J Gastrointest Surg (2007) 11:1033–1038
DOI 10.1007/s11605-007-0184-1

Modified Jejunoileal Bypass Surgery with Biliary Diversion for Morbid Obesity and Changes in Liver Histology During Follow-up

Iraj Fazel · Akram Pourshams · Shahin Merat · Roya Hemayati · Masoud Sotoudeh · Reza Malekzadeh

Published online: 19 May 2007

Abstract
Background and aims Bariatric surgery is the most effective treatment for morbid obesity. The classic procedure, jejunoileal bypass, has many complications including rapid progress of liver disease. The senior author (I.F.) has developed a modification of jejunoileal bypass, which we believe overcomes many of the shortcomings of the classic procedure.
Methods Consecutive patients referring for bariatric surgery were included. A modified jejunoileal bypass in which the defunctionalized limb is eliminated by anastomosing its ends to the gall bladder and cecum was performed. Liver biopsies were taken during operation and at a mean of 16 months later. The patients were followed for 5 years.
Results Forty-three patients were enrolled. The mean value of weight and body mass index (BMI) fell from 128 kg and 46 kg/m^2 before operation to 85 kg and 31 kg/m^2 at 5 years, respectively ($p<0.001$). There was no significant change in the degree of liver steatosis and necroinflammation. The mean liver fibrosis score increased from 0.1 to 0.9 ($p=0.015$). No sign of advanced liver disease was observed during the 5-year follow-up.
Conclusion The modified jejunoileal bypass is very effective in inducing and maintaining weight loss for 5 years and does not lead to hepatic failure or rapid progression of liver disease.

Keyword Obesity · Morbid · Bariatric Surgery · Jejunoileal bypass · Fatty Liver · Liver cirrhosis

Introduction

Obesity is an important health problem whose incidence is increasing rapidly in most parts of the world. Iran is not an exception, and obesity has reached epidemic proportions with more than 25% of the population affected and over 60% overweight.[1,2]

I. Fazel (✉)
Department of Surgery, Medical School,
Shahid Beheshti University of Medical Sciences,
P.O. Box 19395/4655, Tehran, Iran
e-mail: fazel@ams.ac.ir

A. Pourshams · S. Merat · R. Hemayati · M. Sotoudeh · R. Malekzadeh
Digestive Disease Research Center,
Shariati Hospital, Medical Sciences/University of Tehran,
Tehran, Iran

But for morbid obesity, defined as body mass index (BMI) greater than 40 kg/m^2, nonsurgical treatments are rarely effective.[3] Recent studies have shown that the weight loss induced by bariatric surgery normalizes the metabolic abnormalities associated with obesity and hepatic steatosis, including hepatic insulin sensitivity, and decreases the hepatic expression of factors involved in the progression of liver disease.[4,5]

Bariatric surgical procedures can be divided into restrictive and malabsorptive procedures. Combinations of these two techniques are also commonly used. Restrictive procedures are generally simpler to perform, but their effectiveness is not as prominent or as long-lasting as malabsorptive procedures. Malabsorptive procedures are highly effective in reducing weight but carry a considerable risk of metabolic complications.[6–8] Rapid progression of liver disease and even end-stage liver disease has been reported.

The classic malabsorptive procedure is jejunoileal bypass, which is now seldom practiced. The procedure involves dividing the proximal jejunum and anastomosing the proximal end to the distal ileum. In this procedure, the

long-bypassed segment of the jejunum forms a defunctionalized limb occasionally referred to as a "blind loop". Stasis in the defunctionalized limb leads to bacterial overgrowth whose products are directly delivered to the liver via the portal vein. It is believed that this bacterial overgrowth is responsible for many of the serious metabolic complications associated with this procedure. Furthermore, the disturbance of bile metabolism and delivery of excessive bile into the colon is a cause for intractable diarrhea, which is also a frequent complication. Advanced liver disease is one of the grave complications of jejunoileal bypass and reversal of the procedure is indicated if this complication occurs.[9–11] Unfortunately, despite reversal, liver disease may persist or even continue to progress in many patients.[12,13]

There are many modifications of the classic jejunoileal bypass procedure, which attempt to reduce complications mainly by eliminating the defunctionalized limb. Here we present a new modification with a long-term follow-up of patients focusing on liver histology. In our modification, the defunctionalized limb has been eliminated and bile metabolism and recirculation has been improved by anastomosing the redundant jejunal loop between the gall bladder and cecum.

