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ANALYSIS OF SURGICAL COMPLICATIONS AFTER 397 HEPATIC TRANSPLANTATIONS

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Abstract

The results of 397 consecutive orthotopic hepatic transplantations in 333 recipients were reviewed. One or more surgical complications developed in 172 of 323 Patients (55 per cent), excluding ten intraoperative deaths. The six month mortality rate among the patients with surgical complications (55 of 172; 32 per cent) was statistically higher than that among patients without such complications (16 of 151; 11 per cent) ($p<0.001$; chi-square, 58.36). Surgical complications included exploratory laparotomy for bleeding or infection in 74 (22 Per cent), reconstruction of the bile duct for biliary obstruction or leakage in 55 (17 per cent), external biliary drainage for biliary leakage in four (1 per cent), tracheostomy in 80 (24 per cent), thoracotomy in 12 (4 per cent) and splenectomy in seven (2 per cent). The incidence of biliary obstruction (16 per cent mortality rate) and leakage (48 per cent mortality rate) was 18 per cent (34 of 193) and 2 per cent (four of 193) each after choledochocholedochostomy, which was 3 per cent (five of 187) and 9 per cent (17 of 187) each after choledochojejunostomy. Biliary obstruction (16 per cent mortality rate) was more common after choledochocholedochostomy ($p< 0.005$; chi-square, 23.01), whereas the incidence of more serious biliary leakage (48 per cent mortality rate) was higher after choledochojejunostomy ($p<0.005$; chi-square, 8.97). It is concluded that orthotopic hepatic transplantation remains an unforgiving extensive surgical procedure, in which choledochocholedochostomy remains the first-choice reconstruction of the biliary tract because of its lower mortality.

First performed in 1963 (1), orthotopic liver transplantation (OLTx) has evolved to become an accepted modality for the treatment of end-stage hepatic disease (2). Results of recent reports on OLTx from multiple centers indicate a one year patient survival rate of greater than 70 per cent (3–5). Nevertheless, OLTx is an extensive surgical procedure with a narrow margin of safety (6), and a single error at any stage of the operation can cause the demise of the patient (7). This study was done to identify the incidence and significance of various surgical complications after 397 OLTx in adults.

PATIENTS AND METHODS

During the 18 months between 1 July 1986 and 31 December 1987, 333 adult patients underwent 397 OLTx for end-stage hepatic disease at the Presbyterian University Hospital, University of Pittsburgh. Of these 397 procedures, 318 (80 per cent) were the initial transplantations; the other 79 (20 per cent) were retransplants, consisting of 65 second (16 per cent), 13 third (3 per cent) and one fourth OLTx. Excluding ten intraoperative deaths, 387

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transplants in 323 patients were studied. Records and charts of the patients were reviewed retrospectively to study postoperative surgical complications. Surgical complications were defined as any surgical procedure other than retransplantation performed within the first six months after OLTx.

Hepatic allografts were harvested using a rapid perfusion technique (8) or its modification with hepatic hilar dissection prior to aortic cross-clamp. The grafts were preserved in Euro-Collins solution during the first 16 months and University of Wisconsin solution for the last two months. OLTx was performed in a standard manner with the use of venovenous bypass (6,9). Methods of reconstruction of the biliary tract consisted of choledochocholedochostomy over a T tube in 193 (49 per cent), choledochojejunostomy in 187 (47 per cent) and Waddell-Calne's method in two transplants (1 per cent) (10,11). In the other five transplants in four patients, the bile duct was drained externally.

Postoperative immunosuppression consisted of cyclosporine and corticosteroids (12). Steroid-resistant rejection was treated with orthoclone OKT3 (Ortho Pharmaceutical Co.). In the rare severe instances of cyclosporine-related mental confusion, azathioprine was substituted for cyclosporine. Chi-square analysis was used for statistical analyses in this study.

RESULTS

One or more surgical complications developed in 172 of 323 patients (55 per cent). The six month mortality rate of the patients with such complications (32 per cent; 55 of 172) was significantly higher than that of those without complications (11 per cent; 16 of 151) ($p<0.002$; chi-square, 58.36). The cause of death among the 16 patients without surgical complications was infection in six (pneumonia in five and cytomegalovirus infection in one patient), primary graft nonfunction in three, tumoral recurrence in two, intracranial hemorrhage in two, rejection in one patient, lymphoproliferative disorder in one and congestive heart failure caused by primary pulmonary hypertension in one. The incidence and six month patient mortality of each surgical complication among the 172 patients with such conditions after OLTx are discussed herein.

