Institute of Liver & Biliary Sciences



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Bariatric Surgery and NAFLD/MAFLD

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OUTLINE

- BARIATRIC SURGERY: PROCEDURES AND MECHANISMS
- CLINICAL EFFECTIVENESS OF BARIATRIC SURGERY IN NAFLD WITHOUT ADVANCED LIVER DISEASE
- BARIATRIC SURGERY IN CIRRHOSIS
- BARIATRIC SURGERY IN LIVER TRANSPLANT CANDIDATES
- OUTCOME OF LIVER TRANSPLANTATION AFTER PRIOR BARIATRIC SURGERY
- LIVER FAILURE AFTER BARIATRIC SURGERY
- BARIATRIC SURGERY AND ALCOHOL

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Bariatric surgery (BS) vs Metabolic surgery (MBS)?

Shift in the goal: from weight loss to control of metabolic disease

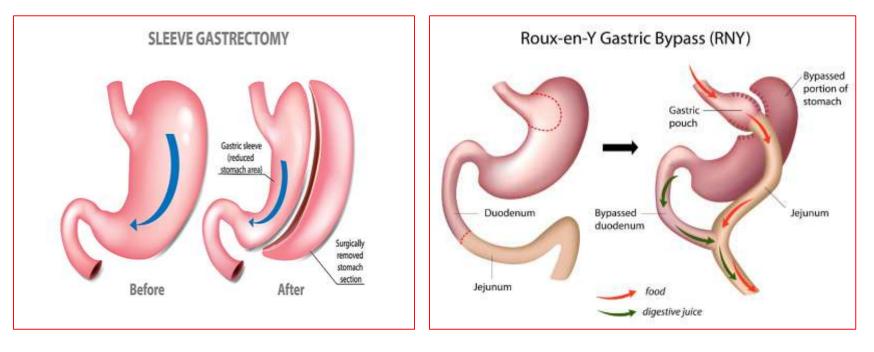
	Bariatric surgery	Metabolic surgery
Purpose	Weight loss	Glycemic/metabolic control; CV risk reduction
Indication criteria	BMI-centric	Uncontrolled type 2 diabetes, metabolic syndrome, NASH, increased CV risk
Operations	Traditional (RYGB,	Traditional (RYGB, SG, BPD, LAGB)
	SG, BPD, LAGB)	Investigational (DJB, IT endoscopic duodenal Sleeve)
Measures of outcome	Weight loss (excess weight loss)	Glycemic control, blood pressure, lipid control, CV risk reduction, weight loss
Presumed mechanisms of action	Restriction to food intake/malabsorption	Several, complex, neuroendocrine

Surgical procedures

Restrictive

- Vertical banded gastroplasty (VBG)
- Adjustable gastric banding (AGB)
- Sleeve gastrectomy (SG)
- Largely Restrictive, Moderately Malabsorptive
 - Roux-en-Y gastric bypass (RYGB)
 - Mini Gastric bypass (MGB)
- Largely Malabsorptive, Mildly Restrictive
 - Biliopancreatic diversion (BPD)
 - Duodenal switch (DS)

Most commonly done techniques are the sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB)



Indications for BS and MBS vary across Asia-Pacific Countries [2018 survey]

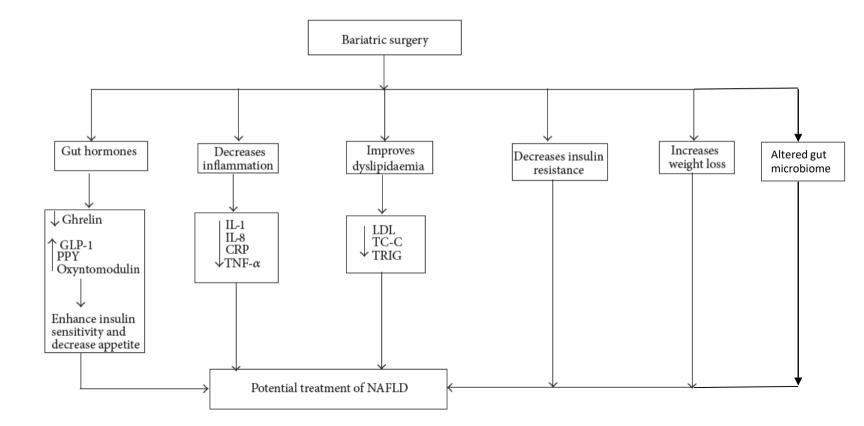
Country	Indication			
	Bariatric surgery (BMI)	Metabolic surgery (BMI)		
East Asia				
Japan	≥35	\geq 32 with DM or other two diseases		
Korea	\geq 35 or \geq 30 with disease	\geq 27.5 with DM		
China	≥ 32.5	\geq 27.5 with DM or other two diseases		
Taiwan	\geq 37 or \geq 32 with diseases	\geq 32.5 or \geq 27.5 with DM or other diseases		
Hong Kong	\geq 35 or \geq 30 with two diseases	\geq 27.5 with uncontrolled DM		
Southeast A				
Philippines		≥32		
Malaysia		≥32 with DM or other two diseases		
Singapore	\geq 37.5 or \geq 32.5 with disease	≥ 27.5		
Indonesia	≥ 35	\geq 30 with uncontrolled DM or MS		
Thailand	≥35	≥32 with DM or other two diseases		
South Asia				
India	\geq 37.5 or \geq 32.5 with diseases	≥27.5		
Oceania	\frown			
Australia	\geq 40 or \geq 35 with disease	≥30 with disease or bad family history or Asia		
West Asia		\frown		
KSA	≥40	\geq 35 with DM or other diseases		
UAE	\geq 40 or \geq 35 with diseases	None		
Qatar	\geq 40 or \geq 35 with disease or \geq 30 with uncontrolled DM	None		
Kuwait	≥40	\geq 35 with DM or other diseases or \geq 30 with severe MS		
Turkey	≥35	None		