Methods

Patients

Consecutive patients referring for bariatric surgery during a 21-year period from 1982 to 2002 were included. Patients were included if they were between 10 and 65 years old, had a BMI of 35 or greater, had failed at least 6 months of nonsurgical treatment, and were committed to long-term follow-up. Exclusion criteria included active alcohol or substance abuse, advanced concomitant disease severe enough to preclude surgery, lack of support from family, psychological problems including suicidal ideation, and of course, not consenting to the procedure.

Operative Procedure

All procedures were performed by a single surgeon (I.F.). The procedure is a modified jejunoileal bypass (MJB) originally developed by one of the authors (I.F.). The entire length of the small bowel is measured and divided at two points: 15 cm distal to the Treitz ligament, and 45 cm proximal to the ileocecal valve. The bowel continuity is established with end-to-end anastomosis of the proximal 15 cm of the jejunum to the distal 45 cm of the terminal ileum. Finally, the proximal end of the bypassed segment is anastomosed to the gall bladder, and the distal end to the cecum (Fig. 1). Gall stones were removed if found. Appendectomy and liver biopsy was done in all patients.

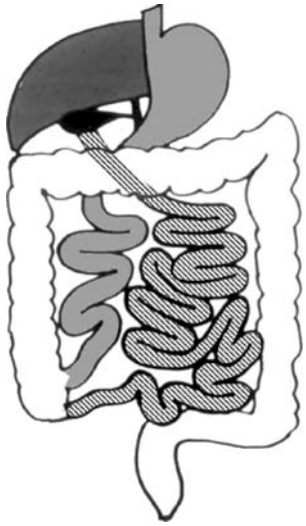

Figure 1 Anatomy of the gut after modified jejunoileal bypass.

Patient Follow-up

Patients were followed by clinical observation and detailed laboratory tests every 3 months. They all received vitamins and mineral supplements. Measurements were recorded and analyzed at post operative months 0, 3, 12, 36, and 60. A second liver biopsy was performed after 1 year or later in patients who agreed.

Pathologic Scoring of Liver Histology

The degree of necroinflammation and fibrosis was scored according to the modified hepatitis activity index (HAI) proposed by Ishak et al. in which necroinflammation is scored between 0 and 18 and hepatic fibrosis is scored between 0 and 614. The degree of steatosis was scored according to the percentage of hepatocytes having fat droplets (Table 1).

All histologic scorings were made by a single pathologist who was unaware of the clinical characteristics of the patients.

Results

Fifty-two patients referred for bariatric surgery during the study period. Nine patients chose other types of operation

Table 1 Scoring of Hepatic Steatosis

Percent of hepatocytes containing fat droplets	Steatosis score
0	0
1–25	1
26–50	2
51–75	3
76–100	4

and 43 patients underwent MJB. The initial characteristics of patients who underwent MJB are given in Table 2.

Surgical Success

One patient, the oldest one in the series, developed mechanical bowel obstruction caused by technical reasons and was reoperated. She developed renal and cardiopulmonary failure and passed away a few days after the reoperation.

Reversal of Procedure

A reversal procedure was performed on six patients (14%) during the follow-up period. One patient developed acute abdominal pain 6 months after MJB. She was found to have a 20-cm-long segmental gangrene of jejunum and as no etiology was found, the bypass was reversed. The reason for reversal in the other patients was severe uncontrollable osteomalacia in one, severe weakness without weight loss in one (in spite of parenteral vitamin supplementation), and severe continuing weight loss (protein-calorie malnutrition) in three. All patients undergoing reversal regained their preoperation weight within 6 months.

Changes in Weight and BMI

The patients were followed up for 5 years. Measurements were made at months 0, 3, 12, 36, and 60. The mean (±SD) value of weight and BMI fell from 128 (±22) kg and 46 (±7) kg/m^2 before operation to 85 (±20) kg and 31 (±7) kg/m^2, respectively, at month 60. The changes in weight and BMI are charted in Fig. 2 and Table 3. The decreases in weight and BMI were significant ($p<0.001$) at each measurement compared to the previous one. The exceptions are measurements at month 60, which show a small increase compared to month 36. This Increase is not statistically significant ($p=0.3$ for both weight and BMI).

