

Histological Findings in the Liver Before and After Gastric Bypass

Attila Csendes, MD¹; Gladys Smok, MD²; Ana Maria Burgos, MD¹

¹Department of Surgery and ²Gastrointestinal Pathology, University Hospital, Santiago, Chile

Background: Bariatric surgery results in massive loss of excess weight, changes in co-morbidities and improvement in quality of life. In these patients, liver histology taken before or during surgery reveals several histological abnormalities. In a prospective study of patients previously submitted to gastric bypass, we determined the changes in liver histology late after the surgery.

Methods: In 16 out of a total of 557 patients who were submitted to open gastric bypass, a second liver biopsy was taken during the repair of an incisional hernia, performed at a mean of 17 months after the gastric bypass.

Results: All patients had lost weight, now having a mean BMI of 28.6 kg/m² (which had been 44.3 kg/m² before gastric bypass). One patient with normal pre-operative liver histology remained normal at the second study. 11 out of 15 who had had liver abnormalities returned to a normal condition or had only minimal change (73.3%). 2 patients (13.3%) showed improvement, while 1 patient presented a slight worsening of liver condition. One patient who had had liver cirrhosis showed no change.

Conclusion: Gastric bypass for morbid obesity is followed by a dramatic improvement or normalization of liver histological abnormalities in the great majority of the patients. Liver cirrhosis in the one patient remained unchanged.

Key words: Morbid obesity, gastric bypass, liver histology, hepatic steatosis

Introduction

Obesity is increasing, reaching epidemic proportions in many countries.¹ Obese patients exhibit a high incidence of co-morbidities, with non-alcoholic fatty liver disease (NAFLD) being a very common find-

ing.² The spectrum of histological changes of the liver in patients with morbid obesity can fluctuate from normal in a small proportion of patients, to different degrees of NAFLD, including non-specific inflammation and fibrosis, a condition known as non-alcoholic steatohepatitis (NASH), and even cirrhosis in 1 to 2% of the patients.³⁻¹⁴ The histologic alterations of the liver have been described in detail in several publications during the last 2 years.⁷⁻¹⁴ Gastric bypass is the most effective surgical procedure to achieve major and permanent loss of weight in these patients.¹⁵⁻¹⁸ As a consequence, the histological abnormalities of the liver could regress to a normal or close to normal condition after bariatric surgery. The purpose of the present prospective study was to determine the potential reversibility of the established liver abnormalities in a group of 16 morbidly obese patients studied during and 1 to 2 years after surgery.

Materials and Methods

Patients Studied

Since August 1999, a prospective protocol was followed for patients with morbid obesity submitted to Roux-en-Y gastric bypass with resection of the bypassed stomach.¹⁹ A total of 557 patients were included up to Dec 2004, submitting all to the open resectional gastric bypass, as described.^{19,20} In all, a liver biopsy was taken during surgery and the patients are being followed according to the protocol. Sixteen patients developed an incisional hernia after surgery and were submitted to reoperation, performing hernioplasty with a polypropylene mesh. In all these patients with prior upper midline laparotomy inci-

Reprint requests to: Attila Csendes, MD, Department of Surgery, Clinical Hospital U. of Chile, Santos Dumont 999, Santiago Chile. Fax: 56-2-7775043; e-mail: acsendes@med.uchile.cl

sions, the peritoneal cavity was open when the peritoneal sac was resected. During this procedure, a second liver biopsy was taken. Preoperative written informed consent was obtained from all patients.

Histological Evaluation

A 20 x 25 mm wedge of the liver was excised and immediately fixed in 10% formalin. The specimens were embedded in paraffin and block sections were cut at intervals of 5 mm. All sections were stained with hematoxylin and eosin, Van Gieson staining and Peris staining.

All liver samples were examined by a pathologist specialized in liver disease (G.S.) blindly, ie., without knowing to which patient the sample belonged. The parameters analyzed included the presence, severity, type and localization of fat, and the presence or absence of fibrosis and cirrhosis. The following definitions were employed, according to the histological criteria published by Brunt et al.²¹

Mild steatosis = <33% of hepatocytes with fat vacuoles.

Moderate steatosis = 33-66% of hepatocytes with fat vacuoles.

Severe steatosis = >66% of hepatocytes with fat vacuoles.