Ohta M etal. Bariatric/Metabolic Surgery in the Asia-Pacific Region: APMBSS 2018 Survey. Obes Surg. 2019 Feb;29(2):534-541.

East/South East/South Asians lower BMI cut-off

Society	Bariatric surgery	Metabolic surgery	
Korean Society for the Study of Obesity (2020)	BMI ≥ 35 kg/m2	Comorbidities with BMI \geq 30 kg/m2	
		Uncontrolled T2D with BMI \geq 27.5 kg/m2	
Joint Committee in the Japanese Society for Treatment of Obesity, the Japan Diabetes Society, and the Japan Society for the Study of Obesity (2021)		BMI ≥ 32 kg/m2 with diabetes or two or more non- diabetic obesity-related health disorders	
Chinese Society for Metabolic & Bariatric Surgery, Chinese College of Surgeons, and Chinese Medical Doctor Association (2019)	BMI ≥ 37.5 kg/m2 (strong recom) BMI 32.5–37.5 kg/m2 (recom)	Comorbidities (\geq 2) with BMI 27.5–32.5 kg/m2	
Obesity and Metabolic Surgery Society of India Guidelines (2016)	BMI >37.5 kg/m2	BMI > 32.5kg/m2 with the presence of T2D / any obesity related co-morbidities	
International Federation for the Surgery of Obesity: Asia Pacific Chapter (IFSO-APC: 2011)	BMI >35 kg/m2	BMI >30 kg/m2 with T2DM or metabolic syndrome BMI >27.5kg/m2 with inadequately controlled T2DM or metabolic syndrome, the surgical approach may be considered as a non-primary alternative to treat.	

BS/MBS and NAFLD: Proposed mechanisms

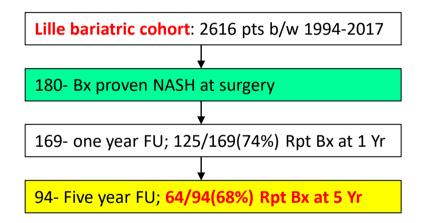


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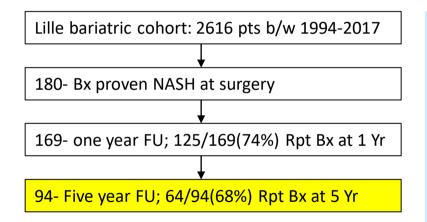
Bariatric Surgery Provides Long-term Resolution of Nonalcoholic Steatohepatitis and Regression of Fibrosis

Centre Hospitalier Universitaire de Lille, Lille, France



Bariatric Surgery Provides Long-term Resolution of Nonalcoholic Steatohepatitis and Regression of Fibrosis

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Criteria for bariatric Sx:

Morbidly (BMI >40 kg/m2) or severely obese (BMI >35 kg/m2), with at least 1 comorbidity factor (eg, arterial hypertension or diabetes mellitus), for at least 5 years and were resistant to medical treatment

No medical or psychologic contraindications to bariatric Surgery

Did not drink excessively

No history of long-term consumption of hepatotoxic drugs, and;

Screened negative for chronic liver disease.

