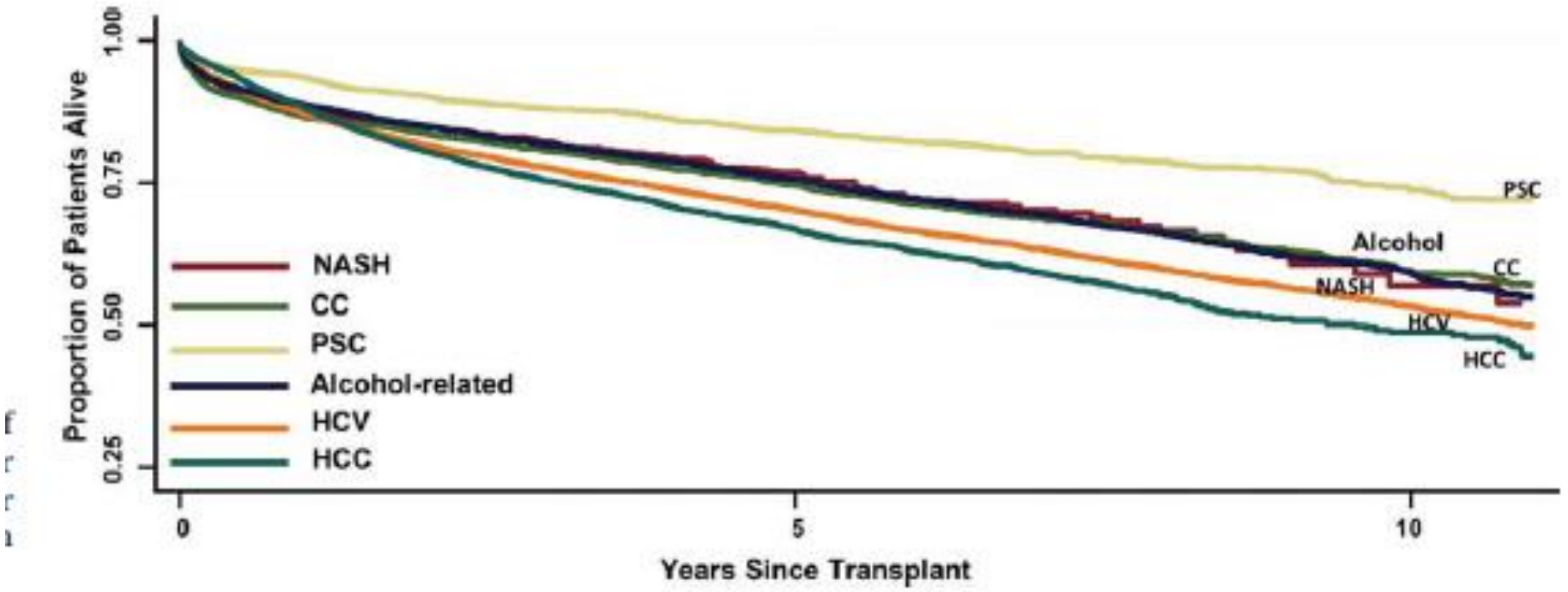
- SRTR 2004-2011
- N=38,194
- Compared <18.5, 18.5-45, >45.
- BMI<18.5 associated worse survival
- No difference in outcomes for obese patients



Orci Transpnt Int. 2012: 26;170-6.

Long term outcomes: NASH

- SRTR data analysis of transplant for NASH 1997-2010

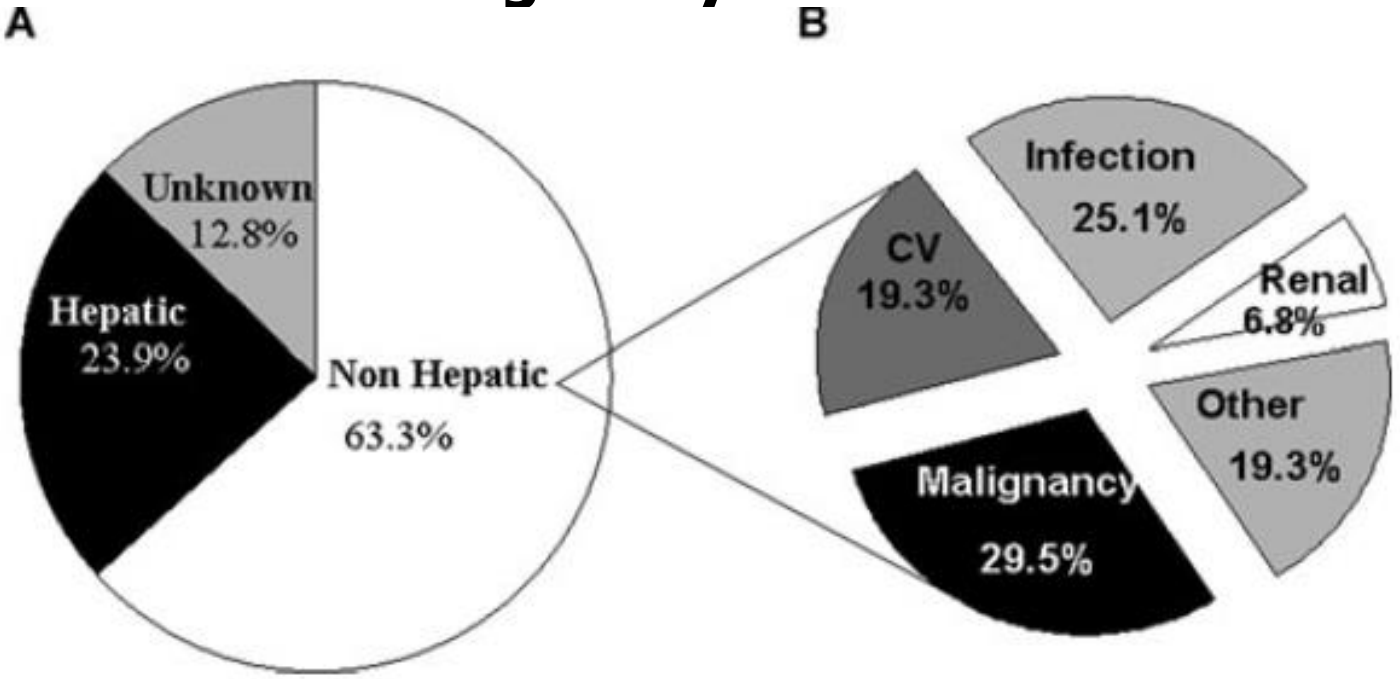


Afzali et al, 2012, Liver Transpl 18:29-37.

Author	year	N	BMI cohort	findings
Fujikawa et al, 2006	1990-2005, US center	700	<25 25-30 >30	**No difference** in cost, LOS, re-op, surgical complications, graft or patient
Nair 2009 et al	2005-07, US center	193	<30 30-34.9 35-39.9 >39.9	**No differences** in resource utilization, surgical complications, patient or graft
Schaffer et al 2009	1999-2003, Canadian	167	<30 30-34.5 ≥35	**Increased** wound complications, longer LOS
Mattina et al, 2012	1997-08, US center	813	<25 25.1-30 30.1-35 35.1-40 >40	**Increased**: OR time, LOS, infection, transfusion, infection, OR complication
Agopian et al, 2012	1993-2011 US center	1235	<18.5 18.5-20 20.1-25 25.1-30 30.1-35 35.1-40 >40	**Increased** OR time, LOS and blood loss, **No Difference graft/patient survival**
Hakeem et al, 2013	1994-2009, UK center	1325	<18.5 18.5-20 20.1-25 25.1-30 30.1-35 >35	**Increased** hospital and ICU stay, increased infection