Exploratory laparotomy

Hemorrhage—Sixty-nine exploratory laparotomies were performed for hemorrhage upon 49 patients (15 per cent) (Table I). The source of hemorrhage was intraperitoneal in 56 and within the gastrointestinal tract in 11. The exploration yielded negative findings in the other two patients. Of the 56 exploratory laparotomies performed for intraperitoneal hemorrhage, definitive source of bleeding was identified on 30 occasions (22 patients), while no specific site could be identified on 26 occasions (19 patients).

For gastroduodenal bleeding, the most common bleeding site was the Roux-en-Y jejunojejunostomy anastomosis site (eight of 11). Two patients bled from gastritis, for whom subtotal gastrectomy or vagotomy and pyloroplasty were performed; both died, one of recurrent bleeding from the remnant stomach and the other of a leak from pyloroplasty. Cytomegalovirus gastroenteritis accounted for the gastrointestinal bleeding in six patients.

The six month mortality rate of the patients who underwent exploration for bleeding was 51 per cent (25 of 49). Patients at high risk for death included ones for whom definitive bleeding sources could not be identified (13 of 19) and ones with multiple bleeding sites (eight of 12), which were significantly higher than four of 15 when a single bleeding source was identified ($p<0.01$; chi-square, 6.86).

Infection—Thirty-one laparotomies were performed upon 25 patients (8 per cent) for suspected intra-abdominal sepsis (Table II). A definitive focus was identified on 21 occasions in 18 patients, while the exploration yielded negative findings in the other ten instances. Patients in whom bile peritonitis developed secondary to biliary leakage are discussed in the section dealing with biliary leakage.

Peritonitis or intra-abdominal abscesses accounted for nine of 21 laparotomies with positive findings, whereas anastomotic leakage or intestinal perforation was the cause of sepsis in eight. The mortality rate of patients with positive findings from laparotomy was 56 per cent (ten of 18), while none died as a result of exploration with negative findings.

Operations upon the gastrointestinal tract—Seven patients (2 per cent) underwent laparotomy for obstruction of the small intestine. The causes were adhesions in five, internal hernia through a window of the mesentery below a Roux-en-Y limb of the jejunum in one patient and an incarcerated incisional hernia requiring resection of the small intestine in one. None died postoperatively.

One patient underwent vagotomy and pyloroplasty for a duodenal ulcer with pyloric obstruction on the 17th postoperative day and survived. One patient underwent a distal pancreatectomy for a pancreatic fistula and abscess on the 43rd postoperative day; this patient died two months later of sepsis. One patient underwent emergent subtotal colectomy for pseudomembranous colitis on the 138th postoperative day and survived. Another patient required colostomy for pseudo-obstruction of the colon on the first postoperative day, but later died of overwhelming sepsis.

Splenectomy—Seven patients underwent splenectomy (2 per cent). The indications consisted of trauma in one patient, penetration of the spleen during left closed thoracostomy in one, splenic infarct in two patients, splenic abscess in one patient, idiopathic thrombocytopenia purpura in one and pseudoaneurysm of the splenic artery three months after transplantation in another. None had splenectomy-related complications develop; two died of unrelated causes.

Hepatic arterial exploration—Seven patients underwent surgical exploration of the hepatic artery (2 per cent) for an attempted reconstruction. One patient had a ruptured infected mycotic aneurysm of the aortodonor iliac arterial graft anastomosis; this patient exsanguinated during an attempted axillobifemoral extra-anatomic by-pass. In five patients, the hepatic artery was thrombosed and reconstruction was attempted. This was successful in only one patient; the other four patients required retransplantation for recurrent hepatic arterial thrombosis, two of whom died subsequently—one because of systemic cytomegalovirus infection and the other, sepsis. The hepatic artery was patent in another patient.

Biliary complications

Biliary obstruction—Thirty-nine reconstructions were performed for biliary obstruction upon 38 patients (12 per cent) (Table III). Clinical presentation of biliary obstruction was cholangitis or hepatic dysfunction characterized by a rise in the levels of total bilirubin and alkaline phosphatase. The diagnosis was established by either a T-tube cholangiogram or percutaneous transhepatic cholangiogram. Ultrasonography was not sensitive in the detection of early intrahepatic dilation of the bile duct. The incidence of biliary obstruction was 18 per cent (34 of 193 grafts) after choledochocholedochostomy and 3 per cent (five of 187 grafts) after choledochojejunostomy ($p<0.005$; chi-square, 23.01).

