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## Gastrointestinal Complications of Hepatic Transplantation

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**I**N THE largest series of orthotopic liver transplants, now numbering 150 patients, the largest number of major complications have arisen in the gastrointestinal (GI) tract. Of these, hepatic complications comprise the majority, and they have been previously described by both leading centers.<sup>1,2</sup> A smaller number of complications have arisen elsewhere in the gastrointestinal tract, but because of their alarming mortality, they have depressed the otherwise improving picture of hepatic transplantation.

### CLINICAL MATERIAL

Gastrointestinal complications occurring in this series of hepatic transplants include bleeding from both upper and lower GI tracts, perforations and fistula, and abdominal abscesses. Many of these complications have previously been described in renal transplantation.<sup>3-6</sup> Problems with biliary drainage have arisen both in the transplant, as has been described, and also in the gastrointestinal tract where biliary-enteric continuity is reestablished. Enteric leaks at this site constitute one group of gastrointestinal complications unique to hepatic transplantation. The colon complications also appear distinct from those encountered in renal transplantation and have occurred in a much younger age group.<sup>7</sup> Abdominal abscesses have been related to a variety of causes, and wide peritoneal drainage is advocated.

### Hemorrhage

Gastrointestinal bleeding has been one of the more frequent complications following liver transplantation. Relatively small enteric bleeds chemically detectable in stools or gastric aspirate occur in the majority of transplant recipients. Clinically significant hemorrhage occurred in 34/150 patients (23%). In 12 of these 34 patients, definitive therapy

was withheld because bleeding was felt to be only one factor in an otherwise terminal patient. The remaining 22 patients all required surgical intervention for enteric bleeding. Of these, only 5 ultimately survived this complication.

Peptic ulcer disease was the most frequent etiology of gastrointestinal bleeding (Table 1). Duodenal ulcers occurred in five patients, of which two survived this complication. One survivor responded to vagotomy and gastroenterostomy, while the other required first a vagotomy and pyloroplasty followed by antrectomy. Gastroenterostomy or resection alone were not successful. Two patients developed gastric ulcers. One patient with high fundal ulcers required subtotal gastrectomy for ulcer resection and survived. The other patient underwent vagotomy and gastroenterostomy but the bleeding site was not recognized. The 12 patients with untreated terminal enteric bleeds all demonstrated peptic ulcer disease. Gastric ulcer was most frequent, followed by gastritis and duodenal ulcer. Various types of gastric lavage were employed without benefit.

Nonpeptic upper gastrointestinal bleeding arose in a variety of cases (Table 2). Four patients bled from esophageal varices. While varices persist endoscopically following he-

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**Table 1. Upper Gastrointestinal Bleeding: Peptic Disease**

Etiology	Therapy	Number
Duodenal ulcer	Vagotomy and gastroenterostomy	1 (s)
	Vagotomy and pyloroplasty	3 (s)
	Gastric resection	2 (s)
	Gastroenterostomy only	1
Gastric ulcer	Subtotal gastrectomy	1 (s)
	Vagotomy and gastroenterostomy	
Terminal peptic bleed	No therapy	12

(s). Successful therapy.

patric transplantation, they do not bleed in the absence of portal-vein thrombosis. All four patients with variceal bleeding demonstrated either thrombosis or cavernous transformation of the portal vein. The Sengstaken-Blakemore tube was used in all four patients with temporary success. One patient went on to sclerotherapy of his varices, but again bled several days later, requiring ligation of varices. This operative ligation appeared unduly treacherous because of the recent sclerotherapy, the esophagus being edematous and friable.

The enteroenterostomy of the Roux-en-Y jejunostomy was the site of bleeding in two patients. In neither patient was it identified clinically. One patient underwent pyloroplasty before the enteroenterostomy was opened and the bleeding site ligated. The other patient had both an abscess and bleeding from the enteroenterostomy, which was

discovered at autopsy. There were individual cases of bleeding from operative trauma to the small bowel, small bowel ulcers, disruption of a duodenostomy closure, and cystic artery bleeding at the gallbladder anastomosis.

Lower gastrointestinal bleeding was sometimes difficult to distinguish clinically from duodenal bleeding (Table 3). Three patients had ulcerations in the right colon and underwent either right or subtotal colectomy. None survived. Two patients had massive colonic bleeds from pneumatosis cystoides intestinalis involving the colon. Both survived following subtotal colectomies.