Table 2 Initial Characteristics of 43 Patients Undergoing Modified Jejunoileal Bypass

Characteristics	Values
Age (years, mean ± SD)	35±10
Sex (M/F)	11/32
Weight (kg, mean ± SD)	128±22
Height (cm, mean ± SD)	167±8
BMI (kg/m^2, mean ± SD)	46±7
Hgb (g/dL, mean ± SD)	14.5±1.8
AST (IU/L, mean ± SD)	35±21
ALT (IU/L, mean ± SD)	34±18
Fasting blood sugar (mg/dL, mean ± SD)	120±42
Triglycerides (mg/dL, mean ± SD)	167±76
Total cholesterol (mg/dL, mean ± SD)	213±72

Preoperative Liver Histology

Needle biopsy of the liver was performed in all 43 patients undergoing MJB during the procedure. However, only 32 samples were adequate for histologic examination. Only one patient had a fibrosis score (stage) of one, all other patients were zero. There was no significant correlation between HAI and degree of steatosis.

Postoperative Liver Biopsy

Only 14 patients consented to the second liver biopsy. The second biopsy was performed at a mean of 16.0±0.5 months after operation. The fibrosis score was zero in three patients, one in 10 patients, and two in one patient.

For 13 patients, liver biopsies were available before and after operation. Among this group, the mean HAI score had changed from 2.2 to 3.3 ($p=0.37$), the mean steatosis score from 1.5 to 1.6 ($p=0.99$), and the mean fibrosis score from 0.1 to 0.9 ($p=0.015$)

Changes in Alanine Aminotransferase (ALT)

The changes in alanine aminotransferase (ALT) from operation till 60 months postop are charted in Fig. 3. Although a trend for increased ALT is seen at month 3 and thereafter a trend for decreased ALT is seen, none of these trends reach statistical significance.

Metabolic Profile

Twenty percent of patients were hyperglycemic (fetal bovine serum [FBS]>115) before operation and 5 were on oral hypoglycemic agents. All these patients had normal FBS 1 year after operation and were off oral hypoglycemic agents. Thirty percent had hyperlipidemia with elevated triglyceride (TG) and/or low-density lipoprotein (LDL) cholesterol; all showed improvement after surgery.

Clinical Follow-up

All patients who did not undergo reversal operation (36 patients) were satisfied with the operation and the degree of weight loss. The most common postoperative complains were easy fatigability and flatulence.

None of the patients developed nephrolithiasis, cololelithiasis, megaloblastic anemia, or symptoms of the “blind loop syndrome” during the 5-year follow-up.

No liver failure was observed. Prothrombin time, platelet count, and albumin levels were normal in all cases and no splenomegaly was seen. In follow-up endoscopies, no patient had esophageal varices or portal hypertensive gastropathy.