The stricture occurred at the anastomotic site in 25 instances, at the distal bile duct presumably because of dysfunction of the ampulla of Vater in 13 and at the exit site of the T tube in one

instance. In all but one patient with choledochocholedochostomy, reconstruction was performed by choledochojejunostomy. The other patient had a revision of the anastomosis. Patients whose initial reconstruction was by choledochojejunostomy had a simple revision of the anastomosis. The six month mortality rate among these patients who underwent reconstruction was 16 per cent (six of 38).

Biliary leak—Twenty-nine laparotomies were done for biliary leaks upon 21 patients (6 per cent). Frank bile peritonitis developed in seven of these patients at seven to 58 days postoperatively (22.2±6.4 days). The location of the biliary leak could be identified in 21 instances: the anterior wall in ten, anterolateral wall in two, posterior wall in one instance and the T-tube exit site of the recipient common bile duct in three instances. The other five patients had complete disruption of the bile duct. The incidence of biliary leakage after choledochojejunostomy was 9 per cent (17 of 187 grafts), which was significantly higher than 2 per cent (four of 193 grafts) after choledochocholedochostomy ($p < 0.005$; chi-square, 8.97). The method of reconstruction of the bile duct after biliary leakage for four patients with a choledochocholedochostomy was converted to a choledochojejunostomy. For patients with an initial choledochojejunostomy, 13 of the 17 underwent revision of the anastomosis, while the other four underwent external biliary drainage; two later required laparotomy for a dislodged external drainage catheter. In only two patients did biliary leakage develop during the first postoperative week. The mortality rate after biliary leakage was 48 per cent (ten of 21 patients).

Extra-abdominal procedures

Tracheostomy—Eighty-two tracheostomies were performed upon 80 patients (25 per cent). The indications for tracheostomy were pneumonia, respiratory failure associated with sepsis or multiorgan failure, inability to be weaned off a respirator as a result mainly of cachexia and cerebrovascular accident. Thirty-seven of 80 patients with a tracheostomy died within six months after OLTx, caused by the underlying complications in all but one patient who died of tracheal hemorrhage from an ulcer. Two patients underwent a second tracheostomy for pneumonia from *Pneumocystis carinii* or *Pseu domonas aeruginosa* more than one month after the initial tracheostomy.

Thoracotomy—Fifteen thoracotomies were performed upon 12 patients (4 per cent) (Table IV). In three, the cause was massive hemothorax after insertion of chest tube; all three died, one of whom died of recurrent hemothorax in spite of four thoracotomies for attempted hemostasis. The incidence of hemothorax after tube thoracostomy or insertion of a pigtail catheter (13) was 1.8 per cent (three of 168 occasions). The other nine patients underwent thoracotomy for a diagnostic open biopsy of the lung.

Hernia—Three patients underwent repair of inguinal hernias on postoperative days 21, 31 and 46, respectively. One repair was performed as a semiemergency for incarceration.

Vascular operations—One patient underwent replacement of the aortic valve for aortic regurgitation secondary to endocarditis on postoperative day 158. Another patient underwent sternotomy for accidental penetration of the left ventricle during an attempted insertion of a pigtail catheter into the left pleural cavity for drainage of an effusion. Two patients underwent excision of a false aneurysm of the radial and femoral arteries, respectively. All four patients survived these vascular complications without morbidity.

Miscellaneous—Miscellaneous surgical procedures were performed for either diagnostic or therapeutic purposes (Table V). Two patients underwent placement of a Denver shunt on post-operative days 16 and 62, respectively. Both are alive and well without ascites.

DISCUSSION

The high incidence of surgical complications after OLTx in our series is consistent with the fact that OLTx is a technically demanding operation that is almost always performed upon moribund patients (1–6). As to the poor prognosis associated with hemoperitoneum of undetermined origin, this seems to be related to poor function of the allograft immediately after OLTx. Of the 19 patients who were operated upon for hemoperitoneum of undetermined origin, five of the 13 initial grafts required replacement, of which three failed to function. Considering the high mortality and morbidity associated with poor function of the hepatic allograft (14), a parameter predictive of allograft function is in urgent need.

Bleeding from a Roux-en-Y choledochojejunostomy during the first two weeks postoperatively seems to be attributable to incomplete hemostasis of the mucosa at the jejunojejunostomy site, which probably begins to bleed after absorbable sutures lose tensile strength. For its prevention, minimal manipulation of the mucosa during jejunojejunostomy seems important, especially because of the friability of the tissue caused by poor nutritional status, collateral vasculature related to portal hypertension and poor healing of tissue from postoperative immunosuppression. The majority of bleeding in the gastrointestinal tract occurring more than three weeks postoperatively, on the other hand, is attributable to cytomegalovirus gastroenteritis. Generally, we observe a policy to perform laparotomy when more than 4 units of blood are transfused within 24 hours or when there is any evidence of hemodynamic instability because of bleeding. An erythrocyte-tagged radionuclide scan has been valuable in identifying the source of bleeding.