Impact of obesity on Long term outcome

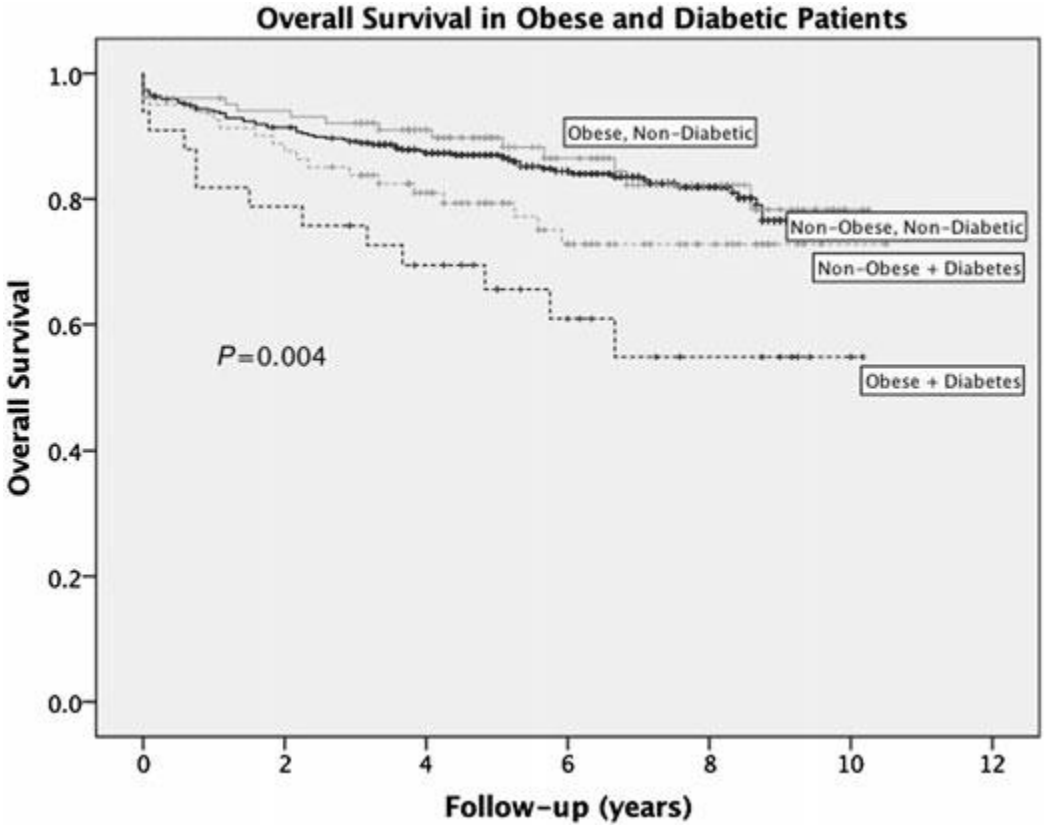
- Long term outcomes using NIDDK data set (multi-center, prospective dataset)
- **Long-term risks for mortality** included age, **DM**, renal insufficiency, and **causes of mortality** included **CV** and **malignancy**



Watt et al AJT 2010:

Impact of obesity on long term outcome

- Multi-center Australian LT cohort N=617 2002-2009
- **Obese plus Diabetes** associated with worse outcomes at 5 years post LT.
- Obese non-DM and non-obese DM were both similar to non-obese, non-DM.



Adams et al:Journal of Gastroenterology and Hepatology 31 (2016) 1016–1024

Long term Impact of obesity: recurrent NAFLD?

- Recurrent NAFLD (n=11) vs de novo NAFLD (n=80)
- Recurrent NAFLD appears earlier and is more severe

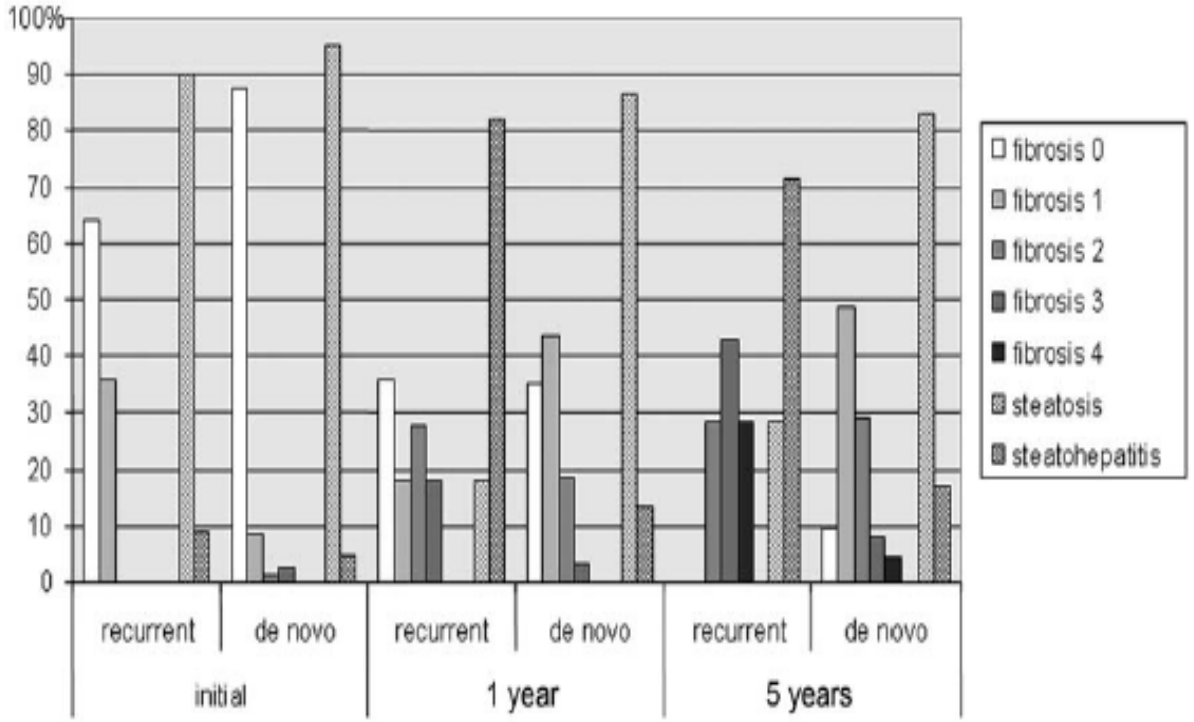
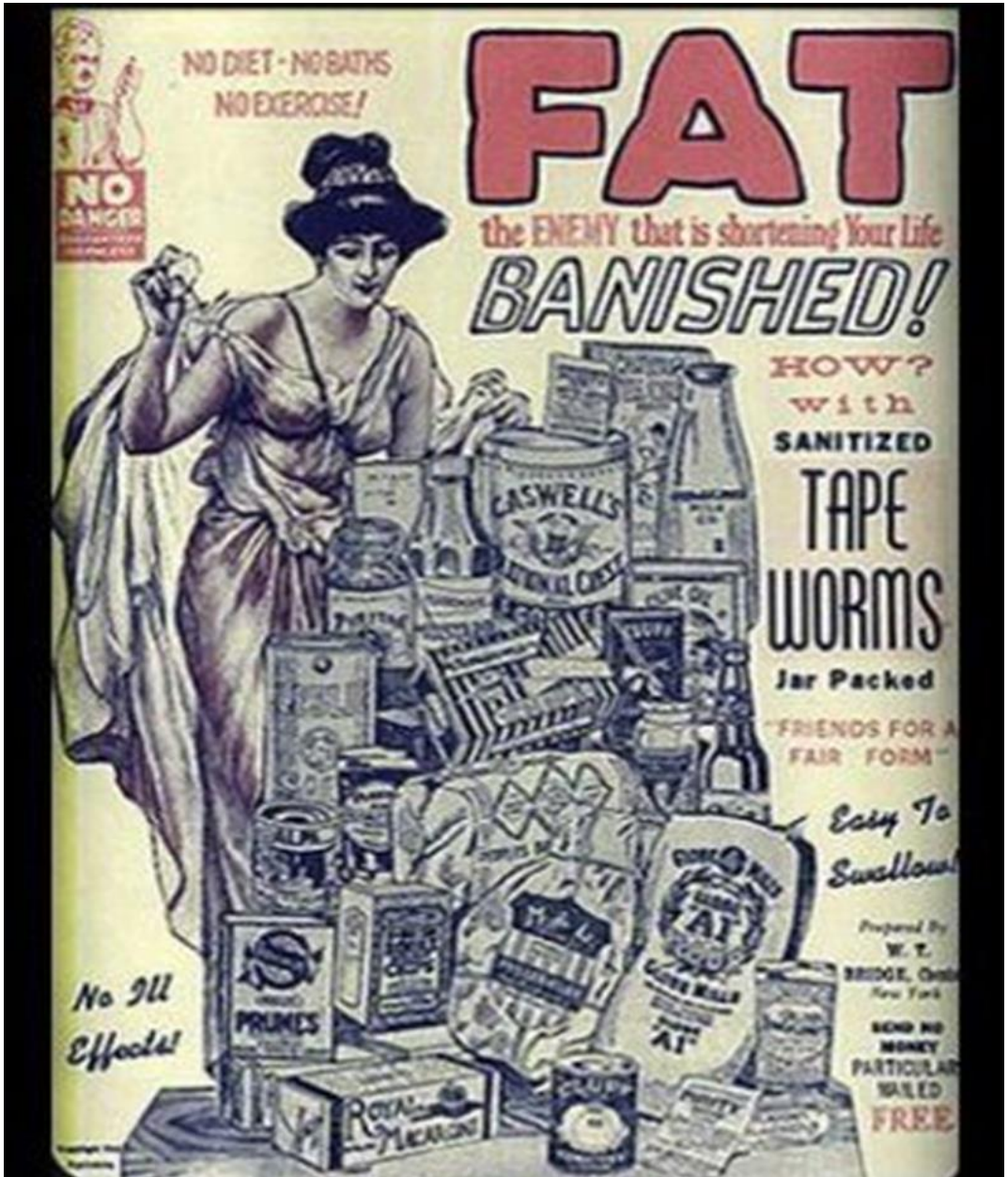


