Non-Alcoholic Fatty Liver Disease:
Is Bariatric Surgery the Answer?

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Surgery B Department
Rabin Medical Center
Morbid obesity

• Obesity is a growing epidemic.

• Worldwide obesity has more than doubled since 1980.

<table>
<thead>
<tr>
<th>Weight</th>
<th>BMI values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy weight</td>
<td>18.5–24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0–29.9</td>
</tr>
<tr>
<td>Obese</td>
<td>30 and above</td>
</tr>
</tbody>
</table>
World Health Organization:

- Globally there are more people who are obese than underweight.

- Overweight and obesity are linked to more deaths worldwide than underweight.
Diabetes prevalence is tracking obesity

Obesity prevalence 1994

Diabetes prevalence 1994

Notes: Rates reflect prevalence among adults. Obesity is defined as BMI $\geq 30$.
Source: Centers for Disease Control and Prevention (CDC)

World Health Care Congress, 31 March 2006
Diabetes and obesity (cont’d)

Obesity prevalence 1999

- Yellow: <10-14%
- Red: <15-19%
- Dark red: ≥20%

Diabetes prevalence 1999

- White: <4%
- Light blue: <4-6%
- Dark blue: >6%

Notes: Rates reflect prevalence among adults. Obesity is defined as BMI ≥ 30.
Source: Centers for Disease Control and Prevention (CDC)

World Health Care Congress, 31 March 2006
Diabetes and obesity (cont’d)

Obesity prevalence 2004

Diabetes prevalence 2004

Notes: Rates reflect prevalence among adults. Obesity is defined as BMI ≥ 30.
Source: Centers for Disease Control and Prevention (CDC)

World Health Care Congress, 31 March 2006
United States

- 1/3 of adults are reported as being obese and by 2025 this number is expected to increase to 45%-50%.

Mid-life mortality:

- **Overweight** patients had a **20%-40%** increase.
- **Obese** individuals had **200%-300%** increase in mortality.

Medical Complications of Obesity

- Pulmonary disease
  - abnormal function
  - obstructive sleep apnea
  - hypoventilation syndrome
- Idiopathic intracranial hypertension
- Stroke
- Cataracts
- Coronary heart disease
  - Diabetes
  - Dyslipidemia
  - Hypertension
- Severe pancreatitis
- Cancer
  - breast, uterus, cervix
  - colon, esophagus, pancreas
  - kidney, prostate
- Nonalcoholic fatty liver disease
  - steatosis
  - steatohepatitis
  - cirrhosis
- Gall bladder disease
- Gynecologic abnormalities
  - abnormal menses
  - infertility
  - polycystic ovarian syndrome
- Osteoarthritis
- Skin
- Gout
- Phlebitis
  - venous stasis
National Institutes of Health guidelines for Bariatric surgery:

- BMI is greater than 40 kg/m$^2$.

- BMI 35 kg/m$^2$ or over who have high-risk comorbidities such as heart disease, DM, hyperlipidemia, and OSA.
ה_Pin: קים מנוהים לביצוע נחותות בריאותי במבוגרים

מסרוה:

הדרת דרישות התהובה המ مجردים המ consectetur נחותות בריאותי;

كبיעת התהווה ל đaיצוד הערכה טром נחותות ומיזק לאזר נחותה;

הדרת אופני הדינון על פועל התהווה הרגאיות הבריאותיות;

كبיעת התהווה ל đaיצוד נחותות בריאותי במעון ובמקנים בכל גל 18.
החותמות מוניצפות ליתויים בבריאותיהם במגוניים מעל גל 18 נобще ליום הפרצה החודש.

40\(\text{BMI} \leq 35\)

ע"פ הפרטים הבאים הממחולות הנלויות:
- סוכרת מסוג 2
- יער לחץ דם
- מחלה לב אספומית
- דיסלפידים
- רומ נשים בשונה
- הפרעות בפיזיות משניות לכלשהונת
- ביעיות אוטורפידיות משניות לכלשהונת ומנוגנות בשתייה של פלואוריד
- אוטואוטרופית
- בכר שומני
- אורות טרוםBOVEובולי

35\(\text{BMI} > 30\)

במגונים השעורים נוחות בריאייטן קיים ובעלים בו
- בוחלים עם סוכרת מסוג 2, נשאר הסוכרת איננה מאוזנת כלשהי באנטיביוטים מספר טיפולי תרופתי
- אופטימלי.
Fig. 1. Alterations in adipose and hepatic tissue related to weight change.
The effect of liposuction on metabolic parameters:

- Visceral adipose - more metabolic activity than subcutaneous adipose tissue.