Percutaneous needle biopsy of the liver is a very useful diagnostic technique for postoperative management of the recipients of OLTx. It often leads to optimal immunosuppression by allowing differentiation of rejection, ischemic injury and viral infection. This procedure, however, is rarely associated with hemoperitoneum or right pneumothorax. In general, coagulopathy or thrombocytopenia with a platelet count of less than 60,000 per cubic millimeter should be corrected before a hepatic biopsy, and the presence of more than minimal ascites or elevated central venous pressure from high positive end expiratory pressure, or both, should be considered a relative contraindication (15).

Negative findings from exploratory laparotomy in ten of 31 patients seem rather high; however, there were no deaths after negative exploration and none of the deaths among the patients without surgical complications were attributable to surgically correctable intra-abdominal complications. We continue this emphatic approach when the source of sepsis cannot be determined by noninvasive diagnostic procedures (16).

Five of the six patients in whom peritonitis developed after OLTx had undergone several previous laparotomies for intraperitoneal hemorrhage. The presence of residual hematoma is a common cause of intraperitoneal sepsis, and vigorous lavage of the peritoneal cavity, as well as meticulous removal of clots, should be performed during any exploratory laparotomy for hemorrhage.

For intestinal anastomoses in patients with cytomegalovirus infection of the gastrointestinal tract, frozen sections of the resection margins may be beneficial. If the margins are affected by cytomegalovirus, a primary anastomosis should probably be avoided as gastrointestinal leakage is usually fatal.

Biliary obstruction, especially after a choledochocholedochostomy, was the most common biliary complication. Ampullary dysfunction accounted for 20 per cent of the obstructions and is probably the result of a devascularization or a denervation of the ampulla of Vater (17). Partial devascularization of the common bile duct seems to be the principal cause of

anastomotic obstruction. To prevent this devascularization of the common bile duct, minimal manipulation of the bile ducts of the donor and recipient during hepatic procurement and OLTx is important. Because of the low mortality demonstrated in this series and others (10,18) and the easy access to bile and the biliary tract, we believe that choledochocholedochostomy remains the first-choice reconstruction of the bile duct in OLTx unless there is a contraindication, such as cholangiocellular carcinoma, sclerosing cholangitis or significant discrepancy in ductal size.

As to the extremely high incidence of tracheostomy, this reflects the moribund state of the patients who undergo OLTx. Cachectic patients with end-stage liver disease can have fatigue develop rather rapidly from spontaneous breathing and inability to clear bronchial secretions. After learning from painful lesions of aspiration pneumonia from premature extubation, we have adopted an aggressive approach in performing tracheostomy after OLTx for patients with severe muscle wasting or suboptimal early function of the allograft.

The development of pleural effusion is extremely common after OLTx (19), for which insertion of a pigtail catheter with the use of the Seldinger technique has been advocated mainly to reduce the incidence of hemothorax (13). As pleural effusion develops within several days after OLTx in most recipients, the drainage procedure is often performed in the presence of coagulopathy and thrombocytopenia for patients with well-developed collaterals in the chest wall because of portal hypertension. These factors in association with the blind nature of the procedure seem to explain the high incidence of hemothoraces in this study.

SUMMARY

The results of 397 OLTx in 333 patients described herein indicate that OLTx remains an unforgiving extensive surgical procedure. A single technical failure often leads to death of the recipient.

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TABLE I

Exploratory laparotomy for bleeding after orthotopic transplantation of the live

Source of bleeding	Death within six months	POD
Intraperitoneal, N=56	19/41	11±13
Hepatic artery anastomosis, N=6	3/6	17±17
Venous anastomosis, N=4	2/3	7.5±3.7 (1, 9, 10, 10)
Subcapsular hematoma, N=3	1/3	34.6±22 (4, 45, 55)
Other, N=14	5/13	9.1±11.0
Gallbladder bed, N=2		
Greater lacerations, N=2		
Hepatic laceration gland, N=2		
Right adrenal gland, N=2		
Not Specified, N=6		
Biopsy of liver or PTC site, N=3	1/3	12±8 (3, 10, 23)
No specific bleeding source, N=26	13/19	10.0±10.5
Gastrointestinal, N=11	7/10	23±21
Jejunonjejunostomy, N=8 (4)*	4/8	24.8±24.0
Stomach, N=2 (1)*	2/2	7±5 (2, 12)
Cecum, N=1 (1)*	1/1	(24)
Negative exploration, N=2	1/2	9±3 (6, 12)

*Number of patients whose gastrointestinal bleeding was caused by cytomegalovirus gastroenteritis.