Gastrointestinal bleeding has arisen at intervals of several days to over a year post-transplant. Frequently, small enteric bleeds occur during this interval, and because these bleeds may be the prelude to a later hemodynamically significant bleed, vigorous diagnos-

**Table 2. Upper Gastrointestinal Bleeding: Nonpeptic Disease**

Etiology	Therapy	Number
Esophageal varices	Sengstaken-Blakemore	4
	Sclerotherapy	1
	Oversew	1 (s)
Enteroenterostomy (Roux-en-Y)	Repair	2 (s)
Small bowel	Resection	1
	Pyloroplasty	1
Disrupted duodenal closure	Repair	1
Gallbladder (cystic artery bleed)	Repair	1

(s). Successful therapy.

**Table 3. Lower Gastrointestinal Bleeding**

Etiology	Therapy	Number
Cecal ulceration		3
	Right colectomy	2
	Ileoproctostomy	1
Pneumatosis Cystoides		2
Intestinales	Ileoproctostomy	2 (s)

(s). Successful therapy.

tic maneuvers are indicated. Vital signs, hemoglobin levels, and overt and occult enteric blood loss are carefully monitored. Panendoscopy has been crucial in all bleeding episodes regardless of how minor they appear. Colonoscopy has been used but has not had a direct therapeutic benefit. Proctoscopy is useful, as anal disease is quite frequent, and the bleeding site sometimes is obscure even at surgery. Radiographic studies have been helpful in minor bleeding, but in the major bleeds included here, hemodynamic instability precluded this delay.

### Perforation

Gastrointestinal perforations and fistulas were less frequent but even more lethal complications than bleeding. The preponderance of leaks were secondary to the establishment of biliary drainage. In the 150 patients in this series, 198 biliary procedures have been performed. Choledochocholedochostomy obviates the need for entry into the gastrointestinal tract and thus eliminates enteric leaks from biliary drainage. This has been used in 33 patients and is our preference for adults with suitable ducts. Cholecystoduodenostomy was the earliest drainage technique and has a low incidence of leakage (8%), but was abandoned for other reasons (Table 4). The majority of the 14 choledochoduodenostomies were conversions from previous cholecystoduodenostomies. The incidence of leakage in choledochoduodenostomies was an unacceptable 43%, but responsibility must rest primarily on the "failed" cholecystoduodenostomies. The combination of a biliary leak and high enteric fistula was lethal in all patients. Surgery was directed at providing

**Table 4. Enteric Leaks Secondary to Biliary Drainage**

Etiology	No Leaks (No. Procedures)
Cholecystoduodenostomy	5 (65)
Choledochoduodenostomy	6 (14)
Roux-en-Y jejunostomy (at new enteroenterostomy)	8 (48)
Roux-en-Y jejunostomy (at choledochojejunostomy)	1 (26)

alternative biliary drainage and either draining or closing the duodenum.

Currently, when choledochocholedochostomy is not feasible, Roux-en-Y jejunostomy to either gallbladder or common duct is preferred. Enteric leaks have arisen at the enteroenterostomy in 17% of the newly constructed Roux-en-Y jejunostomies. Leaking enteroenterostomies have been corrected by reinforcing small leaks or reconstructing the anastomosis. Of these eight repairs, two needed revision. One reinforced leak disrupted, requiring reconstruction of the enteroenterostomy. The other, also a reinforced leak, developed a second leak at a separate site that had not appeared compromised at the previous laparotomy. This site was successfully reinforced. While leaks at the enteroenterostomy may occur at any time up to 4 weeks, once this anastomosis has healed, the roux limb biliary drainage may be safely revised at the free end if necessary. The existence of a preexisting Roux-en-Y jejunostomy is thus regarded as an asset among potential transplant recipients. Like the duodenal fistulas, these enteroenterostomy leaks have been highly lethal with only one survivor among eight leaks.