Figure 1. Distribution of fibrosis stages and prevalence of steatohepatitis in the 2 study groups according to the time after LT.

Vallin et al LT 2014:20;1064-71

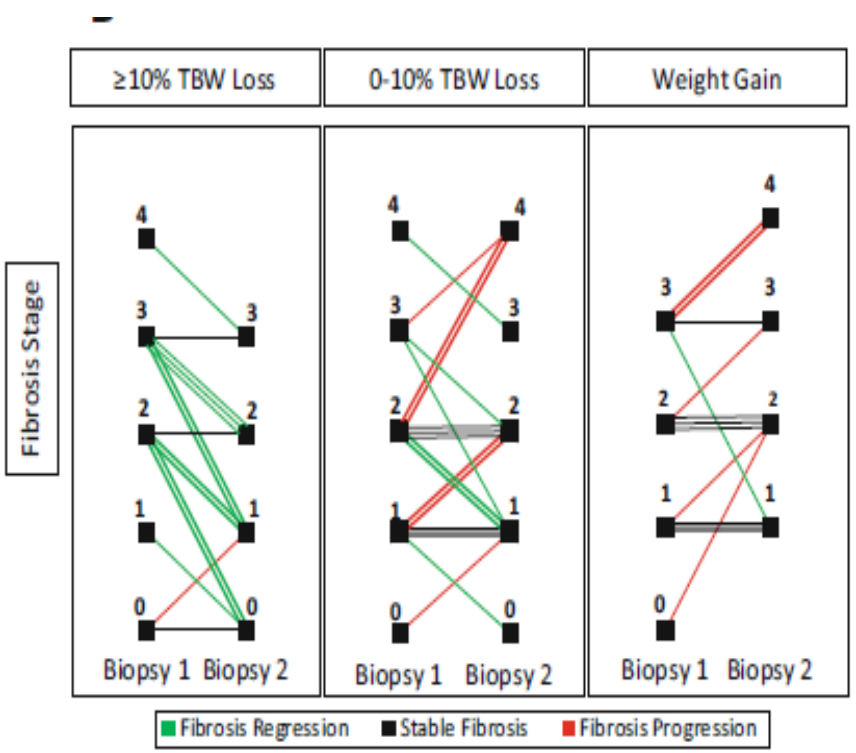
Options for treatment

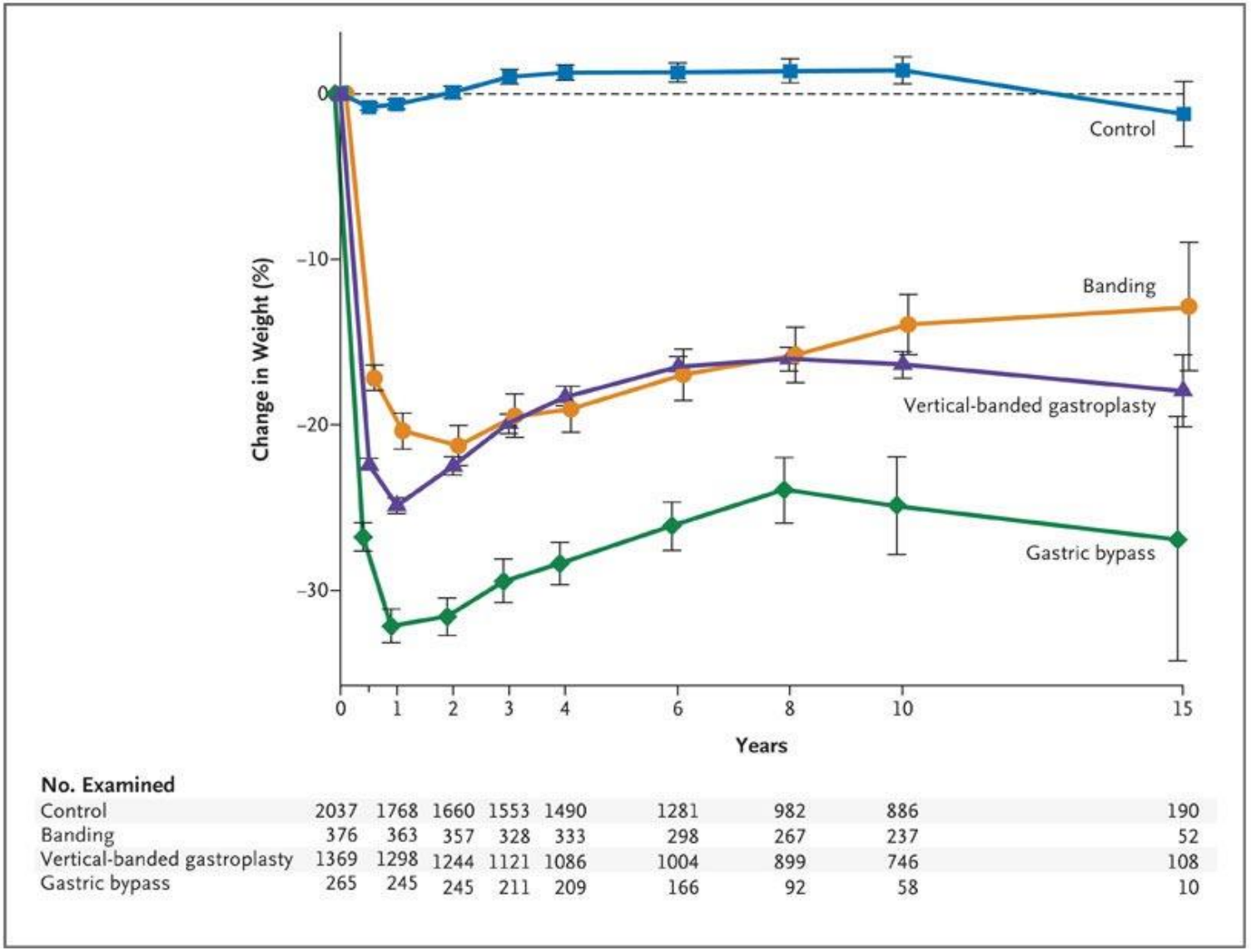


Impact of weight loss on liver fibrosis:

Glass et al. (Dig Dis 2015 60:1024–1030)

- **45 patients**, followed for mean of 4.6 years with **serial biopsies** every 5 years
- Mean fibrosis stage=2, two patients with cirrhosis.
- 12 patients with bariatric surgery, 6 more who lost weight with medical management
- On multivariate analysis, only **weight loss of >10 % TBW predicted fibrosis regression, OR 8.14**