Values expressed for postoperative days are means plus or minus the standard deviation; numbers in parentheses are the specific postoperative days.

POD, Postoperative days and PTC, percutaneous transhepatic cholangiogram.

TABLE II

Exploratory laparotomy for infection after orthotopic transplantation of the live

Indication	Deaths within six months	POD
Peritonitis, N=6	3/6	14±6
Abscess, N=3	1/3	19.6±7.5 (9, 24, 26)
Anastomotic leak, N=5	4/4	22.0±10.2
Jejunojejunostomy, N=3	3/3*	19.0±11.7 (7, 15, 35)
Ileocolostomy, N=1	1/1*	31
Pyloroplasty, N=1	1/1	22
Intestinal perforation, N=3	1/3	56.0±58.6
Small intestine, N=2	0/2+	71±67 (4, 138)
Colon, N=1	1/1	26
Infected pancreatic pseudocysts, N=4	1/2	23±13 (9, 23, 26, 44)
Negative exploration, N=10	1/10‡	21.1±26.0
Total, N=3	11/25	23.4±27.0

*One patient had leak from jejunojejunostomy and ileocolostomy simultaneously caused by cytomegalovirus enteritis.

+One patient had a lymphoproliferative disorder.

‡Three patients had exploratory laparotomy for peritonitis or abscess previously.

Patients in whom peritonitis developed because of bile leak were excluded. Values expressed for postoperative days are means plus or minus the standard deviation; numbers in parentheses are the specific postoperative days.

TABLE III

Biliary complications after orthotopic hepatic transplantation

Cause	Deaths within six months	POD
Biliary obstruction, N=39	6/38	65.5±49.0
Anastomosis stricture, N=21	5/21	71.3±53.0
Ampullary dysfunction, N=8	0/8	78.6±25.0
Stent displacement, N=3	0/3*	65.3±78.0 (8, 11, 177)
Mucocele of cystic duct, N=2	0/2	43.5±19.5 (24, 63)
Bile cast formation, N=1	1/1	26
Gallstones, N=1	0/1	88
Recurrent sclerosing cholangitis, N=1	0/1	68
Kinking of common bile duct, N=1	0/1	26
Duodenal diverticulum, N=1	0/1	8
Bile leak, N=29	10/21	37±31
Bile duct necrosis, N=6	3/3	29.6±17.5
Dislodged T tube, N=2	1/2	32.5+25.5 (7, 58)
Hepatic arterial thrombosis, N=1	1/1	24
Technical failure, N=20	5/15	39.9+35.0

*Ampullary dysfunction and stem dislodgment developed in one patient values expressed for postoperative days are means plus or minus the standard deviation, numbers in parentheses are the specific postoperative days POD postoperative days.

TABLE IV

Indications for thoracotomy after orthotopic hepatic transplantation

Indication	Deaths within six months	POD
Hemothorax, N=6*	3/3	13±6
Open lung biopsy, N=9+	5/9	65±41

*Chest tube insertion injury.

+Positive in five instances: lymphoproliferative disorders, two; *Pneumocystis carinii* infection, one; cytomegalovirus pneumonia, one, and possible graft-versus-host disease, one.

Values expressed for postoperative days are means plus or minus the standard deviation.

POD, Postoperative day.

TABLE V

Miscellaneous surgical procedures after orthotopic hepatic transplantation

Procedure	Postive results	POD
Diagnostic purpose		
Lymph node biopsy, N=3	1*/3	44±19 (19, 47, 66)
Biopsy of the ear, N=1	1/1+	12
Biopsy of the breast, N=1	0/1‡	90
Brain aspiration, N=2	2/2§	146±30 (116, 126)
Therapeutic purpose		
Sternotomy, N=1	1/1¶	12
Evacuation of intracranial hematoma, N=1	0/1	138
Denver shunt, N=2	2/2	39±23 (16, 62)

*Lymphoproliferative disorders.

+Squamous cell carcinoma.

‡Fibrocystic disease.

§Brain abscess.

¶Lymphangioma of the neck and themediastmum.

POD, postoperative day.