Autopsy Findings Following Gastric Bypass Surgery for Morbid Obesity

Judy Melinek, MD; Edward Livingston, MD; Galen Cortina, MD, PhD; Michael C. Fishbein, MD

● ***Background.*—Roux-en-Y gastric bypass, currently the most frequently performed surgical procedure for morbid obesity, has a low but significant mortality rate. There are limited data documenting the findings at necropsy in patients who have died following this procedure.**

***Objective.*—To determine cause of death and pathologic processes present in obese subjects dying after gastric bypass surgery.**

***Patients.*—We studied 10 patients who underwent autopsy following gastric bypass surgery for morbid obesity between the years 1994 and 2000.**

***Results.*—There were 6 men and 4 women. The mean age of the patients was 48 years (range, 28–62 years). The mean preoperative weight was 162 kg (range, 112–245 kg), and the mean body mass index was 54 kg/m² (range, 39–76 kg/m²), similar to all patients undergoing gastric bypass at our institution during the same period. Five deaths were directly attributable to technical complications. Five deaths were attributed to underlying comorbid conditions. One patient died of cirrhosis and one of pulmonary hemorrhage. Three patients died from pulmonary embolism. However, 8 of 10 patients had microscopic evidence of pulmonary emboli, despite prophylaxis for deep vein thrombosis. Most patients had some degree of steatohepatitis and hepatic fibrosis (80% and 70%, respectively). There were no deaths from primary cardiac events.**

***Conclusions.*—In patients who die after Roux-en-Y gastric bypass, half die due to technical complications, whereas the other half die of complications of their obesity. Clinically, only 20% of patients were suspected to have pulmonary emboli, yet at autopsy, 80% of patients had pulmonary emboli. In morbidly obese patients undergoing Roux-en-Y gastric bypass, there is an unexpectedly high rate of clinically silent pulmonary emboli contributing to morbidity and mortality.**

(*Arch Pathol Lab Med.* 2002;126:1091–1095)

Morbid obesity (body mass index [BMI] of more than 35 kg/m²) occurs in 2% to 5% of the population of Europe and the United States. Morbid obesity is accompanied by such attendant health risks as coronary artery disease, hypertension, diabetes, gallstones, breast cancer, degenerative arthritis, obstructive sleep apnea, and obesity hypoventilation syndrome.[1–3] Morbidly obese patients who are untreated have only a 1 in 7 chance of reaching their life expectancy. Medical management and dietary treatments have been shown to have limited long-term success, whereas surgical techniques have gained in popularity.[4,5] The surgical procedures currently available include vertical banded gastroplasty, Roux-en-Y gastric bypass (RYGB), and, most recently, laparoscopic approaches.[6] Of these, RYGB is the most frequently performed, with or without some modifications.[7] Surgical treatment, although effective, has a low but significant mortality, ranging from 1.5% to 8%.[8–10] Lethal early complications following RYGB include pulmonary embolism (PE), gastrointestinal hemorrhage, sepsis secondary to wound infections or anastomotic leaks, intra-abdominal abscess formation, small bowel obstruction, and unexplained sudden deaths in patients with increased heart mass but otherwise negative autopsy findings.[11,12] In light of the large number of patients currently undergoing RYGB, there are relatively few autopsy studies documenting the findings at autopsy in a series of patients who die after RYGB surgery for obesity.

Accepted for publication April 24, 2002.

From the Departments of Pathology and Laboratory Medicine (Drs Melinek, Cortina, and Fishbein) and General Surgery (Dr Livingston), UCLA School of Medicine, Los Angeles, Calif.

Reprints: Michael C. Fishbein, MD, Department of Pathology and Laboratory Medicine, UCLA CHS A2-179, 10833 Le Conte Ave, Los Angeles, CA 90095-1713 (e-mail: mfishbein@mednet.ucla.edu).