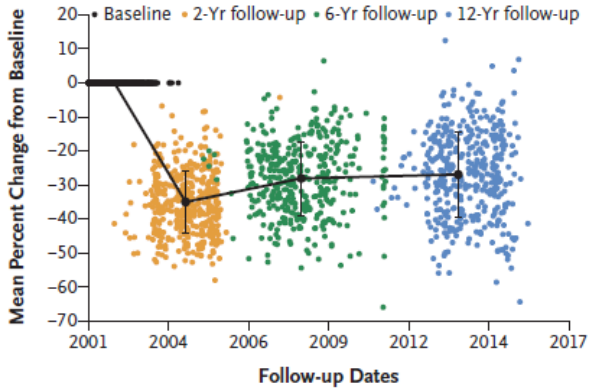
No. Examined									
Control	2037	1768	1660	1553	1490	1281	982	886	190
Banding	376	363	357	328	333	298	267	237	52
Vertical-banded gastroplasty	1369	1298	1244	1121	1086	1004	899	746	108
Gastric bypass	265	245	245	211	209	166	92	58	10

Bariatric surgery provides effective long-term weight loss

*Sjostrom et al NEJM 2007;357:741-752

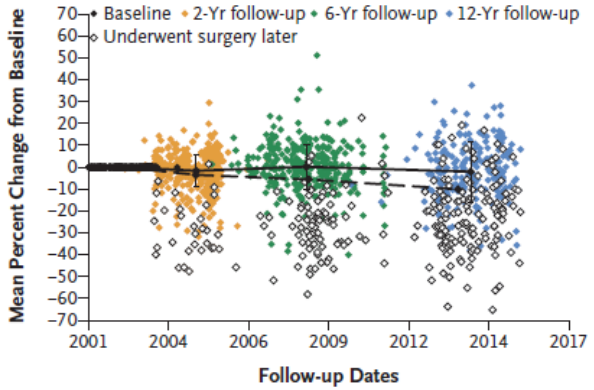
12 year outcomes post Roux-Y Gastric bypass: Adams et al NEJM 2017: 377; 1143-55.

A Mean Percent Change in Body Weight from Baseline to Years 2, 6, and 12 in the Surgery Group



No. of Patients	Baseline	2 Yr	6 Yr	12 Yr
Surgery group	418	409	379	387
Deaths	—	3	9	14
Total	418	412	388	401

B Mean Percent Change in Body Weight from Baseline to Years 2, 6, and 12 in Nonsurgery Group 1



No. of Patients	Baseline	2 Yr	6 Yr	12 Yr
Nonsurgery group 1	417	373	294	217
Underwent surgery later	—	28	89	146
Deaths	—	3	11	25
Total	417	404	394	388

- Bariatric surgery provides effective long-term weight loss
- 95% reduction in new-onset DM at 12 years
- 51% resolution of DM type II at 12 years

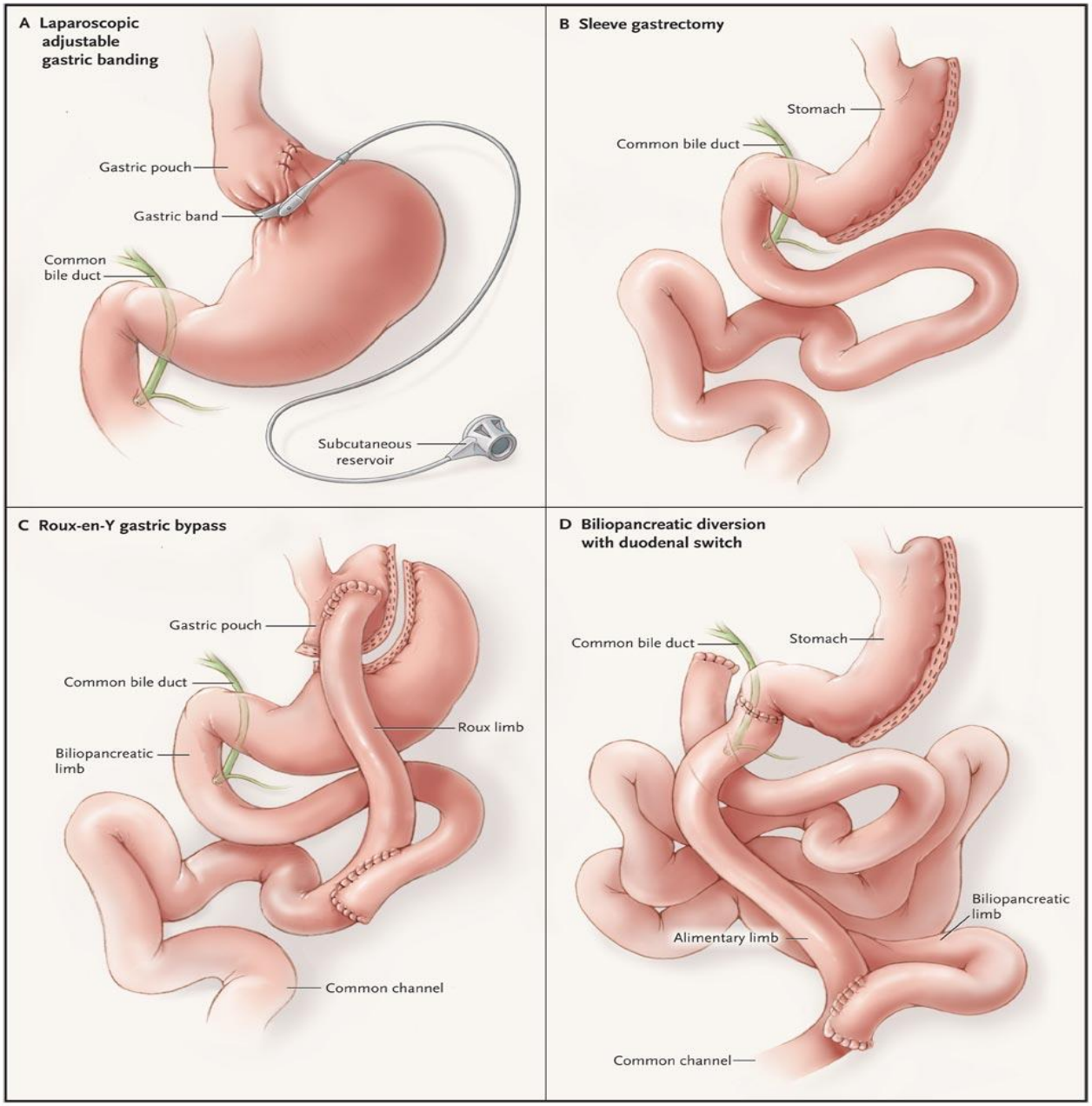
Bariatric surgery procedures

Restrictive

- **Lap band:** reversible, low rate of serious complications. Less effective weight loss, and >50% failure rate at 10 years. ? Access to distal varices
- **Gastric sleeve:** slower weight loss, low rate of complications, appears durable (**early**). Not reversible. Preserves access to biliary tree and varices.