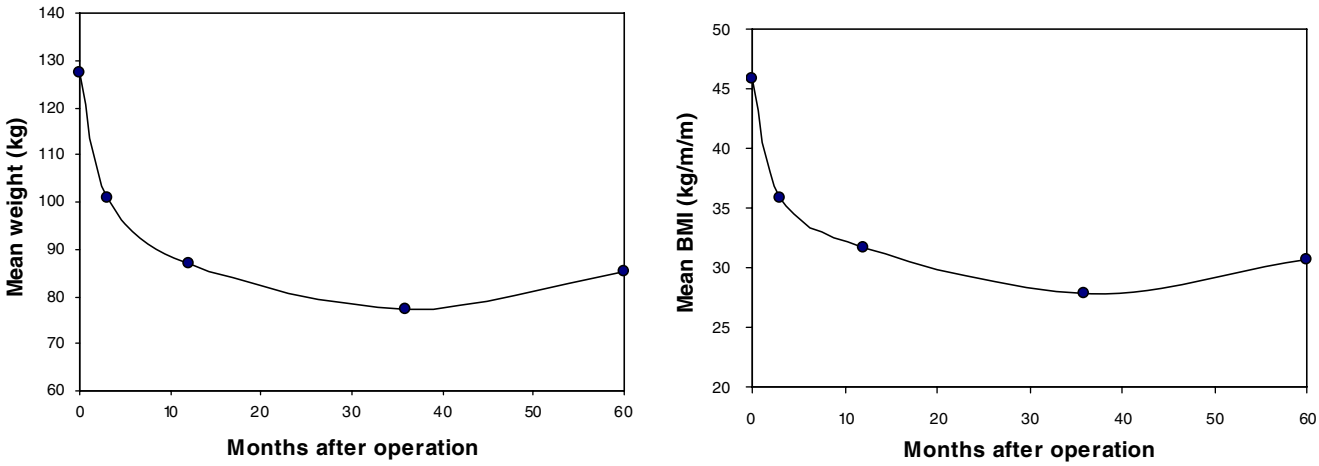

Figure 2 Changes in weight and BMI from operation till 5 years postoperation.

The mean number of bowel movements within 2 months post operation was 6.5 per day. The diarrhea was well controlled in all cases with 1–2 tablets of diphenoxylate per day. The mean number of bowel movements fell to 3–4 per day during further follow-up. Except for the patients who underwent reversal, no patient was admitted because of complications of surgery.

It is interesting to mention that two of our cases (5%) complained of constipation after the operation. They both had a preoperative history of anismus-type constipation also known as outlet obstruction constipation.

Discussion

Further progression of liver disease and even end-stage liver disease has been reported after malabsorptive bariatric surgery. There are various explanations for this finding. Rapid weight loss has always been associated with progression of steatohepatitis.[15–17] Deficiencies of protein and various nutrients such as vitamins and minerals have also been implicated. One of the widely accepted explanations is the implication of stasis and bacterial overgrowth in the defunctionalized limb produced during the operation. Many researchers believe the bacterial overgrowth results in portal endotoxinemia or endogenous ethanol production, which subsequently induces steatosis and steatohepatitis in a liver that may be sensitized by obesity.[18–20]

The classic malabsorptive procedure, jejunoileal bypass, produces a long defunctionalized limb. It is believed that stasis and bacterial overgrowth in this defunctionalized limb accounts for many serious complications seen with this procedure. There have been many modifications of this procedure to overcome this problem.[21] The biliopancreatic diversion (BPD), with or without the duodenal switch procedure, tries to overcome the defunctionalized limb problem by routing biliary and pancreatic secretions through the defunctionalized limb.[22,23] The flow of bile and pancreatic juice prevents stasis and bacterial overgrowth, but the length of intestine where bile, pancreatic juice, and food mix is very small. Thus, malabsorption of protein and lipid soluble vitamins is quite frequent.[24]

Table 3 Changes in Weight and BMI of Patients Undergoing Modified Jejunoileal Bypass

	N	Weight (kg) ± SD	BMI (kg/m^2) ± SD
Before operation	43	128±22	46±7
3 months post operation	37	101±18	36±5
12 months post operation	32	87±17	32±6
36 months post operation	36	77±14	28±5
60 months post operation	30	85±20	31±7

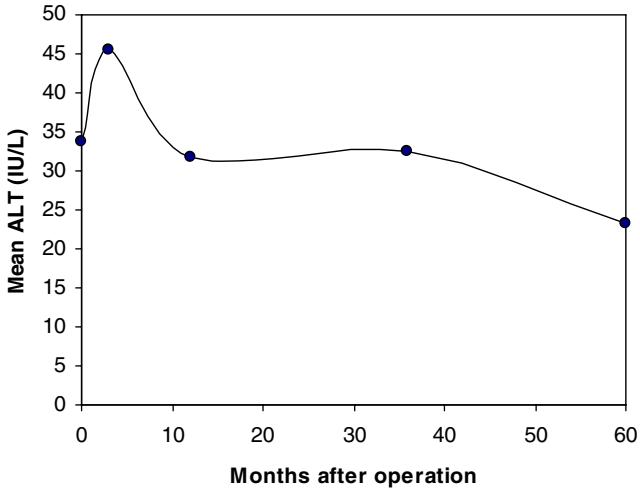

Figure 3 Changes in alanine aminotransferase (ALT) after modified jejunoileal bypass.