Lassailly etal. Gastroenterology 2020; 59:1290–1301

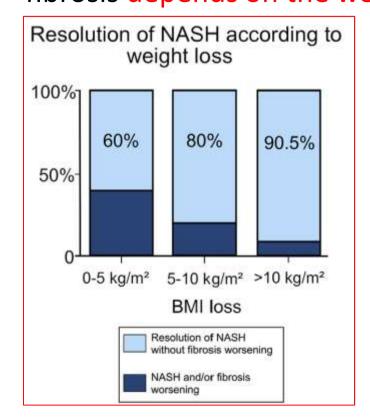
Bariatric Surgery Provides Long-term Resolution of Nonalcoholic Steatohepatitis without worsening of fibrosis at 5 years in majority (84%)

Bariatric procedures	Total=180	
Gastric band	39 (21.7)	
Gastric bypass	119 (66.1)	
Sleeve gastrectomy	21 (11.7)	
Shunt	1 (0.5)	

Resolution of NASH without worsening of fibrosis at 5 years after bariatric surgery (n=64 patients). Paired biopsy analysis P < .001 100 80 Percentage 60-84.4% 40-20-15.6% Baseline 5 years NASH and/or Fibrosis worsening No NASH & No Fibrosis worsening

Lassailly etal. Gastroenterology 2020; 59:1290–1301

Resolution of Nonalcoholic Steatohepatitis without worsening of fibrosis depends on the weight lost

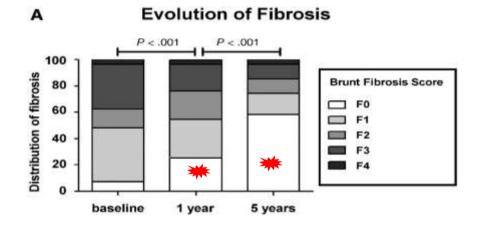


BMI loss >10 kg/m2=90% NASH resolution

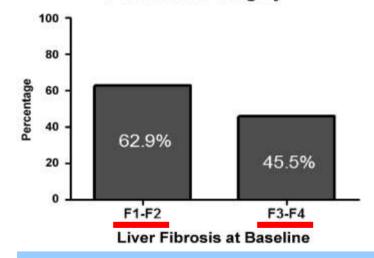
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Bariatric Surgery Provides Long-term Regression of Fibrosis

в



The reduction of fibrosis is progressive, beginning during the first year and continuing through 5 years Rate of Fibrosis Resolution 5 Years After Surgery



Fibrosis resolution: defined by a F0 fibrosis score on liver histology at 5 years.

Whether RYGB or LSG is more effective in improving NASH?-Meta-analysis 2021

Meta-analysis: 45 studies

24: exclusively on RYGB; 14: exclusively on SG; 7: evaluating both RYGB and SG

23: follow-up with liver biopsies, 22: only biochemical assessment

9940 individuals; age 40.8 ± 6.9 years; female (71.9%)

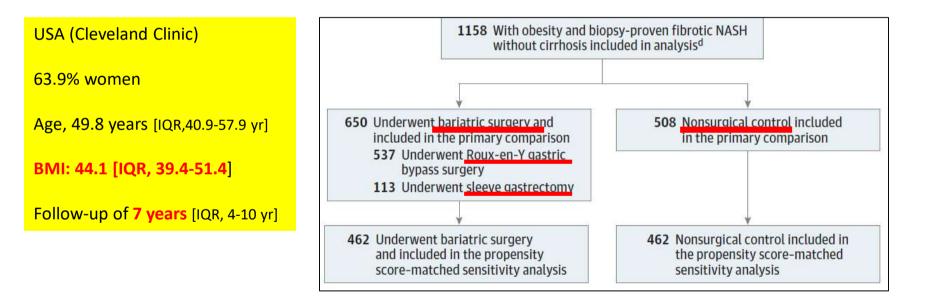
Baseline BMI was 46.5 ± 4.7 kg/m2; Follow-up : 14 ± 6 months

No difference was found between RYGB and SG regarding the histopathological outcomes

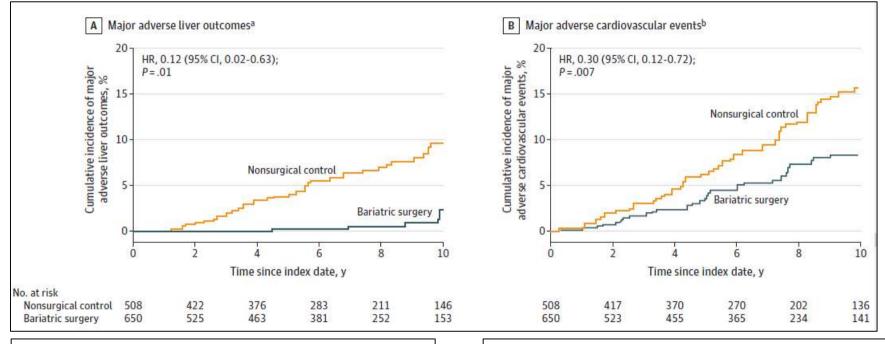
SG and RYGB are equivalently effective for treating NAFLD/NASH

Barreto de Brito e Silva. Etal. Obesity Surgery (2021) 31:2762–2772

BS associated with a significantly lower risk of incident major adverse liver outcomes and major adverse cardiovascular events (MACE) in NASH and obesity (vs nonsurgical care).