METHODS

The case histories and autopsy findings of 10 patients who died following gastric bypass surgery for morbid obesity between the years 1994 and 2000 were reviewed. In all cases, the medical records of the patients were reviewed for the assessment of clinically apparent premorbid conditions and the documentation of preoperative weight and BMI. Gross photographs taken at the time of autopsy were evaluated and hematoxylin-eosin–stained histologic sections from archived material were reviewed. Lung sections were reviewed for evidence of PE and pulmonary hypertension, which was graded on the following scale: 0, none; I, medial hypertrophy without intimal hyperplasia; II, medial hypertrophy with mild intimal thickening; III, severe intimal and medial thickening; and IV, plexiform lesions.[13] Liver sections were evaluated for steatosis and necroinflammatory activity. Their changes were graded as none (−), mild (+), moderate (++), or severe (+++). Masson's trichrome stains of liver sections were performed on archived blocks to stage the degree of fibrosis, which was staged as absent (−), mild perisinusoidal (+), moderate perisinusoidal with periportal fibrosis (++), severe perisinusoidal and periportal fibrosis with extensive bridging (+++), and cirrhosis (++++).[14]

RESULTS

In our institution, 1067 patients underwent a gastric bypass procedure between December 1993 and July 2000.[15,16]

Table 1. Case Summaries*

Patient No.	Sex	Age, y	Survival, d	Surgery	Weight, kg	BMI, kg/m²	Cause of Death
1	M	43	3	RYGB	223	66.4	Pulmonary embolism
2	M	43	6	RYGB	140	54.5	Anastomotic dehiscence
3	M	48	12	RYGB	245	75.7	Pulmonary hemorrhage secondary to pulmonary hypertension
4	F	59	14	RYGB	134	47.7	Small bowel necrosis
5	F	44	15	RYGB	112†	38.8†	Pulmonary embolism
6	F	47	17	RYGB	147	50.2	Pulmonary embolism
7	F	28	34	RYGB	146	53.5	Intraoperative injury to hepatic artery
8	M	62	69	RYGB	165	51.9	Wound dehiscence with enterocutaneous fistula
9	M	51	211	Laparoscopic RYGB, then open	166	56.0	Small bowel necrosis
10	M	51	858	RYGB	142	43.4	Cirrhosis

* BMI indicates body mass index; RYGB, Roux-en-Y gastric bypass. The patients' mean age was 48 years, mean days of survival was 124, mean weight was 162 kg, and mean BMI was 54.0 kg/m².

† At autopsy.

The rate of major complications was 5.8% and the mortality rate was 1.3%, representing 14 deaths. During the same period, we performed 10 autopsies of patients who underwent gastric bypass surgery for morbid obesity (Table 1). There were 6 men and 4 women operated on from March 28, 1994 to August 24, 2000. Their mean age was 48 years (range, 28–62 years). The mean weight at the time of surgery was 162 kg (range, 112–245 kg), and the mean BMI was calculated as 54 kg/m² (range, 39–76 kg/m²). The heaviest patient (patient 3) weighed 318 kg on admission and had massive edema. He was treated with diuretics to a preoperative dry weight of 245 kg. The average weight and BMI of the group that underwent autopsy (162 kg and 54 kg/m², respectively) were similar to the average weight and BMI of all patients undergoing gastric bypass at our institution.

Seven of 10 patients who underwent autopsy had gastric bypass operations performed at our institution; 3 were hospitalized at our institution after surgery performed at other institutions. At UCLA, the stomach is stapled, not divided, to create a 30-cm³ proximal gastric pouch. The jejunum is divided 30 cm distal to the ligament of Treitz, and the distal cut end is connected to the pouch, side to side, to create a 1.0-cm anastomosis. Forming a side-to-side jejunostomy 40 to 75 cm distal to the gastrojejunostomy completes the procedure. Nine surgical procedures were open RYGB. One procedure (case 9) was begun as a laparoscopic RYGB but was converted to an open laparotomy because of difficulties with the jejunostomy anastomosis and mesenteric foreshortening. Postoperative deaths occurred in a range of 3 to 858 days. We defined early death as within 1 month or during initial hospitalization for surgery; there were 7 early and 3 late deaths. The first postoperative death occurred suddenly from a massive PE on the third postoperative day (case 1); the last survivor, who was found to have cirrhosis at the time of RYGB, died of complications from end-stage liver disease more than 2 years later.