The modified bypass procedure we have used in this study connects the proximal end of the defunctionalized limb to the gall bladder and the distal end to the cecum. Thus, flow of bile from gall bladder to cecum through the formerly defunctionalized limb overcomes stasis. Furthermore, because of the wide opening between the gall bladder and the intestine, gall stones, common in the standard procedure, are not formed. Not all the bile secreted from the liver goes through the gall bladder and the extra loop. Some of the bile goes through the common bile duct to the duodenum and is available for the absorption of fat soluble vitamins. Furthermore, the pancreatic secretions are added to food at the normal site and are in contact with food as long as possible in the shortened intestine. The terminal ileum is preserved in the path of digested food, thus B12 deficiency and megaloblastic anemia is eliminated.

Another frequent complication observed in classic jejunoileal bypass is nephrolithiasis, which is believed to be caused by excess absorption of unbound oxalate from the gut. No case of nephrolithiasis was seen in our series. We believe that as bile metabolism and circulation is minimally disturbed in MJB, the amount of oxalurea is less marked.

The procedure is not very complicated to perform and we had only one mortality in our series (2%), which is similar to the mortality reported by others.[25]

In this study, we have shown that the MJB procedure is highly effective in reducing weight and maintaining weight loss for at least 5 years. The changes in liver histology as indicated by HAI and the steatosis score were not significant at a mean of 16 months after operation. Although the degree of fibrosis has significantly increased during this period, the magnitude of this advancement, 0.8 scores, is not large and of uncertain clinical significance. More important is the absence of rapid progression of liver disease or significant liver-related morbidity as seen in subjects undergoing classic jejunoileal bypass. Of course, longer follow-up is required to study the long-term effects on liver histology.

A similar result has been obtained by Stratopoulos et al.,[26] who studied patients losing weight after a restrictive procedure. In this study, 51 patients underwent first and second liver biopsies at an average of 18 months apart. Fibrosis improved in almost 50% of their patients, but 12% had increase in fibrosis. No patient had rapid progression of liver disease.

In a large study by Kral et al.,[27] which included 689 patients, 104 patients underwent a second liver biopsy after a mean of 41 months. Severe fibrosis (stages 3–5) decreased in 28 patients, whereas mild fibrosis (stages 1–2) appeared in 42. In general, however, the degree of fibrosis decreased over time. Even in the 11 patients having cirrhosis in the first biopsy, the fibrosis stage decreased from a mean of 5 to 3 and in seven patients cirrhotic nodules disappeared.

From our study and others it appears that some patients experience worsening of liver fibrosis by bariatric surgery. However, this worsening is generally mild and not clinically significant. In general, even severe liver disease improves. Considering the numerous improvements observed in other obesity comorbidities, the risk of mild increased fibrosis in some patients is well justified.[25]

Conclusion

The MJB is very effective in inducing sustained weight loss without causing clinically significant liver disease. We believe that many of the shortcomings and complications of classic jejunoileal bypass are overcome by this modification and MJB is a viable option for the morbidly obese patient, especially those willing to eat just as well after operation or those failing gastric bypass. Further study on this procedure is warranted.

References

1. Malekzadeh R, Mohamadnejad M, Merat S, Pourshams A, Etemadi A. Obesity pandemic: an Iranian perspective. Archives of Iranian Medicine 2005;8:1–7.
2. Bahrami H, Sadatsafavi M, Pourshams A, Kamangar F, Nouraie M, Semnani S, Brennan P, Boffetta P, Malekzadeh R. Obesity and hypertension in an Iranian cohort study; Iranian women experience higher rates of obesity and hypertension than American women. BMC Public Health 2006;6:158.
3. Lara MD, Kothari SN, Sugerman HJ. Surgical management of obesity: a review of the evidence relating to the health benefits and risks. Treatments in Endocrinol 2005;4:55–64.
4. Klein S, Mittendorfer B, Eagon JC, Patterson B, Grant L, Feirt N, Seki E, Brenner D, Korenblat K, McCrea J. Gastric bypass surgery improves metabolic and hepatic abnormalities associated with nonalcoholic fatty liver disease. Gastroenterology 2006;130:1564–1572.
5. Mottin CC, Moretto M, Padoin AV, Kupski C, Swarowsky AM, Glock L, Duval V, da Silva JB. Histological behavior of hepatic steatosis in morbidly obese patients after weight loss induced by bariatric surgery. Obes Surg 2005;15:788–793.
6. Gastrointestinal surgery for severe obesity. NIH consensus development conference, March 25–27,1991. Nutrition 1996;12:397–404.
7. Brolin RE. Update: NIH consensus conference. Gastrointestinal surgery for severe obesity. Nutrition 1996;12:403–404.
8. Schneider BE, Mun EC. Surgical management of morbid obesity. Diabetes Care 2005;28:475–480.
9. Holzbach RT. Hepatic effects of jejunoileal bypass for morbid obesity. Am J Clin Nutr 1977;30:43–52.
10. Moxley RT, III, Pozefsky T, Lockwood DH. Protein nutrition and liver disease after jejunoileal bypass for morbid obesity. N Engl J Med 1974;290:921–926.
11. Geiss DM, Shields S, Watts JD. Reversibility of hepatic failure following jejunoileal bypass. Arch Surg 1976;111:1362–1365.
12. Dean P, Joshi S, Kaminski DL. Long-term outcome of reversal of small intestinal bypass operations. Am J Surg 1990;159:118–123.
13. Styblo T, Martin S, Kaminski DL. The effects of reversal of jejunoileal bypass operations on hepatic triglyceride content and hepatic morphology. Surgery 1984;96:632–641.