BS associated with a significantly lower risk of incident major adverse liver outcomes and major adverse cardiovascular events (MACE) in NASH and obesity (vs nonsurgical care).



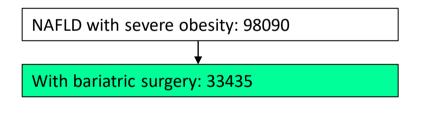
MALO: defined as the first occurrence of progression to clinical or histological cirrhosis, development of hepatocellular carcinoma, liver transplantation, or liver-related mortality after the index date.

MACE defined as the first occurrence of coronary artery events, cerebrovascular events, heart failure, or cardiovascular mortality after the index date.

Bariatric Surgery Reduces Cancer Risk in Adults With Nonalcoholic Fatty Liver Disease and Severe Obesity

USA, Retrospective cohort study of 18 to 64 years old newly diagnosed NAFLD patients with severe obesity (ie, BMI ≥40 kg/m2) between 2007 and 2017:

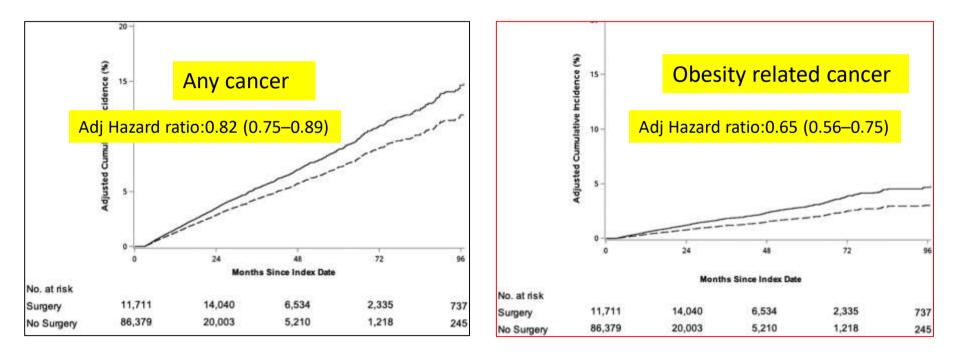
With at least 12 mo f/u, and no h/o cancer before.



Bariatric procedures	Total=33435	
Open RYGB	733 (2.19)	
Open VBG/SG	272 (0.81)	
Lap AGB	4788 (14.32)	
BPS-DS	3221 (9.63)	
Lap SG	11,420 (34.16)	
Lap RYGB	12,663 (37.87)	
Other	338 (1.01)	

AGB, adjustable gastric band; BPS-DS, biliopancreatic diversion/duodenal switch; lap, laparoscopic; other, other partial gastrectomy; SG, sleeve gastrectomy; VBG, vertical-banded gastroplasty.

Bariatric Surgery Reduces Cancer Risk in Adults With Nonalcoholic Fatty Liver Disease and Severe Obesity



Obesity related cancers: Colon cancer, rectal cancer, postmenopausal breast cancer, hepatocellular carcinoma, kidney cancer, esophageal cancer, cancer of the gastric cardia, gallbladder cancer, pancreatic cancer, ovarian cancer, endometrial cancer, thyroid cancer, multiple myeloma, and meningioma.

Bariatric Surgery Reduces risk for colon, pancreatic, endometrial, thyroid cancers, hepatocellular carcinoma, and multiple myeloma

Type of obesity-related cancer	Adjusted HR (95% CI)
Any obesity-related cancer	0.65 (0.56–0.75)
Colon cancer	0.66 (0.42–1.00)
Rectal cancer	0.44 (0.10–1.37)
Postmenopausal breast cancer	1.08 (0.74–1.54)
Hepatocellular carcinoma	0.48 (0.24–0.89)
Kidney cancer	0.90 (0.60–1.32)
Esophageal cancer	0.33 (0.06–1.18)

Type of obesity-related cancer	Adjusted HR (95% CI)	
Cancer of the gastric cardia	0.46 (0.03–2.44)	
Gallbladder cancer	0.99 (0.05–12.58)	
Pancreatic cancer	0.46 (0.21–0.93)	
Ovarian cancer	0.70 (0.41–1.15)	
Endometrial cancer	0.49 (0.31–0.73)	
Thyroid cancer	0.61 (0.41–0.89)	
Multiple myeloma	0.33 (0.14–0.69)	
Meningioma	0.52 (0.05–2.90)	