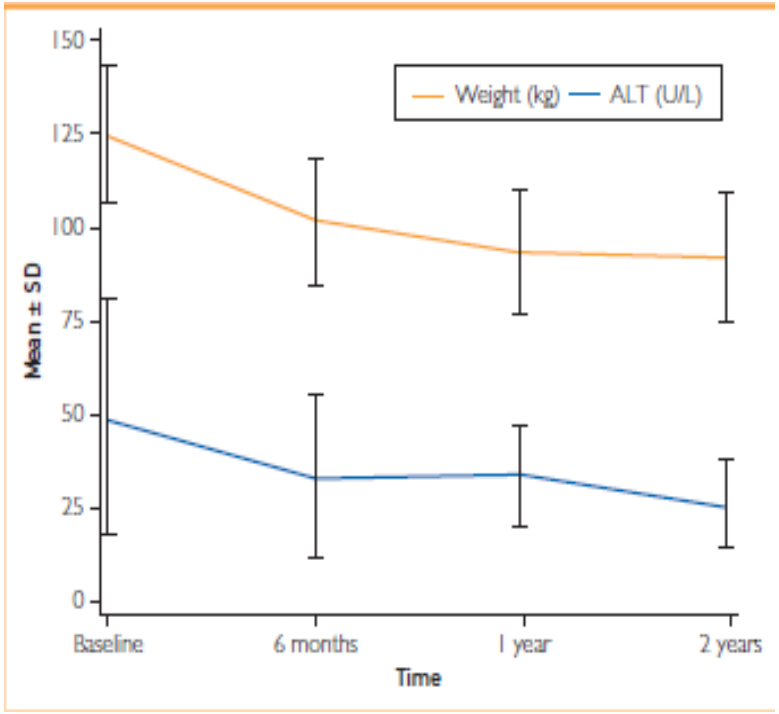
Restrictive +Malabsorptive

- **Roux-en-Y Gastric bypass:** gold standard. Effective, long-term weight loss. Serious complication rate 0.5-2%. No access to distal varices. ? Rapid weight loss
- **Duodenal switch:** rarely used, reserved for very severe obesity. Not appropriate for patients with liver disease.


A Laparoscopic adjustable gastric banding
Gastric pouch
Gastric band
Common bile duct
Subcutaneous reservoir
B Sleeve gastrectomy
Stomach
Common bile duct
C Roux-en-Y gastric bypass
Gastric pouch
Common bile duct
Roux limb
Biliopancreatic limb
Common channel
D Biliopancreatic diversion with duodenal switch
Common bile duct
Stomach
Biliopancreatic limb
Alimentary limb
Common channel

Bariatric Surgery in patients with cirrhosis

- 5 studies (13-23 patients)
- Lap sleeve gastrectomy or RYGB
- Longer OR time and higher complications
- Conclude: bariatric surgery safe, effective in selected patients with **compensated** cirrhosis (child's A.)



Lin et al Obes Relat Dis. 2013;9(5):653–8. Woodford et al Obesity Surg (2015) 1623-9. Shimizu et al Obesity Rel Dis (2013)9;1–6. Rebibo et al Obesity Rel Dis (2014)405-10. Pestana et al Mayo Clin. Proc. (2015)209-15

Bariatric surgery for cirrhosis

Mosko and Nguyen: CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2011;9:897–901

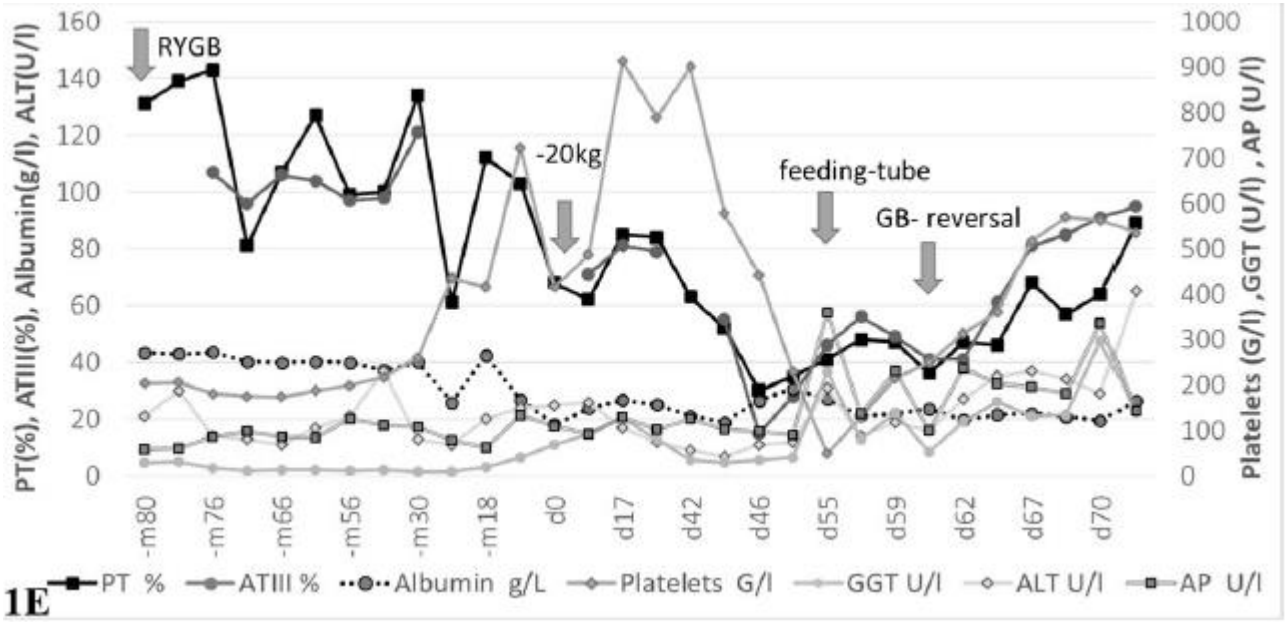
- Nationwide Inpatient Sample (NIS) between 1998 and 2007
- Patients identified as having bariatric surgery and decompensated cirrhosis (n=62), compensated (n=3888) or or no cirrhosis (n=670,950).
- Diagnosis code of ascites or varices required to be classified as decompensated.
- **In-hospital mortality 16.3 % vs 0.9% and 0.3%,(P <.0002)**.
- LOS higher in cirrhosis: 6.7 and 4.4 d vs 3.2 d, respectively; P<.0001.

Significant Liver-Related Morbidity After Bariatric Surgery and Its Reversal—a Case Series

Magdalena Eilenberg[1] · Felix B. Langer[1] · Andrea Beer[2] · Michael Trauner[3] · Gerhard Prager[1] · Katharina Staufer[4]

Obes Surg 2018:28;812-19

- N=10 patients, post-RYGB, median 15 months. 110% excess body weight lost.
- Liver decompensation: reversed by lengthening common limb



Liver Function in Patients With Nonalcoholic Fatty Liver Disease Randomized to Roux-en-Y Gastric Bypass Versus Sleeve Gastrectomy

Kalinowski et al 2017 Annals of Surg 266:738-45

- N=66, randomized to SG vs RYGB, intraoperative liver biopsy plus NAS score. LFTs compared pre and post op 1,3,6 and 12 months.
- Excess weight loss 66% for SG and 62% for RYGB at 1 year
- RYGB induced significantly greater increase in INR, and decreased in serum albumin (versus no change for SG) at 1 month post surgery– resolved by 1 year

<u>Conclude:</u> patients with NASH undergoing RYGB more susceptible to early transient liver dysfunction vs SG

Liver transplantation after bariatric surgery?

- N=11 patients (9 RYGB, 1 sleeve, 1 JI bypass)
- Mean LOS=10 days, mean OR time 405.8 min, 4 re-operations (biliary issues=3, wound=1), 6 u transfusion (no control group)
- Post-op survival similar (81% 1 year and 72% 2 year) for those with bariatric surgery versus 88% and 84% for those LT recipients without prior bariatric surgery