14. Ishak K, Baptista A, Bianchi L, Callea F, De Groote J, Gudat F, Denk H, Desmet V, Korb G, MacSween RN. Histological grading and staging of chronic hepatitis. J Hepatol 1995;22:696–699.
15. Hamilton DL, Vest TK, Brown BS, Shah AN, Menguy RB, Chey WY. Liver injury with alcoholiclike hyalin after gastroplasty for morbid obesity. Gastroenterology 1983;85:722–726.
16. Reid AE. Nonalcoholic steatohepatitis. Gastroenterology 2001; 121:710–723.
17. Angulo P. Nonalcoholic fatty liver disease. N Engl J Med 2002; 346:1221–1231.
18. Yang SQ, Lin HZ, Lane MD, Clemens M, Diehl AM. Obesity increases sensitivity to endotoxin liver injury: Implications for the pathogenesis of steatohepatitis. Proc Natl Acad Sci USA 1997;94:2557–2562.
19. Mezey E, Imbembo AL, Potter JJ, Rent KC, Lombardo R, Holt PR. Endogenous ethanol production and hepatic disease following jejunoileal bypass for morbid obesity. Am J Clin Nutr 1975; 28:1277–1283.
20. Wigg AJ, Roberts-Thomson IC, Dymock RB, McCarthy PJ, Grose RH, Cummins AG. The role of small intestinal bacterial overgrowth, intestinal permeability, endotoxaemia, and tumour necrosis factor alpha in the pathogenesis of non-alcoholic steatohepatitis. Gut 2001;48:206–211.
21. Shaffer EA. Bariatric surgery: a promising solution for nonalcoholic steatohepatitis in the very obese. J Clin Gastroenterol 2006;40:S44–S50.
22. Scopinaro N. Biliopancreatic diversion: mechanisms of action and long-term results. Obes Surg 2006;16:683–689.
23. Hess DS, Hess DW. Biliopancreatic diversion with a duodenal switch. Obes Surg 1998;8:267–282.
24. Guedea ME, Arribas dA, Solanas JA, Marco CA, Bernado AJ, Rodrigo MA, Diago VA, Diez MM. Results of biliopancreatic diversion after five years. Obes Surg 2004;14:766–772.
25. Bouldin MJ, Ross LA, Sumrall CD, Loustalot FV, Low AK, Land KK. The effect of obesity surgery on obesity comorbidity. Am J Med Sci 2006;331:183–193.
26. Stratopoulos C, Papakonstantinou A, Terzis I, Spiliadi C, Dimitriades G, Komesidou V, Kitsanta P, Argyrakos T, Hadjiyannakis E. Changes in liver histology accompanying massive weight loss after gastroplasty for morbid obesity. Obes Surg 2005;15:1154–1160.
27. Kral JG, Thung SN, Biron S, Hould FS, Lebel S, Marceau S, Simard S, Marceau P. Effects of surgical treatment of the metabolic syndrome on liver fibrosis and cirrhosis. Surgery 2004;135:48–58.