Steatohepatitis = morphological liver damage which can be seen in alcoholic or non-alcoholic liver disease (obesity, drugs, diabetes, etc.). It consists of the presence of steatosis plus hepatocellular, portal or lobar inflammation and eventual fibrosis.

Cirrhosis = regeneration nodules surrounded by fibrous tissue.

Results

Table 1 shows the main clinical features of all patients included in the present study. There were 15 women and 1 man with a mean age of 46 years. After gastric bypass and a clinical follow-up of 22 months, there was a significant decrease in BMI from 44.3 kg/m² to 28.6 kg/m² ($P < 0.001$). The excess weight loss after surgery was 72%. All had a ventral incisional hernia, which was repaired with an uneventful course in all. The histological changes of the liver biopsy sample taken during incisional

Table 1. Clinical features of patients with morbid obesity submitted to gastric bypass and liver biopsy before and after surgery (N = 16)

Age (years)	46.2 (21-65)
Gender	15 females, 1 male
BMI before operation	44.3 kg/m ² (37-60)
BMI late after operation	28.6 kg/m ² (22.5-37)
Follow-up	22 months (12-45)
Time between 1st and 2nd liver biopsy	17.5 months (9-33)

BMI = Body mass index

hernia repair compared to findings during gastric bypass are shown in Table 2. Only 1 patient (6.2%) had a normal finding before bypass and remained so late after surgery.

Of the 15 patients who had histological abnormalities before gastric bypass, in 10 patients (66.7%) the liver changes returned to normal appearance. In 2 patients (13.3%), histological abnormalities decreased in severity up to a mild condition, while in 1 patient (6.7%), mild steatosis remained similar. One patient (6.7%) showed histologic progression from mild steatosis to pericellular fibrosis. One patient had had liver cirrhosis which remained similar (6.7%) 2 years after the gastric bypass, but with disappearance of steatohepatitis.

Table 2. Histological changes of liver biopsy before and after gastric bypass

Before gastric bypass		At later operation	
Normal	1	Normal	1
Mild steatosis	7	Normal	5
		Mild steatosis	1
		Pericellular fibrosis	1
Moderate or severe steatosis	3	Normal	2
		Hepatitis without steatosis	1
Steatohepatitis	4	Normal	3
		Mild steatosis	1
Cirrhosis plus steatohepatitis	1	Cirrhosis	1

Discussion

The histological abnormalities of the liver among patients with morbid obesity at bariatric surgery are well known and described. As an example, in the last 2 years (2004 and 2005), 7 different publications have dealt with this topic. The number of patients evaluated during bariatric surgery, by taking liver samples, have varied from 24 to 1,000 patients.⁷⁻¹⁴ In these studies, the incidence of histologic liver damage in the morbidly obese patients is very high, despite acceptable liver function tests in some of the patients.⁵ However, no reliable biochemical data can identify patients with severe liver damage, to obviate the need for liver biopsy for diagnosis and staging of the disease.⁷ It has been shown that routine liver biopsy documented significant liver abnormalities compared to selective liver biopsies.⁸ Hepatic steatosis appears to be higher for males than females.⁹ The presence of NASH is highly prevalent.^{10,12-14}

Therefore, the logical step was to evaluate liver histology late after gastric bypass or any other bariatric procedures, in order to determine whether significant loss of weight is associated with signifi-

cant improvement in the pathologic appearance of the liver. The results of the present study indicate that after a rapid and considerable loss of weight as a consequence of gastric bypass, liver histological abnormalities which were present in 94% of the patients before surgery, improved significantly in 87% of the patients, reaching normal liver histology in 67% of them. It has been reported that in a small percentage of patients, the rapid loss of weight could induce the appearance of hepatitis or mild fibrosis, suggesting that this rapid fat mobilization, probably associated with inadequate protein and vitamin intake during this weight loss, could deteriorate or increase the pre-existent liver damage.²² This was not the case in our patients.

We reviewed extensively the literature concerning histological studies of the liver in patients with morbid obesity and found several papers dealing with this topic. The first studies published in the 1970s were related to the liver condition after jejunoileal bypass. Hocking et al²³ described a 7% incidence of liver cirrhosis after surgery, while Vryberg et al²⁴ reported 15% development of reversible hepatic insufficiency.

