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

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

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

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

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>BMI cohort</th>
<th>Findings</th>
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<td>Fujikawa et al, 2006</td>
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<td>700</td>
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<td>Schaffer et al 2009</td>
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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.

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
Bariatric surgery provides effective long-term weight loss

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

- 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.
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.)

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 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.
• 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

Conclude: 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

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

- 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

<table>
<thead>
<tr>
<th>Pre-Transplant BMI (kg/m²)</th>
<th>Pre-RYGB BMI (kg/m²)</th>
<th>OLT-RYGB Interval (months)</th>
<th>Post-RYGB BMI (kg/m²)</th>
<th>Follow-up Duration Post-RYGB (Months)</th>
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<tbody>
<tr>
<td>32.6</td>
<td>38</td>
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<td>18.7</td>
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<td>35.7</td>
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<td>39.4</td>
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<td>14</td>
<td>22.9</td>
<td>55</td>
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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.

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.
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

<table>
<thead>
<tr>
<th>characteristic</th>
<th>N=37 LT</th>
<th>N=7 LT+SG</th>
<th>P-value</th>
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<tr>
<td>MELD at tx</td>
<td>19 (8-35)</td>
<td>32 (11-40)</td>
<td>&lt;0.001</td>
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<td>O.R. time (mean)</td>
<td>4:21 (2:54-7:51)</td>
<td>4:59 (4:16-7:39)</td>
<td>0.59</td>
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<td>Mean BMI at LT</td>
<td>33 (28-40)</td>
<td>48 (39-52)</td>
<td>&lt;0.001</td>
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<tr>
<td>% DM post LT</td>
<td>34% (12/35)</td>
<td>0% (0/7)</td>
<td>0.03</td>
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<tr>
<td>BMI at last f/u</td>
<td>36 (25-45)</td>
<td>28 (23-35)</td>
<td>0.003</td>
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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 $3.9 \pm 13.3\%$ vs. LT+SG cohort $34.8 \pm 17.3\%;$ p<0.001
Long-term outcomes of patients undergoing simultaneous Liver Transplantation and Sleeve Gastrectomy
Zamora-Valdez et al, Hepatology Feb 2018

*BMI (kg/m²)

Listing  | Transplant  | 4 months  | 1 year  | 2 years
---|---|---|---|---

* After controlling for baseline BMI
Long-term outcomes of patients undergoing simultaneous Liver Transplantation and Sleeve Gastrectomy

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

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


- 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 $\geq 10\%$ 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