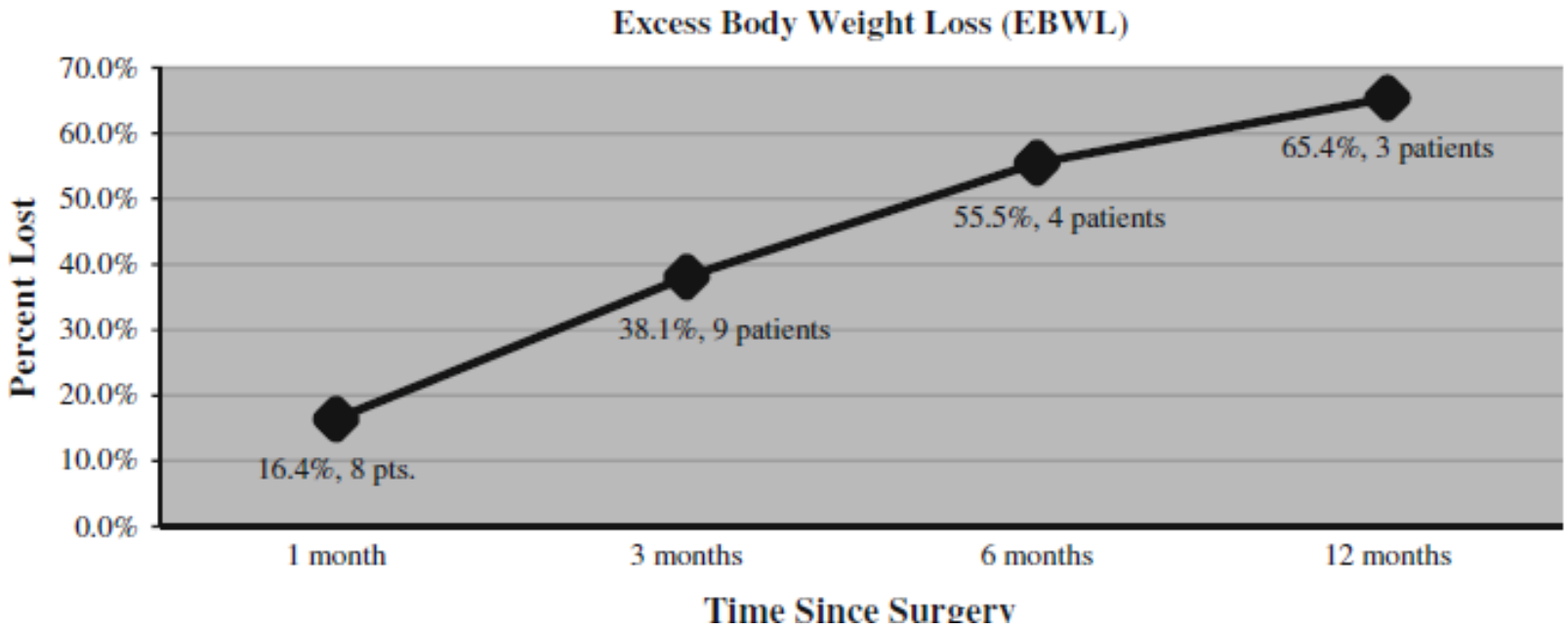
Sarwan et al Liver Trans 2017:23; 1415-21.

Bariatric surgery in Decompensated Cirrhosis

- Before transplant : not an option for patients with Child's B/C,
- After transplant
- Concurrent with transplantation

Post LT bariatric surgery

- Lin et al: Lap gastric sleeve post LT n=9 patients
- Mean time from transplant 5.9 years, age=56, BMI=41, OR time 165 minutes (lysis of adhesions), hospital stay 5.6 days
- Mean f/u 6 months
- 3 patients required re-op in first 30 days



Lin Surg Endo 2013: 27;81-85

Post LT bariatric surgery

- Al-Nowaliti et al (LT 2013;19(12):1324-9): open RYGB post LT n=7 patients
- Mean time from transplant 2.6 years, age=56, BMI=44
- Mean f/u 5 years
- 2 patients died in first 1 year, and 1 reversal

Pre-Transplant BMI (kg/m^2)	Pre-RYGB BMI (kg/m^2)	OLT-RYGB Interval (months)	Post-RYGB BMI (kg/m^2)	Follow-up Duration Post-RYGB (Months)
32.6	38	38	18.7	103
35.7	46	26	32.5	6
39.4	46	19	24.3	9
38.7	39.5	31	24.5	48
26.3	55.9	32	28	98
27.8	45	26	34.4	96
39.4	40	14	22.9	55
34.27	44.34	26.57	26.47	59.14

Post LT bariatric surgery

- N=6 post LT SG. (3 open, 3 lap). Performed at average of 43 months post LT.
- Mean follow up 37 months
- Median LOS =9 days, 1 leak with subsequent prolonged stay/multiple reoperations/death. One complication > 30 days (infected mesh requiring re-op).
- Mean BMI 28 post procedure.

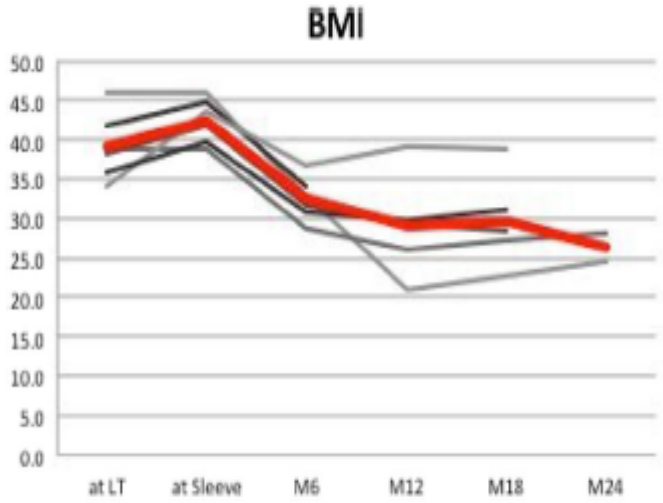


Fig. 1 BMI and %EWL at LT, at SG, 6,12, 18, and 24 months following sleeve gastrectomy (*gray lines* indicate each patient and *red line* the average of BMI and %EWL of all six patients). LT indicates Liver

Osseis et al Obes Surg 2017 Aug 3.
doi: 10.1007/s11695-017-2843-y7:

Perioperative bariatric surgery: MCR Approach

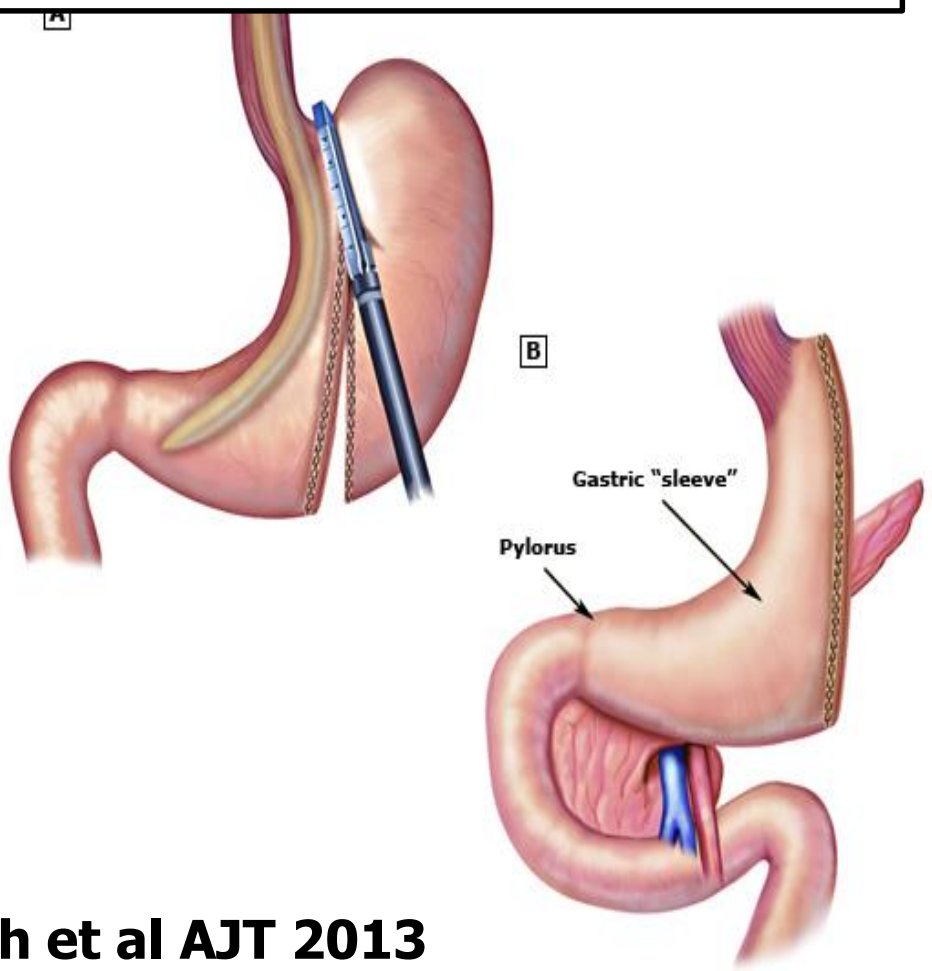
- Why? **Previously, approach was inconsistent**
- Enroll all pre-transplant patients with BMI>35 in an obesity management protocol: 4 step approach, goal is BMI<35
  - Calorie restricted diet
  - Food record
  - Weigh and record.
  - Activity: determine restrictions, pedometer, etc.