Laparoscopic Sleeve Gastrectomy (SG) associated with significant risk reductions in all cancer outcomes (vs other procedures)

Bariatric procedures	Any cancer HR (95% CI)	Obesity-related cancers HR (95% CI)
Open RYGB	0.63 (0.37–1.03)	1.04 (0.46–2.34)
Open VBG/SG	1.12 (0.46–2.77)	0.68 (0.14–2.62)
Lap AGB	0.90 (0.71–1.12)	0.60 (0.39–0.91)
BPS-DS	0.75 (0.56–1.00)	0.62 (0.37–1.02)
Lap SG	0.77 (0.65–0.90)	0.60 (0.44–0.80)
Lap RYGB	0.81 (0.70–0.93)	0.77 (0.59–1.01)
Other	0.33 (0.11–0.83)	0.35 (0.05–1.42)

Laparoscopic Sleeve Gastrectomy (SG) associated with significant risk reductions in all cancer outcomes

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Safety in cirrhosis

• An increasing number of Bariatric Surgery procedures performed in patients with cirrhosis described over the last decade.

• Mostly retrospective analyses of incidental findings at the time of surgery.

High mortality in decompensated cirrhosis

USA, 2008 to 2013 Nationwide Inpatient Sample (NIS) database to study the trends and outcomes of bariatric surgery in patients with cirrhosis.

Undergoing Roux-en-Y gastric bypass (RYGB) or vertical sleeve gastrectomy (VSG)

RYGB or VSG admissions: 558017	Variable	No cirrhosis (n = 554,828)	Compensated cirrhosis (n = 3086)	Decompensated cirrhosis (n = 103)
No cirrhosis: 554828 Compensated Cirrhosis: 3086 [0.55%]	Mortality	563 (0.1%)	20 (0.6%)	20 (19.4%)
Decompensated cirrhosis: 3086 [0.55%]	Length stay, median (IQR)	1.5 (1.0–2.0)	1.7 (1.2–2.6)	3.4 (2.0–7.6)

Decompensation defined by: presence of ascites, HE, variceal bleeding, or SBP

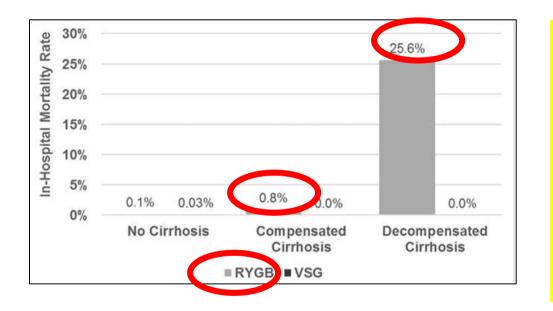
Mumtaz etal. Obes Surg. 2020 Sep;30(9):3444-3452

VSG preferred over RYGB post 2010

Trends of RYGB and VSG from 2008 to 2013 90,000 80.000 Number of Admissions 70,000 60,000 50,000 40,000 RYGB VSG 30,000 20,000 10,000 0 2008 2009 2010 2011 2012 2013 Year

Mumtaz etal. Obes Surg. 2020 Sep;30(9):3444-3452

VSG safer than RYGB



Sleeve Gastrectomy favoured: Shorter operative time Lower technical complexity Better postoperative outcomes Preservation of access to the biliary tree (for potential need for transplantation) Limited impact on absorption of immunosuppression post LT

Center experience also a predictor of mortality in patients undergoing bariatric surgery on Multivariable logistic regression

Variable	Adjusted odds ratio (95% CI)	p value
Cirrhosis None Compensated Decompensated	Reference 1.88 (0.65, 5.46) 83.8 (19.3, 363.8)	<0.001
Age	1.06 (1.04, 1.08)	<0.001
Sex, male versus female	2.59 (1.76, 3.81)	<0.001
Elixhauser comorbidity Index, \geq 3 versus < 3	5.30 (3.45, 8.15)	<0.001
Procedure, RYGB versus VSG	3.90 (1.79, 8.48)	<0.001
Low-volume center (< 50 gastric bypasses/year)	5.25 (3.38, 8.15)	<0.001