The first study after gastric bypass came from Denmark, when Ranlov and Hardt²⁵ evaluated 7

Table 3. Reported histologic findings of liver biopsy after bariatric surgery

Author	Years	N	Operative procedure	Method of post-operative liver biopsy	Postoperative histological findings
Ranlov ²⁵	1990	15	VGB – 7 RYGBP – 8	Percutaneous	Steatosis present preop 73%, postop 40%. No fibrosis.
Silverman ²⁶	1995	91	RYGBP	Laparotomy	65 patients reduced steatosis (71.4%). 18 patients no steatosis (19.8%), 5. Patients minimal steatosis (5.5%), 3. Patients increased steatosis (3.3%).
Luyckx ²²	1998	69	VGB	Laparotomy	Normal 45% (preop 13%). Steatosis 38% (preop 83%). Hepatitis 26% (preop 14%).
Mottin ²⁷	2005	90	RYGBP	Percutaneous	49 (54.4%) normal. 25 (27.8%) improved steatosis. 16 (17.8%) same degree steatosis.
Stratopoulos ²⁸	2005	51	VGB	Percutaneous	Steatosis improved in 43 (84.3%). Steatohepatitis improved in 44 (86.2%). Fibrosis improved in 24 (47%).
Csendes (present study)	2006	16	RYGBP	Laparotomy	Normal in 11 (68.7%). Improved in 4 (25%). More severe in 1 (6.2%).

VGB = vertical banded gastroplasty, RYGBP= Roux-en-Y gastric bypass, Preop = preoperative, Postop = postoperative.

patients after gastric bypass and 8 patients after gastroplasty; at liver biopsy taken 1 year after surgery (Table 3), they found a decrease of steatosis from 73 to 40%, together with a marked decrease in individual grading of fatty changes. In no case was fibrosis present. They described for the first time that these bariatric operations could reverse the liver steatosis in patients with morbid obesity.

Silverman et al²⁶ in 1995 reported liver biopsies taken in 91 patients who had previously been submitted to gastric bypass at 2 to 61 months after the surgery, comparing them to their preoperative findings. The majority had 1 postoperative biopsy, while 11 patients had 2 biopsies and 2 patients had 3 postoperative biopsies. They found that 65 patients had decreased steatosis, 23 patients had no or minimal steatosis, while 3 had patients increased steatosis. Among 13 patients with perisinusoidal fibrosis, this histological change was eliminated in 10 and reduced in 1. They concluded that most hepatic fatty changes and perisinusoidal fibrosis were reduced or eliminated following a successful gastric bypass.

Luyckx et al²² evaluated 69 patients before and 27 months after gastroplasty, with a mean decreased body weight of 32 kg after surgery. Nine patients (13%) had normal findings before surgery. After gastroplasty, in the 60 patients with prior abnormal findings, normal histology was now found in 22 (37%), which is less compared to our value of 67%. They found a significant improvement in steatosis, while a significant increase in hepatitis was noticed (from 14% to 26%). The prevalence of cirrhosis was unchanged, exactly similar to our findings.

Mottin et al²⁷ evaluated liver pathological findings among 90 patients submitted to open gastric bypass, taking percutaneous liver biopsies 1 year after operation. Before surgery, all had liver steatosis. After operation, liver histology was normal in 54% of the patients, improved in 28%, and showed a similar degree of steatosis in 18% of the patients. None showed worsening in the histology.

Stratopoulos et al²⁸ studied 51 patients before and at 8-17 months after vertical banded gastroplasty, by percutaneous liver biopsy. Steatosis and steatohepatitis improved significantly (84 and 86% respectively). Liver fibrosis improved in nearly half of the patients.

The 6 authors who evaluated liver histology after bariatric surgery (Table 3), have performed the procedure of liver biopsy by percutaneous method in 3

studies, and by laparotomy in 3 studies taking the biopsy during any upper abdominal operation that any patient underwent late after the bariatric procedure. In 4 studies, open Roux-en-Y gastric bypass and in 2 studies, vertical banded gastroplasty had been performed. All studies have shown that most histologic liver abnormalities in morbidly obese patients return to a normal condition or are reduced in severity after a successful decrease in weight after any bariatric procedure.

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