Technical complications are summarized in Table 2. Operative complications were the ultimate cause of death in 3 early and 2 late deaths (Figure, A and B). Complications occurred in 2 other patients, but were not considered to be the cause of death. There were no intraoperative hemorrhagic complications in any of the patients.

Five deaths were attributable to the patients' underlying comorbid condition. There was one death (case 3) from pulmonary hemorrhage secondary to severe pulmonary hypertension (Figure, C through E). There was one late death due to cirrhosis (case 10). There were 3 deaths from PE 3, 15, and 17 days after surgery. However, PE was a cause of death only in the early postoperative period (<17 days). Although only 3 deaths were due to PE, there was microscopic evidence of PE in 8 of 10 cases, with both recent and remote evidence of pulmonary infarction (Table 3). Two patients (cases 7 and 10) had had placement of inferior vena cava filters, which were found properly positioned at autopsy but were covered with thrombi. Those 2 patients both had evidence of remote and recent PE. However, in neither case was PE considered to be the cause of death.

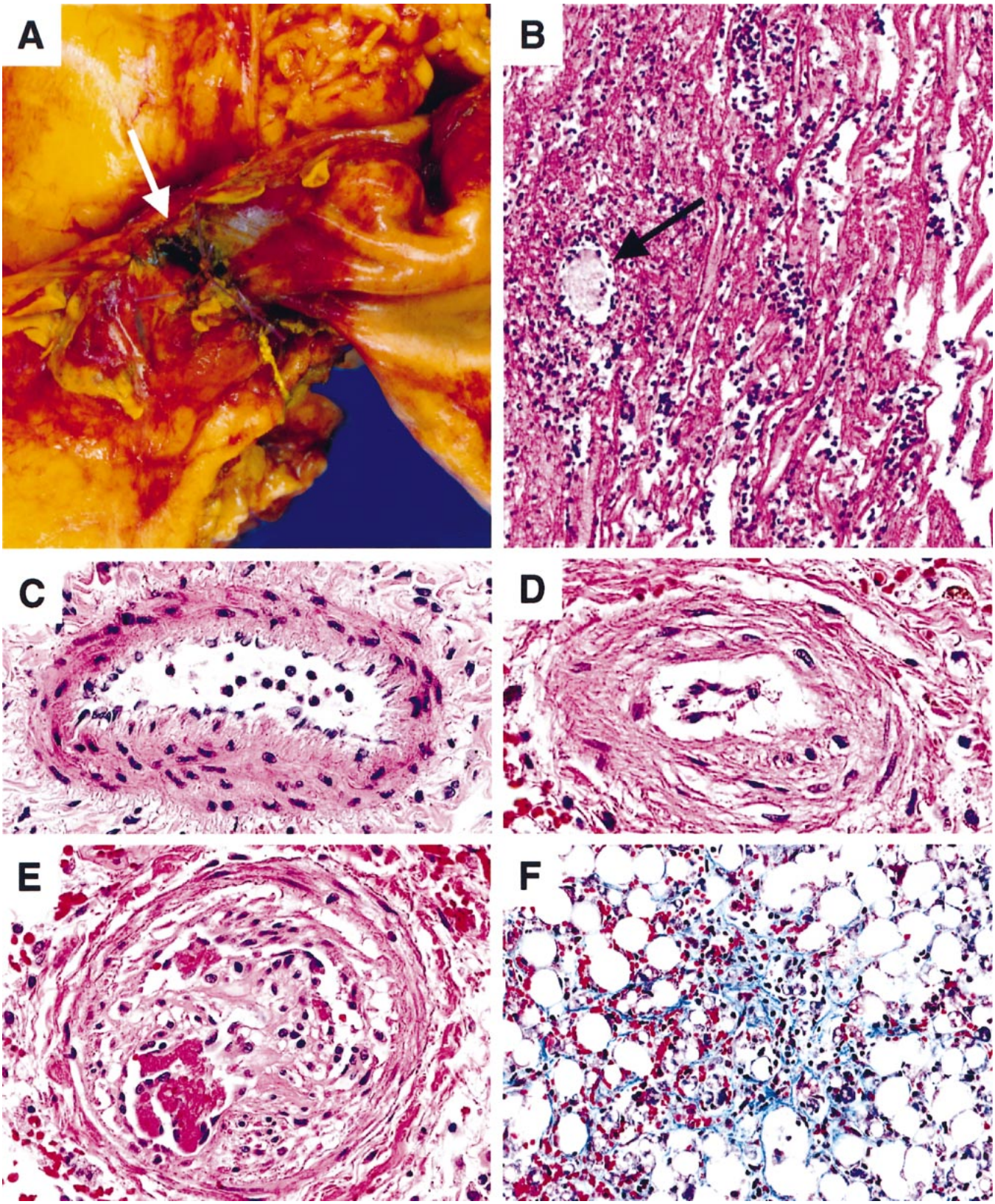
Table 2. Postoperative Complications

Patient No.	Complication	Sequelae of Complication
2	Anastomotic leak	Peritonitis, sepsis, death
3	Wound infection	. . .
4	Jejunal necrosis	Peritonitis, sepsis, death
6	Intestinal obstruction	. . .
7	Hepatic artery ligation	Massive hepatic necrosis, death
8	Wound dehiscence	Enterocutaneous fistula, death
9	Mesenteric vein thrombosis	Intestinal necrosis, sepsis, death

Five patients had histologic evidence of pulmonary hypertension. Two patients showed minimal changes consisting of medial hypertrophy without intimal thickening, 1 patient had vessels with both medial hypertrophy and mild intimal hyperplasia, and 2 patients had more severe intimal proliferation. Plexiform lesions were not observed.