- Liposuction: no changes were observed in obesity-related metabolic derangements or proinflammatory cytokines.

Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. 
## Success Rate of Weight Loss Treatments for Morbid Obesity

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Average Weight Loss (% Total)</th>
<th>% Excess Weight Loss at Five Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>4–6%</td>
<td>0%</td>
</tr>
<tr>
<td>Diet/Behavior Modification</td>
<td>8–12%</td>
<td>1.6% (10 Years)</td>
</tr>
<tr>
<td>Drug Therapy</td>
<td>&lt; 10%</td>
<td>10%</td>
</tr>
<tr>
<td>Gastric Bypass Surgery</td>
<td>65–85%</td>
<td>Up to 100%</td>
</tr>
<tr>
<td>Laparoscopic Adjustable Gastric Banding</td>
<td>45–50%</td>
<td>56%</td>
</tr>
</tbody>
</table>
Surgical treatments for patients who are morbidly obese were pioneered as early as the 1950s
Estimated Number of Bariatric Operations Performed in the United States, 1992-2003

Bariatric operations in Israel:

2006 – 1,600 Surgeries
2010 – 5,500 Surgeries
2016 - 10,000 Surgeries
Bariatric Procedures

Adjustable Gastric Banding

Rou-X-En-Y Gastric Bypass

Sleeve Gastrectomy

Biliopancreatic Diversion and Duodenal Switch (BPD+DS)

Biliopancreatic Diversion BPD (Scopinaro)
Surgical Procedures - Current Bariatric

• **Restrictive**
  – Vertical Banded Gastroplasty - VBG, SRVG
  – Laparoscopic Adjustable Gastric Banding
  – Sleeve gastrectomy

• **Malabsorptive**
  – Laparoscopic Duodenal Switch
  – Biliopancreatic Diversion

• **Restrictive and Malabsorptive**
  – Laparoscopic Roux-en-Y Gastric Bypass
  – Omega loop gastric bypass (mini ?)
Changes in Bariatric surgery

- Increasing weight of candidates
- Lower morbidity mortality and postoperative hospital stay
- Laparoscopy
- Operations in extreme ages
- Change in the indications for operations
The bariatric population:

- Most patients undergoing bariatric surgery have some degree of hepatic steatosis:
  - 85% - 95% of morbidly obese populations seem to have NAFLD.
  - 25%-33% have NASH
  - 1%-3% will have cirrhosis incidentally found in the operating room.
Lose weight before surgery
Gut peptides:

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- Ghrelin
- GLP-1
- PYY

Gut Peptides:

- Patients who undergo RYGB have shown a marked reduction in hepatic lipid content and improved hepatic insulin sensitivity well before significant weight loss occurs.

- These benefits to the liver are directly related to gut peptides (GLP-1 and PYY).
Bariatric surgery - mechanisms:

- **Gut hormones**: 
  - ↓ Ghrelin
  - ↑ GLP-1, PPY, Oxyntomodulin
  - Enhance insulin sensitivity and decrease appetite