Unfortunately, the existence of a previous Roux-en-Y jejunostomy implies previous hepatic surgery. Previous Roux-en-Ys have been injured three times during particularly difficult hepatectomies resulting in fistulas (Table 5). These have not been difficult to manage if well drained, and one patient has survived this complication. Other segments of bowel injured during hepatectomy that developed fistulas are duodenum, one patient; ileum, one patient; colon, two patients. All

**Table 5. Enteric Leaks Independent of Biliary Drainage**

Etiology	Number
Operative trauma to preexisting Roux-en-Y	3
Operative trauma to ileum	1
Operative trauma to duodenum	1
Operative trauma to colon	2
Duodenal "blow-out" after Bilroth II	1

were recognized and initially repaired at transplant except for the ileal injury, which was probably related to the use of electrocautery. None of these patients survived. One duodenal stump "blew out" following a Bilroth II in the postoperative period. Open drainage permitted this to mature into an end-duodenal fistula, and the patient survived.

Enteric leaks, because of immunosuppression, have sometimes been rather subtle. Free air, when present on a roentgenogram, has been diagnostic. Other times, clinical condition and abdominal signs may provide the only clue. The threshold for laparotomy, particularly in difficult donor hepatectomies and recent biliary-enteric anastomoses, must remain low. When a suppurative process is encountered in the abdomen, biliary drainage must be maintained or reestablished if it is in jeopardy and the primary process well drained.

#### *Pancreatitis*

While mild edematous pancreatitis has been a frequent autopsy finding, only two patients have developed hemorrhagic pancreatitis. One patient with an extensive resection of a hepatoma involving a portion of the distal stomach and pylorus at the time of transplant developed hemorrhagic pancreatitis. Resection of the pancreatic body and tail were followed shortly by her death. The other case of hemorrhagic pancreatitis was not detected clinically but was an autopsy finding.

#### *Abscess*

With the mortality of enteric fistulas and abdominal abscesses unacceptably high, con-

**Table 6. Open-Wound Management**

Etiology	Number
Fistula secondary to biliary drainage	
Combined biliary-enteric fistula	5
Biliary fistula only (choledochocholedochostomy)	3
Abdominal abscess	
Primary drainage of abscess	3
Abscess drainage at biliary revision	2
Abscess drainage at retransplant	1
Hepatic necrosis	1
Open management for incomplete hemostasis	
Splenic vein rupture	1
50% pancreatectomy	1

ventional methods of limited drainage have proven inadequate. Complete open drainage of the entire abdominal wound has permitted frequent thorough irrigation and dressing changes. By this method, biliary or enteric fistula are freely drained and secondary abscesses have been avoided. The most frequent indication for open-wound management has been biliary or combined biliary-enteric fistulas (Table 6). Abscesses drained primarily or in combination with other surgical procedures have also been managed with completely open wounds. Two further cases where pancreatic hemostasis could not be achieved, one following rupture of the splenic vein and the other following partial pancreatectomy for hemorrhagic pancreatitis, have required open-wound management. Those patients healing the primary fistula or abdominal abscess are allowed to heal their wounds secondarily or by delayed primary closure. Interestingly, intestinal obstruction, an occasional complication of major surgery or large wounds, has been exceedingly rare. Only one patient developed obstruction following transplant, and this was due to extensive metastatic disease.

#### SUMMARY

In this series of 150 orthotopic hepatic transplants, clinically significant gastrointestinal hemorrhage occurred in 34 patients (23%). Five patients (15%) survived this complication. Enteric perforations occurred

in 20 patients following 198 biliary-enteric procedures. Only one patient survived. Enteric perforations unrelated to biliary procedures fared only slightly better with one survivor among eight perforations. These

results clearly do not warrant complacency. Modifications advocated are an aggressive diagnostic approach and early reoperation with establishment of extensive peritoneal drainage where necessary.

#### REFERENCES

1. Starzl TE, Putnam CW, Hansborough JF, et al: *Surgery* 81:212, 1977
2. Calne RY, Williams R: *Br Med J* 1:471, 1977
3. Hadjiyannakis EJ, Evans DB, Smellie WAB, et al: *Lancet* 2:781, 1971
4. Leapman SB, Vidne BA, Butt KM, et al: *Ann Surg* 183:266, 1976
5. Penn I, Brettschneider L, Simpson K, et al: *Arch Surg* 100:61, 1970
6. Penn I, Groth CG, Brettschneider L, et al: *Ann Surg* 168:865, 1968
7. Koep LJ, Peters TG, Starzl TE: Abstract of the American Society of Transplant Surgeons, Chicago, Ill., June 1978