There were no deaths from myocardial infarction. Surprisingly, no patients had occlusive coronary atherosclerosis. Myocardial necrosis, secondary to hypoxia, was found in 2 patients, but in neither case was this considered the cause of death.

When heart weight at autopsy was compared with expected heart weight normalized for height,[17] 9 of 10 patients had cardiomegaly and 5 had concentric left ventricular hypertrophy (wall thickness, >1.5 cm). Despite the pulmonary vascular changes observed, right ventricular



A and B, Surgical leak identified at autopsy. A, Gross photograph taken at autopsy demonstrates defect (arrow) with associated peritonitis on the adjacent serosal surface (discolored region). B, Microscopic sections demonstrate severe necrotizing peritonitis (hematoxylin-eosin, original magnification ×80). Bowel content (arrow) is present. C and D, Pulmonary hypertension in morbidly obese patients following gastric bypass. C, Mild histologic changes are characterized by medial hypertrophy without intimal thickening. D, In the patient who died from pulmonary hemorrhage, severe intimal and medial thickening are observed. E, Subclinical pulmonary embolism with recanalization (C, D, and E, hematoxylin-eosin, original magnification ×160). F, Severe steatohepatitis in morbid obesity. Masson's trichrome stain highlights perisinusoidal spidery fibrosis (original magnification ×80).

Table 3. Autopsy Findings*

Patient No.	Lung: Pulmonary Hypertension	Lung: Pulmonary Embolism	Liver: Steatosis Grade‡	Liver: Fibrosis Stage§	Heart: Weight (g) vs (Expected)†	Heart: LVW, cm	Heart: RVW, cm	Heart: CAD
1	II	+	++	++	465 (346 ± 40)	2.2	0.4	Mild
2	−	+	+++	+++	450 (302 ± 40)	1.4	0.4	None
3	III	+	+	+++	1100 (340 ± 40)	0.8	0.5	Moderate/Ca^{2+}
4	III	−	++	+	520 (277 ± 30)	1.5	0.4	Moderate/Ca^{2+}
5	−	+	++	−	370 (281 ± 30)	1.0	0.3	Mild
6	−	+	+	+	430 (283 ± 30)	1.7	0.5	None
7	−	+	++‖	−‖	370 (272 ± 30)	1.8	0.9	None
8	I	+	+	−	600 (336 ± 40)	1.8	0.3	Moderate/Ca^{2+}
9	−	−	+++	+++	650 (325 ± 40)	1.7	0.8	Mild
10	I	+	−	++++	320 (342 ± 40)	1.5	0.3	Mild