American Journal of Transplantation 2013; 13: 363–368
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2012.04318.x

Combined Liver Transplantation and Gastric Sleeve Resection for Patients With Medically Complicated Obesity and End-Stage Liver Disease

- **Option for selected patients who have not attained goal weight and have high MELD**
- **Gastric sleeve resection combined with liver transplant**
- **No malabsorption, slower weight loss, technically easier**

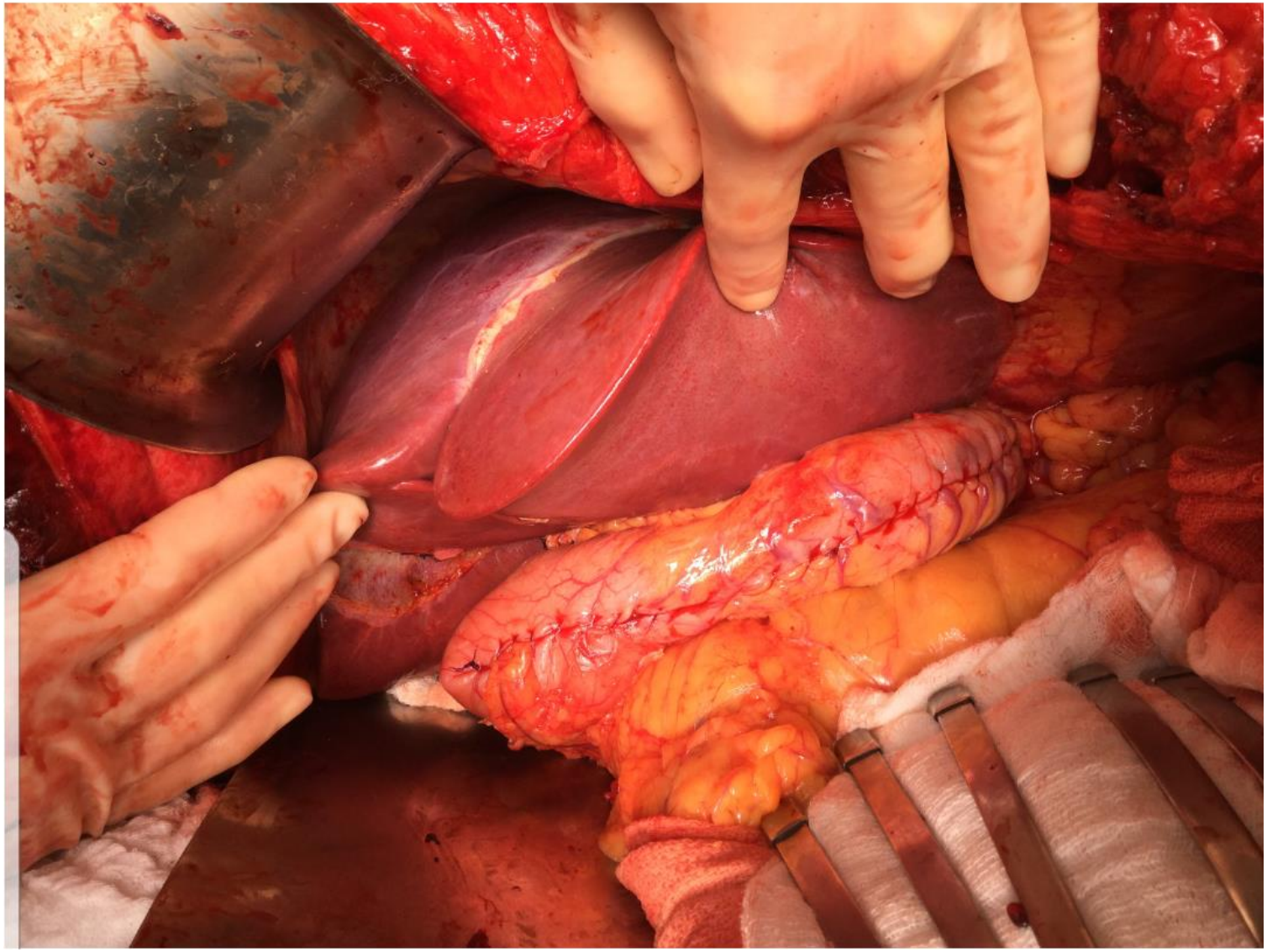


Heimbach et al AJT 2013

Combined LT and sleeve gastrectomy

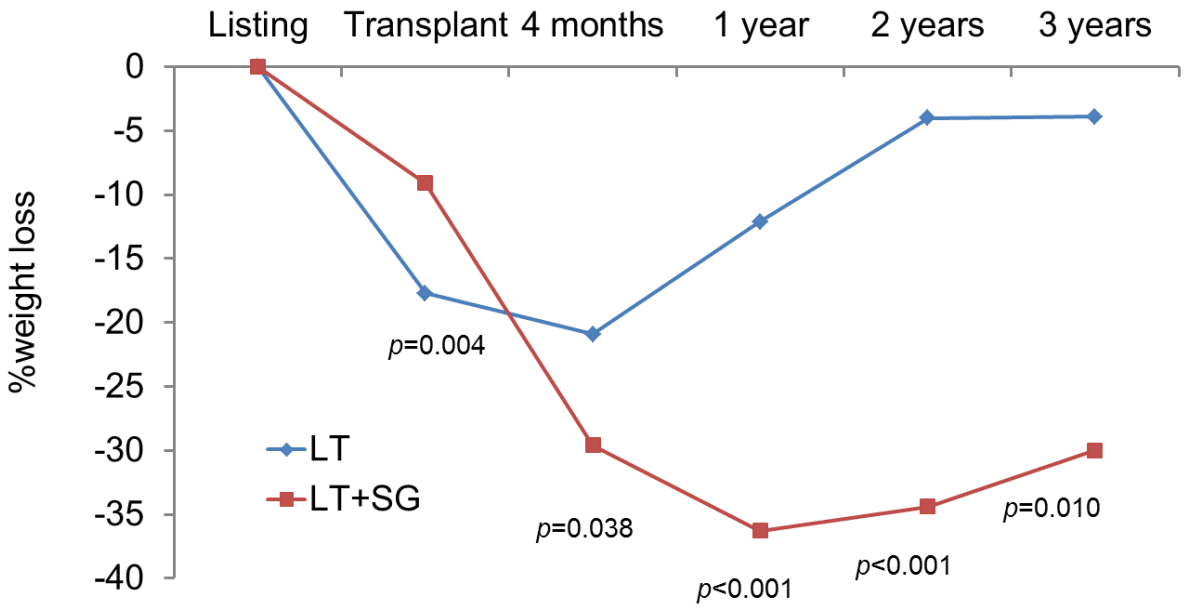
- 37 non-invasive approach versus 7 combined sleeve with LT
- With short term follow up, safe and effective

characteristic	N=37 LT	N=7 LT+SG	P-value
MELD at tx	19 (8-35)	32 (11-40)	<0.001
O.R. time (mean)	4:21 (2:54-7:51)	4:59 (4:16-7:39)	0.59
Mean BMI at LT	33 (28-40)	48 (39-52)	<0.001
% DM post LT	34% (12/35)	0% (0/7)	0.03
BMI at last f/u	36 (25-45)	28 (23-35	0.003



Long-term outcomes of patients undergoing simultaneous Liver Transplantation and Sleeve Gastrectomy