- **Decreases inflammation**: 
  - IL-1, IL-8, CRP, ↓ TNF-α

- **Improves dyslipidaemia**: 
  - ↓ LDL, TC, C, TRIG

- **Decreases insulin resistance**

- **Increases weight loss**

**Potential treatment of NAFLD**
The effects of bariatric surgery on NAFLD

<table>
<thead>
<tr>
<th>Study</th>
<th>Surgery</th>
<th>Total/NASH, N</th>
<th>Cirrhosis, N</th>
<th>Mean Initial BMI (± Standard Error)</th>
<th>Mean Interval to Second Biopsy (months)</th>
<th>Mean Excess Weight Loss (%)</th>
<th>Steatosis</th>
<th>Ballooning</th>
<th>Inflammation</th>
<th>Fibrosis</th>
<th>NASH Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dixon, 2004(^{73})  AGB</td>
<td>36/23</td>
<td>1</td>
<td>47 (±10.6)</td>
<td>25.6</td>
<td>52%</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>82%</td>
</tr>
<tr>
<td>Dixon et al, 2006(^{65}) AGB</td>
<td>60/30</td>
<td>2</td>
<td>45.9 (±7.4)</td>
<td>29.5</td>
<td>32%</td>
<td>↓</td>
<td>Not reported</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>80%</td>
</tr>
<tr>
<td>Mattar et al, 2005(^{61}) RYGB (41)</td>
<td>70</td>
<td>15</td>
<td>56 (±11)</td>
<td>15</td>
<td>59%</td>
<td>↓</td>
<td>Not reported</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Not reported</td>
</tr>
<tr>
<td>Mathurin et al, 2006(^{62}) BIB (71)</td>
<td>121/24</td>
<td>12</td>
<td>49 (±8)</td>
<td>12</td>
<td>19%</td>
<td>↓</td>
<td>Not reported</td>
<td>Not reported</td>
<td>↑</td>
<td>↑</td>
<td>75%</td>
</tr>
<tr>
<td>Kral et al, 2004(^{74}) BPD</td>
<td>104</td>
<td>41</td>
<td>31 (±8)</td>
<td>41</td>
<td>34%</td>
<td>↓</td>
<td>Not reported</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>Not reported</td>
</tr>
<tr>
<td>Mottin et al, 2005(^{59}) RYGB</td>
<td>90</td>
<td>10</td>
<td>46.7 (±0.88)</td>
<td>12</td>
<td>81.4%</td>
<td>↓</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Clark et al, 2005(^{60}) RYGB</td>
<td>16</td>
<td>1</td>
<td>51.1 (±6.1)</td>
<td>10</td>
<td>35.4%</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Not reported</td>
</tr>
<tr>
<td>Csendes et al, 2006(^{63}) RYGB</td>
<td>16/4</td>
<td>1</td>
<td>44.3</td>
<td>17.5</td>
<td>72%</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>100%</td>
</tr>
<tr>
<td>de Almeida et al, 2006(^{64}) RYGB</td>
<td>16</td>
<td>1</td>
<td>53.4 (±8.8)</td>
<td>23.5</td>
<td>42%</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Not reported</td>
</tr>
<tr>
<td>Barker et al, 2006(^{66}) RYGB</td>
<td>19/19</td>
<td>1</td>
<td>47 (±4.4)</td>
<td>21.4</td>
<td>52.4%</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>89%</td>
</tr>
<tr>
<td>Liu et al, 2007(^{67}) RYGB</td>
<td>39/23</td>
<td>18</td>
<td>47.7 (±6.2)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>100%</td>
</tr>
<tr>
<td>Furuya et al, 2007(^{68}) RYGB</td>
<td>18/12</td>
<td>1</td>
<td>51.7 (±7.4)</td>
<td>24</td>
<td>60%</td>
<td>↓</td>
<td>Not reported</td>
<td>↓</td>
<td>Not reported</td>
<td>↓</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Fibrosis

• Interestingly, in the study of Kral et al, bariatric surgery seemed to have differential effects, depending on the degree of baseline fibrosis.

• Patients with minimal fibrosis (stage ≤ 2) showed progressive fibrosis postoperatively, whereas those with advanced fibrosis (stage 2 ≤, including cirrhosis) showed marked regression of fibrosis after surgery.
Prospective study – clinical, metabolic and liver histology at baseline, Yr 1 and Yr 5 after bariatric surgery in 381 adult patients with severe obesity (56% Gastric Band, 21% Gastric bypass, Bilio-intestinal bypass 23%).
Conclusions

• Improvement in steatosis and ballooning occurred mainly within the first year and persisted up to 5 years.

• Fibrosis worsened at 5 years, although 95% of patients had a fibrosis score F1≥ at 5 years.)
Patients with persistent severe steatosis after surgery were found to have more insulin resistance.

Insulin resistance as the hallmark of NAFLD and if insulin resistance is still present postoperatively, it is likely that liver disease will persist as well.
Effect of Bariatric Surgery on Nonalcoholic Fatty Liver Disease: Systematic Review and Meta-Analysis

RAJASEKHHARA R. MUMMADI,^ KRISHNA S. KASTURI,^ SWAPNA CHENNAREDDYGARI,^ and GAGAN K. SOOD‡

^Internal Medicine, ‡Gastroenterology and Hepatology, University of Texas Medical Branch, Galveston, Texas

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2008;6:1396–1402
Results:

• An improvement of histopathologic features of NAFLD in more than three fourths of the patients.