* LVW indicates left ventricular wall thickness; RVW, right ventricular wall thickness; and CAD, coronary artery disease.
† Calculated as 1.9 × height in centimeters − 2.1 ± 40 for men and 1.78 × height in centimeters − 21.58 ± 30 for women.[16]
‡ −, none; +, mild; ++, moderate; and +++, severe.
§ −, absent; +, mild perisinusoidal; ++, moderate perisinusoidal with periportal fibrosis; +++, severe perisinusoidal and periportal fibrosis with extensive bridging; and ++++, cirrhosis.
‖ Evaluation of native liver from surgical specimen; liver at autopsy was a transplant.

hypertrophy (wall thickness, >0.4 cm) was noted in only 2 patients.

At autopsy, 7 of 9 patients had hepatomegaly and 8 of 9 had steatosis (Figure, F). The patient who underwent transplantation for hepatic artery injury also had mild steatosis of the explanted native liver. Hepatic fibrosis was present in 7 patients, with one case demonstrating mixed micronodular and macronodular cirrhosis without steatosis. In life, this patient had known steatohepatitis with bridging fibrosis and a long history of alcohol abuse.

Significant weight loss was seen in the long-term survivors and was proportional to length of survival. One patient (case 9), who survived 211 days, had a total loss of 41 kg, but this was associated with malabsorption and total parenteral nutrition dependence secondary to the extensive bowel infarction, necessitating resection. The patient surviving the longest (patient 10), who survived for 2 years after his operation, lost 82 kg and was cachectic and weighed 60 kg when he died of cirrhosis.

COMMENT

At our institution, 1067 patients underwent a gastric bypass procedure between December 1993 and July 2000. The mortality rate was 1.3%, representing 14 patients, half of whom underwent autopsies. Three additional autopsies were performed on patients who had had their surgical bypass performed at other institutions. In the series studied by Livingston et al,[15,16] risk factors for major complications or deaths included male sex and preoperative weight. Indeed, in the 10 autopsies performed at our institution during the same period, there were more men than women who underwent autopsy, although women were more likely to undergo the procedure than men (78% women vs 22% men). In the subset of patients who underwent autopsy in our study, the average weight and BMI of the group who underwent autopsy (162 kg and 54 kg/m^2, respectively) were similar to the average weight and BMI of all patients undergoing gastric bypass at our institution. Since only half of the patients who died at our institution underwent autopsy (7/14) and since the total number of cases is small, our autopsy series may not be representative of all patients who die after RYGB.

In 8 of 10 patients at autopsy, PE was not detected during life, despite a clinical suspicion of PE. Two of the 10 patients had sufficient clinical evidence of PE to warrant placement of inferior vena cava filters before their deaths. The increased incidence of thrombosis in morbidly obese patients has been attributed to dysregulation of proteins involved in the coagulation and fibrinolytic pathways. Plasminogen activator inhibitor 1, adipsin (complement D), adipocyte complement–related protein (Acrp30), and adiponectin are secreted by adipocytes and have all been implicated in contributing to this increased risk.[18] A previous study[19] has indicated that the autopsy incidence of all unsuspected acute PE in critically ill surgical patients is 9.9%. Interestingly, in that study, there was no relationship between the occurrence of PE and obesity. Many of the patients in that study had known derangements in coagulation parameters due to their underlying illnesses. Our findings reinforce the importance of prophylactic anticoagulation of these high-risk patients and that physicians should have a low threshold of suspicion for PE in the postoperative gastric bypass patient.[20]

The microscopic changes of pulmonary hypertension, evident in many of these patients, have been previously described in the autopsy findings of obese patients with sleep apnea or obesity hypoventilation syndrome.[21] In the study by Ahmed et al,[21] most patients died from biventricular cardiac failure. In our series, moderate coronary atherosclerosis with calcification was not uncommon, but there were no patients with severe occlusive coronary atherosclerosis and none of our postsurgical patients died from primary cardiac events, perhaps related to the relatively young age of the patients.