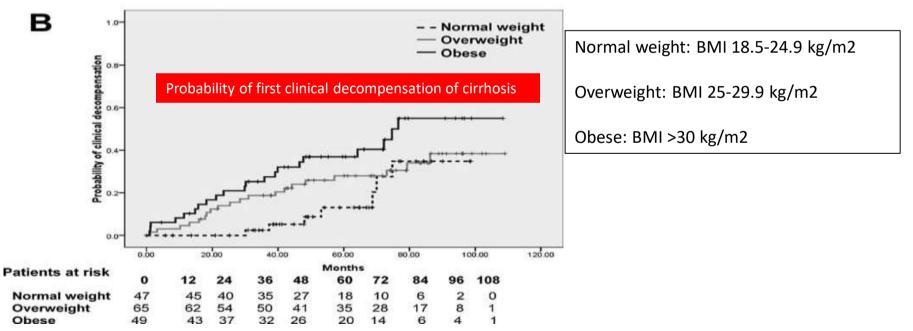
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Obesity Is an Independent Risk Factor for Clinical Decompensation in Patients with Cirrhosis of all etiologies- increases waitlist mortality

European Multicenter; 161 patients with compensated cirrhosis Median follow-up: 59 months



Berzigotti et al. HEPATOLOGY 2011;54:555-561

Paucity of good quality data on bariatric surgery in LT candidates

 Most papers report on small case series or retrospective datasets, and there is a risk of publication bias

• Timing can be before, during, or after LT.

Bariatric surgery before, during, or after LT?- Pros and Cons

	Before	During	After
Pros	Can make patient eligible for LT (if BMI ineligibility exists in the LT programme)*	Single intervention	Allows for operation on a patient with good liver function
Cons	Not recommended in decompensated patients	Additional morbidity and mortality risk in a complex high-risk Patient. Bariatric surgeon available	Higher technical difficultly due to postoperative abdominal adhesions Complications related to
		at LT	immunosuppression

* There are no universal guidelines on the BMI cut-off for transplant eligibility.

Many institutions have BMI limits that exclude morbidly obese patients from transplantation, resulting in prolonged wait times for LTX in this population

Bariatric Surgery **Before LT**: Meta-analysis

8 studies [6 retrospective and 2 prospective cohort]

187 patients, mean age = 50.4 years (74.4% female) underwent bariatric surgery before LTX

Sleeve gastrectomy (SG; 3 studies) laparoscopic SG (LSG; 4 studies) Roux-en-Y gastric bypass(RYGB; 3 studies) biliopancreatic diversion (BPD; 1 study) duodenal switch (DS; 1 study) jejunoileal gastric bypass (JIB; 3 studies).

5 studies conducted bariatric surgery with the intention of improving LTX candidacy

3 studies included patients with prior bariatric surgery unrelated to improving LTX candidacy

Lee Y etal. Surg Obes Relat Dis. 2020 Sep;16(9):1336-1347

Bariatric Surgery **Before LT**: Meta-analysis

30 day mortality- 0%30-day minor complications-4%30-day major complications-1%

2 studies: Complete resolution of T2D: 41.14% Complete resolution of HT: 22.5% Beyond 30 day mortality (all cause)- 7%

At 12-months f/u: BMI change: 45.7 (2.0) to 31.8 (8.3) kg/m2

% reduction of BMI 30.4% after bariatric surgery

5 studies conducted bariatric surgery with the intention of improving LTX candidacy

Time b/w BS and LT: 14 months (7-22 months)

78% being listed for transplant and

33% subsequently receiving LTX

Bariatric Surgery during LT: Meta-analysis

2 studies [1 retrospective and 1 prospective cohort]

32 patients, mean age = 51.9 years (50% female) underwent bariatric surgery during LT

SG was the only type of bariatric surgery performed among these patients.

Lee Y etal. Surg Obes Relat Dis. 2020 Sep;16(9):1336-1347

Bariatric Surgery during LT: Meta-analysis

1 year mortality- 0%

Complete resolution of T2D: 58.3% Complete resolution of HT: 66.7%

At f/u: BMI change: 47.6 (1.1) to 33.3 (2.9) kg/m2

% reduction of BMI 30%

1 study Complications:

Roperation for bleeding: 3(10.3%),

Staple line leak:1(3.4%)

Steroid-resistant rejection:1(3.4%)

HAT:2 (6.8%), one of whom eventually underwent re-transplant.