• The majority of patients experience complete resolution of NAFLD after bariatric surgery, and the risk of progression of inflammatory changes and fibrosis seems to be minimal.
Summery:

• Explosive growth in obesity  
  NAFLD ↑

• NAFLD not only contributes to the development of liver-related morbidity and mortality, it is a predisposing factor for cardiovascular disease and malignancy.
Improvement in the liver histology:

- Steatosis, steatohepatitis, and fibrosis appear to improve or completely resolve in the majority of patients after bariatric surgery results in significant weight loss.

![Diagram of liver histology progression](image-url)
• The only effective treatment for NAFLD is **weight loss**.

• Sustained weight loss can be beneficial in preventing and even reversing NAFLD.

• The only effective treatment for morbid obesity is **bariatric surgery**.
The end.....
**Table 1:** Considerable studies showed that RYGB is associated with marked improvement in NAFLD.

<table>
<thead>
<tr>
<th>Study</th>
<th>Ref</th>
<th>Main outcomes</th>
<th>Type of study</th>
<th>Sample size</th>
<th>Followup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silverman et al., 1995</td>
<td>[20]</td>
<td>Improved steatosis and fibrosis</td>
<td>Retrospective cohort</td>
<td>91</td>
<td>18.4 months</td>
</tr>
<tr>
<td>Clark et al., 2005</td>
<td>[21]</td>
<td>Improved steatosis, fibrosis, and inflammation</td>
<td>Prospective cohort</td>
<td>16</td>
<td>305 ± 131 days</td>
</tr>
<tr>
<td>Mattar et al., 2005</td>
<td>[22]</td>
<td>Improved metabolic syndrome, steatosis, and fibrosis</td>
<td>Prospective cohort</td>
<td>70</td>
<td>15 ± 9 months</td>
</tr>
<tr>
<td>Mottin et al., 2005</td>
<td>[23]</td>
<td>82% improvement in liver steatosis and fibrosis not measured</td>
<td>Retrospective cohort</td>
<td>90</td>
<td>12 months</td>
</tr>
<tr>
<td>Klein et al., 2006</td>
<td>[24]</td>
<td>Decreased factors lead to liver fibrosis and inflammation</td>
<td>Prospective cohort</td>
<td>7</td>
<td>12 months</td>
</tr>
<tr>
<td>Barker et al., 2006</td>
<td>[25]</td>
<td>Improved histology of NAFLD</td>
<td>Prospective cohort</td>
<td>19</td>
<td>21.4 months</td>
</tr>
<tr>
<td>Csendes et al., 2006</td>
<td>[26]</td>
<td>Improved histology in 80%</td>
<td>Prospective cohort</td>
<td>16</td>
<td>22 months</td>
</tr>
<tr>
<td>de Almeida et al., 2006</td>
<td>[27]</td>
<td>Improved steatosis, fibrosis, and inflammation</td>
<td>Prospective cohort</td>
<td>16</td>
<td>23.5 ± 8.4 months</td>
</tr>
<tr>
<td>Furuya et al., 2007</td>
<td>[28]</td>
<td>Improved steatosis and fibrosis</td>
<td>Prospective cohort</td>
<td>18</td>
<td>24 months</td>
</tr>
<tr>
<td>Liu et al., 2007</td>
<td>[29]</td>
<td>Resolved NASH in 60%</td>
<td>Retrospective cohort</td>
<td>39</td>
<td>18 months</td>
</tr>
<tr>
<td>Weiner 2010</td>
<td>[30]</td>
<td>Complete regression of NAFLD in 83%</td>
<td>Retrospective cohort</td>
<td>116</td>
<td>18.6 ± 8.3 months</td>
</tr>
<tr>
<td>Moretto et al., 2012</td>
<td>[31]</td>
<td>Resolved fibrosis in 50%</td>
<td>Retrospective cohort</td>
<td>78</td>
<td>Unavailable</td>
</tr>
</tbody>
</table>