Nonalcoholic steatohepatitis has been attributed to morbid obesity, rapid and profound weight loss in obese subjects, total parenteral nutrition, industrial toxins, poorly controlled diabetes, medications, metabolic disorders (Wilson disease), and unknown causes.[22] At autopsy, steatohepatitis has been reported in 18.5% of markedly obese patients, with accompanying fibrosis seen in 13.8%.[23] A prospective study[24] has shown that in patients undergoing gastric bypass procedures, 36% have some degree of steatohepatitis. The severity of histopathologic abnormalities of the liver correlates with the degree of impaired glycemic status. In our study, steatohepatitis and fibrosis were found in most patients (80% and 70%, respectively). Surveyed surgeons believe that gastric bypass can be per-

formed safely in patients with chronic liver disease.[25] Progression of steatohepatitis and eventual death from hepatic failure were commonly described complications of jejunoileal bypass.[26,27] In contrast, regression of steatosis and some resolution of perisinusoidal fibrosis have been reported following RYGB and gastroplasty procedures.[28,29] In this study, we report only one late death from cirrhosis 2 years after gastric bypass; of note, the patient was cirrhotic at the time of his original surgery.

Gastric bypass surgery for morbid obesity achieves long-term weight reduction of 50% or more of excess body weight in approximately 60% of patients at 5 years.[30] Weight loss has been maintained for periods as long as 10 to 15 years after surgery, with patients showing concomitant improvements in hypertension, diabetes mellitus, sleep apnea, and overall well-being.[31,32] Because of its effectiveness and safety, gastric bypass surgery has had considerable exposure in the mainstream media, resulting in an increased demand for the procedure, which is currently performed in many surgery centers and community practices.[33–35] Although mortality rates after RYGB are low, because so many procedures are being performed, some patients will die after this procedure. Delineation and understanding of the pathologic findings in patients who die after such procedures may help to further reduce the mortality rate in these patients.

We acknowledge Andrew Feda for his reference work and data collection. We also recognize the expert secretarial assistance and word processing skills of Ms Judy Wiltz and the photographic expertise of Ms Carol Appleton.

This study was supported in part by the Piansky Family Trust (Dr Fishbein).