Lee Y etal. Surg Obes Relat Dis. 2020 Sep;16(9):1336-1347

Bariatric Surgery after LT: Meta-analysis

9 studies [7 case series, 2 case report]

64 patients, mean age = 56 years (48.3% female) underwent bariatric surgery after LT

SG (8 studies) and RYGB (3 studies)

The median time between LT and bariatric surgery was 27.5 months (25 to 120)

Lee Y etal. Surg Obes Relat Dis. 2020 Sep;16(9):1336-1347

Bariatric Surgery after LT: Meta-analysis

30 day mortality- 0%30-day minor complications-4%30-day major complications-9%

Complete resolution of T2D: 41% Complete resolution of HT: 48%

At 33.8 mo f/u: BMI change: 43.4 (1.44) to 31.7 (24.8) kg/m2

% reduction of BMI 27%

Beyond 30 day mortality (all cause)- 7.8%

Major Complications:

Incisional hernia

Balloon dilatation

Bile leak

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Impact of Prior Bariatric Surgery on Perioperative Liver Transplant Outcomes

USA, 78 with h/o BS prior to evaluation for consideration of primary LT

156: matched concurrent cohort on age, MELD at evaluation, and etiology

RYGB (63%)

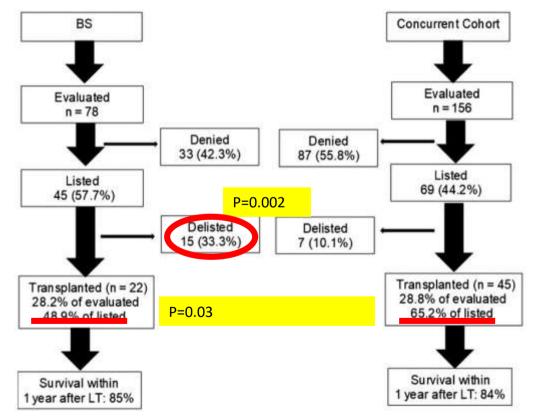
Mean weight loss between the BS and the time for evaluation for LT: 130 pounds

Liver cirrhosis diagnosis: After BS :67.5% At time of BS: 22.5% Before BS: 10%

Median time between the BS and evaluation for LT: 7 years

Idriss etal. Liver Transplantation 2019; 25: 217–227

Rate of LT was lower from the time of listing in BS cohort vs concurrent cohort



Idriss etal. Liver Transplantation 2019; 25: 217–227

Patients malnourished at the time of LT higher in BS vs concurrent cohort

Variable	BS cohort, 78	Concurrent cohort, 156	Ρ
Malnourished by SGA	64.1%	39%	<0.01
Total skeletal surface area, cm2	127 [105-141]	153 [131-191]	0.005

Rates of sarcopenia higher among **patients delisted after listing** (**71.4%** versus 16.7%; *P* = 0.04).

Idriss etal. Liver Transplantation 2019; 25: 217–227

RYGB and its metabolic outcomes exert negative effects on patients on the waiting list and on LT outcomes

Variable	RYGB surgeries	Non-RYGB surgeries	Р
Skeletal muscle index, cm2/m2	42.0 [36.0-45.0]	52.0 [43.0-57.0]	<0.01
Delisting or death after listing	44%	16.4%	0.04

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Deterioration of liver function and development of liver failure can occur after BS/MBS

Jejunoileal bypass (JIB): 10% liver failure on long term.

Procedure abandoned now

Requarth JA etal. Arch Surg. 1995;130(3):318-325.

Biliopancreatic diversion (BPD): liver failure requiring LT can occur- case series

Rarely done now

Addeo P etal. Surg Obes Relat Dis. 2019;15(8):1394-140

Liver failure following Roux-en-Y gastric bypass (RYGB) and oneanastomosis gastric bypass (OAGB)

Austria, Post BS patients presenting with severe liver dysfunction

N=10, (m:f = 2:8; median age 48 years, range 22–66 years)

After median postoperative time of 15 months (range 2–88 months).

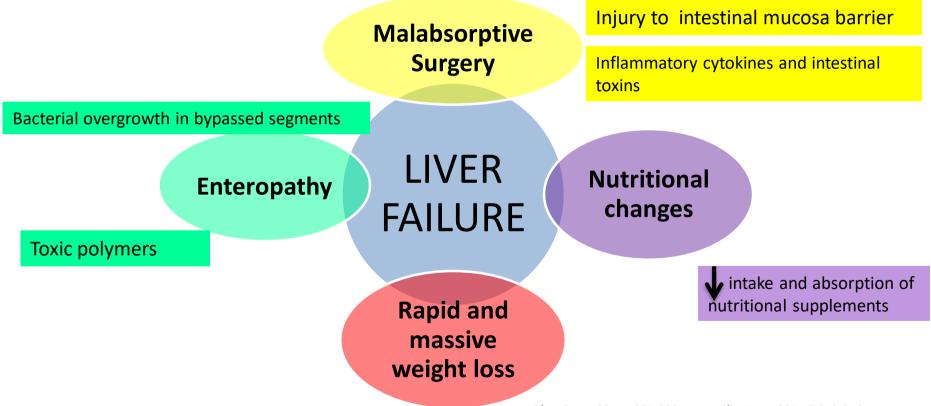
RYGB=3 RYBG→ distal GB=2 Gastric band → OAGB=2 OAGB=3 8= lengthening of the alimentary/ common limb led to an improvement or complete remission of symptoms.