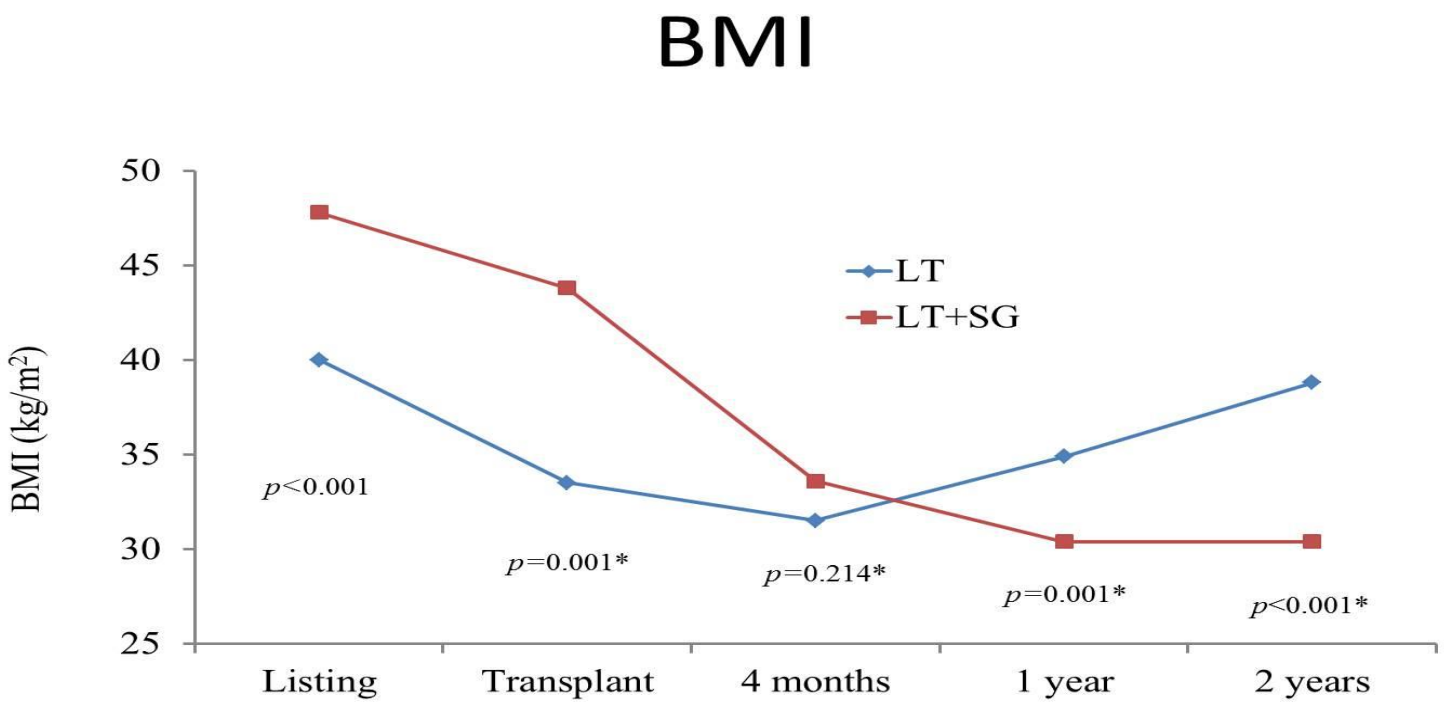
Zamora-Valdez et al, 2018 Hepatology:68(2);485-95



- N=29 LT+SG, with 17 >3 years of follow-up, 36 LT alone
- 29.4% of patients in LT cohort maintained >10% loss in TBW, while 100% of the LT+SG patients did (p<0.001)
- %TBWL= LT cohort 3.9±13.3% vs. LT+SG cohort 34.8±17.3%; p<0.001)

Long-term outcomes of patients undergoing simultaneous Liver Transplantation and Sleeve Gastrectomy

Zamora-Valdez et al, Hepatology Feb 2018



* After controlling for baseline BMI

Long-term outcomes of patients undergoing simultaneous Liver Transplantation and Sleeve Gastrectomy

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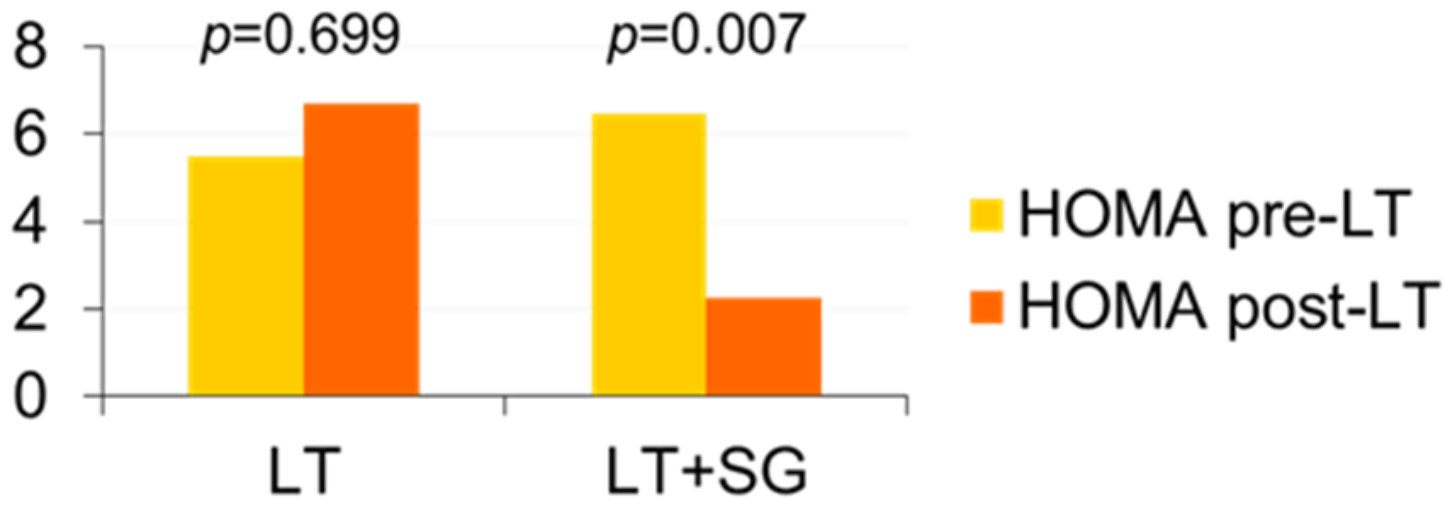

Figure 3. Insulin resistance index (HOMA-IR) before and after transplant (last follow-up).

Less DM, less hypertension, lower triglycerides

Practical tips:

- Standardized approach: specific nutritional, activity, and weight loss goals
- Close follow up (reflux excess weight loss, re-gain)
- Weight distribution/ascites important for technical considerations

Practical tips:

- Closed wound vac for those with edematous pannus (particularly liver kidney)

- Specific diet post LT
  - Clear Liquids for 3 days
  - Full liquids for 3 days
  - Pureed diet for 3 weeks
  - Mechanical soft for 4 weeks
  - Soft diet for 4 weeks

Combined LT+ SG

- Taricotti et al 2016 (Rome). European J of Surg Case Reports. N=1, age 53 HCC/HCV BMI=38, MELD=14. 5 months post-op, BMI=29, and normal allograft function.

- Nesher et al. 2017(Tel Aviv) Obesity Surgery. N=3. Mean BMI=44, Mean MELD=24. Weight loss -27%, improved metabolic comorbidities, at mean follow up of 13 months. 1 bile leak and 1 AKI.

Fig. 1. Gastrografin study following sleeve gastrectomy showing absence of leakage.

Treatment:

Compensated cirrhosis

↓

Goal attain ≥10% body weight loss to improve liver fibrosis, metabolic complications

↓

Non-invasive weight loss

↓

Consider lap sleeve gastrectomy

Decompensated cirrhosis

↓

Transplant candidate?

↓

Non-invasive attempt at weight loss (selected)

↓

Sleeve gastrectomy (during or after LT)

Summary for liver transplant:

- Post LT outcomes for **selected obese** patients are acceptable (Cardiac screening essential)

- Long term outcomes post LT impacted by obesity
  - Lifestyle modification

  - Combined approach may be an option for selected patients who have not attained goal weight (close follow up essential), or consider after transplant

Questions?
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