References

1. Abram S, Johnson C. Prevalence of severe obesity in adults in the United States. *Am J Clin Nutr.* 1980;33:364–369.
2. Seidell JC. Obesity in Europe: scaling an epidemic. *Int J Obes.* 1995; 19(suppl 3):S1–S4.
3. Seidell JC. The impact of obesity on health status: some implications for health care costs. *Int J Obes.* 1995;19(suppl 6):S13–S16.
4. Consensus Development Conference Statement: gastrointestinal surgery for severe obesity. *Ann Intern Med.* 1991;115:956.
5. Brolin RE. Update: NIH consensus conference: gastrointestinal surgery for severe obesity. *Nutrition.* 1996;12:403–404.
6. Fielding GA, Rhodes M, Nathanson LK. Laparoscopic gastric banding for morbid obesity: surgical outcome in 335 cases. *Surg Endosc.* 1999;13:550–554.
7. Nguyen NT, Ho HS, Palmer LS, Wolfe BM. A comparison study of laparoscopic versus open gastric bypass for morbid obesity. *J Am Coll Surg.* 2000;191: 149–155.
8. Sjostrom LV. Mortality of severely obese subjects. *Am J Clin Nutr.* 1992;55(2 suppl):516S–523S.
9. Sagar PM. Surgical treatment of morbid obesity. *Br J Surg.* 1995;82:732–739.
10. Pories WJ, Swanson MS, MacDonald KG, et al. Who would have thought it? an operation proves to be the most effective therapy for adult onset diabetes. *Ann Surg.* 1995;222:339–352.
11. Fobi MAL, Lee H, Holness R, Cabinda DG. Gastric bypass operation for obesity. *World J Surg.* 1998;22:925–935.
12. Drenick EJ, Fisler JS. Sudden cardiac arrest in morbidly obese surgical patients unexplained after autopsy. *Am J Surg.* 1992;155:720–726.
13. Katzenstein ALA. Pulmonary hypertension and other vascular disorders. In: *Katzenstein and Askin's Surgical Pathology of Non-neoplastic Lung Disease.* 3rd ed. Philadelphia, Pa: WB Saunders; 1997:332–360.
14. Brunt EM, Janney CG, Di Bisceglie AM, Neuschwander-Tetri BA, Bacon BR. Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. *Am J Gastroenterol.* 1999;94:2467–2474.
15. Huerta S, Lee S, Heber D, Livingston EH. Risk assessment for major complications of gastric bypass surgery. *Gastroenterology.* 2001;120:A487.
16. Livingston EH, Huerta S, Arthur D, Lee S, DeShields S, Heber D. Male gender is a predictor of morbidity and age a predictor of mortality for patients undergoing gastric bypass surgery. *Ann Surg.* In press.
17. Zeek PM. The weight of the normal human heart. *Arch Pathol.* 1942;34: 820–832.
18. Ahima RS, Flier JS. Adipose tissue as an endocrine organ. *Trends Endocrinol Metab.* 2000;11:327–332.
19. Cullen DJ, Nemeskal AR. The autopsy incidence of acute pulmonary embolism in critically ill surgical patients. *Intensive Care Med.* 1986;12:399–403.
20. Eriksson S, Backman L, Ljungstrom KG. The incidence of clinical postoperative thrombosis after gastric surgery for obesity during 16 years. *Obes Surg.* 1997;7:332–335.
21. Ahmed Q, Chung-Park M, Tomashefski JF. Cardiopulmonary pathology in patients with sleep apnea/obesity hypoventilation syndrome. *Hum Pathol.* 1997; 28:264–269.
22. Chitturi S, Farrell GC. Etiopathogenesis of nonalcoholic steatohepatitis. *Semin Liver Dis.* 2001;21:27–41.
23. Wanless IR, Lenz JS. Fatty liver hepatitis (steatohepatitis) and obesity: an autopsy study with analysis of risk factors. *Hepatology.* 1990;12:1106–1110.
24. Silverman JF, O'Brien KF, Long S, et al. Liver pathology in morbidly obese patients with and without diabetes. *Am J Gastroenterol.* 1990;85:1349–1355.
25. Brolin RE, Bradley LJ, Taliwal RV. Unsuspected cirrhosis discovered during elective obesity operations. *Arch Surg.* 1998;144:84–88.
26. Rucker RD, Chan EK, Horstman J, Chute EP, Varco RL, Buchwald H. Searching for the best weight reduction operation. *Surgery.* 1984;96:624–631.
27. Griffen WO, Young VL, Stevenson CC. A prospective comparison of gastric and jejunoileal bypass procedures for morbid obesity. *Ann Surg.* 1977;186:500–509.
28. Ranlov I, Hardt F. Regression of liver steatosis following gastroplasty or gastric bypass for morbid obesity. *Digestion.* 1990;47:208–214.
29. Silverman EM, Sapala JA, Appelman HD. Regression of hepatic steatosis in morbidly obese persons after gastric bypass. *Am J Clin Pathol.* 1995;104:23–31.
30. Deitel M. Overview of operations for morbid obesity. *World J Surg.* 1998; 22:913–918.
31. Kolanowski J. Surgical treatment for morbid obesity. *Br Med Bull.* 1997; 53:433–444.
32. Choban PS, Onyejekwe J, Burge JC, Flancbaum L. A health status assessment of the impact of weight loss following Roux-en-y gastric bypass for clinically severe obesity. *J Am Coll Surg.* 1999;188:491–497.
33. Grady D. Exchanging obesity's risks for surgery's. *New York Times.* October 12, 2000;sect A:1-9.
34. Rabkin RA. Distal gastric bypass/duodenal switch procedure, Roux-en-Y gastric bypass and biliopancreatic diversion in a community practice. *Obes Surg.* 1998;8:53–59.
35. Deitel M, Shahi B. Morbid obesity: selection of patients for surgery. *J Am Coll Nutr.* 1992;111:457–462.