1= Liver transplantation was required

1= died (septic shock and decompensated liver)

Eilenberg etal. OBES SURG (2018) 28:812–819

Risks factor for Liver Failure after BS/MBS

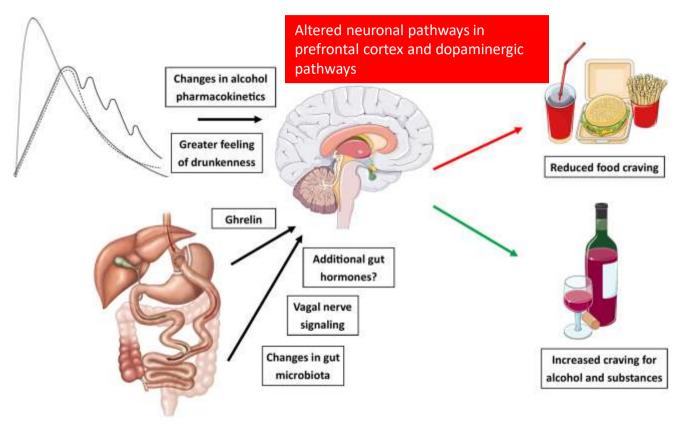


Obes Surg 1994; 4:285-290... Am J Clin Nutr 1987;46:273-276

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- BARIATRIC SURGERY AND ALCOHOL

Potential mechanisms involved in postbariatric surgery alcohol use disorder



Lefere etal. Obesity Reviews. 2021;22:e13294.

Bariatric surgery and Alcohol absorption and elimination

• Conflicting data as to the lifetime and current prevalence of AUD in patients seeking weight loss surgery

Ertelt TW, et al. Surg Obes Relat Dis 2008; King WC, et al. JAMA 2012; Wee CC, et al. Surg Obes Relat Dis 2014; Svensson PA, et al. Obesity (Silver Spring) 2013

- Gastric bypass surgery is associated with:
 - Accelerated alcohol absorption (shorter time to reach maximum concentration)
 - ✓ Higher maximum alcohol concentration
 - ✓ Longer time to eliminate alcohol in both men and women
 - ✓ Increased risk for development of AUD

Klockhoff H, et al. Br J Clin Pharmacol 2002; Hagedorn JC, et al. Surg Obes Relat Dis 2007; Woodard GA, et al. J Am Coll Surg 2011; Horowitz M, et al. Int J Obes 1986; Lee SL, et al. Alcohol Clin Exp Res 2006; Steffen KJ, et al. Surg Obes Relat Dis 2013

• Data less clear regarding altered pharmacokinetics after SG and no evidence that alcohol absorption is affected by gastric banding

SUMMARY AND CONCLUSIONS

- BS/MBS very effective for obesity and metabolic comorbidities including NAFLD/MAFLD
- Indications for BS/MBS vary across Asia-Pacific Countries
- East/South East/South Asians lower BMI cut-off for BS/MBS vs Western/Caucasian Population
- BS/MBS have effects on food intake, gut hormone secretion, metabolic signalling pathways, and adipose tissue dysfunction.

SUMMARY AND CONCLUSIONS

- BS/MBS provides long-term resolution of NASH and fibrosis regression
- BS/MBS associated with significantly lower risk of incident major adverse liver outcomes and major adverse cardiovascular events NASH and obesity
- BS/MBS reduces cancer risk (including HCC) in adults with NAFLD and severe obesity
- BS/MBS- high mortality in decompensated cirrhosis
- BS/MBS can safely be performed in selected patients with liver cirrhosis and an attractive option in carefully selected transplant candidates with severe obesity

SUMMARY AND CONCLUSIONS

- SG and RYGB are equivalently effective for treating NAFLD/MAFLD
- SG –preferred procedure in last decade especially patients with cirrhosis
- Reports of liver failure following BS/MBS esp older bypass procedures
- BS/MBS may be a risk factor for alcohol abuse, the development of ALD in these patients should be monitored.
- BS/MBS should be used after appropriate screening and with close follow-up, and the beneficial effects generally far outweigh the risks.
- Multidisciplinary coordination and approach needed

Future directions

• Need for randomized trials to demonstrate efficacy

Identifying subset likely to benefit: concept of metabolically benign obesity

 Phenotypic and Genotype stratification to assist patient selection for surgical treatment of NAFLD/MAFLD.

Thank You