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The hepatic artery in orthotopic liver transplantation

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Summary

Hepatic artery thrombosis (HAT) is a dreadful complication of orthotopic liver transplantation (OLT). This complication occurred in 27 grafts (68% = 27/393 grafts) in 25 patients (9% = 25/313 patients). HAT was responsible for a high mortality (64% = 16/25 patients) despite a high retransplantation rate (70% = 19/27 grafts). HAT should be suspected in case of fulminant liver failure, delayed bile leak or unexplained fever of sepsis of unknown etiology occurring after liver transplantation. Pulsed doppler examination and arteriogram are the decisive diagnostic procedures. Patients presenting HAT can only be rescued by early diagnosis and retransplantation. Aneurysms of the hepatic arterial supply must also be treated urgently, either by conventional vascular repair if possible or by retransplantation, because or the high incidence of fatal rupture (3/4 patients = 75%).

Introduction

Clinical orthotopic liver transplantation (OLT) is recognized as an effective therapy of end-stage liver disease [7–9]. Despite standardization of donor and recipient operations, still about 10% of the allografts are lost due to surgical complications [2, 3]. This report handles nature, incidence, clinical presentation and treatment of hepatic artery complications in a series of 393 consecutive OLT realized during the cyclosporine-era.

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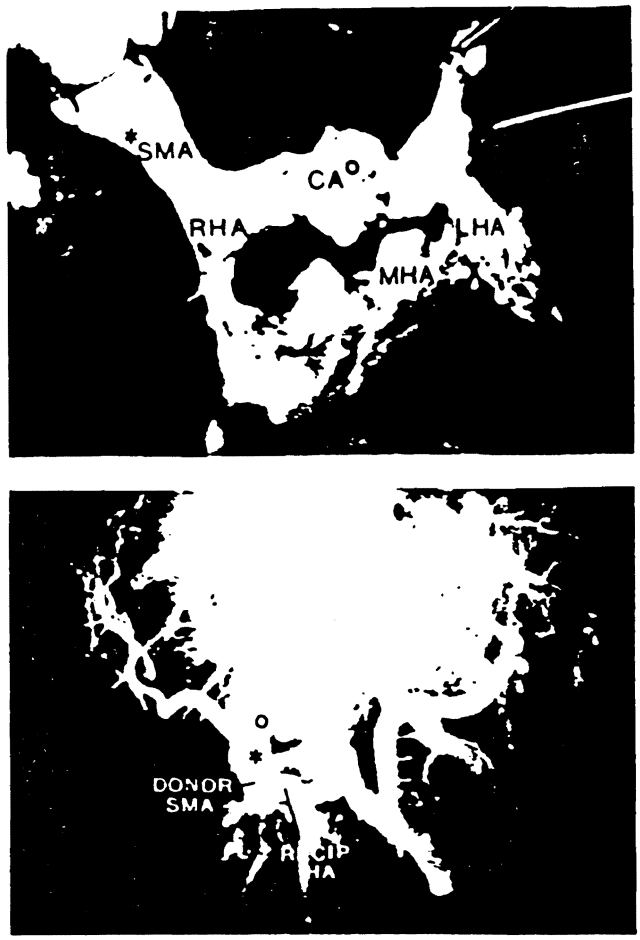


Fig. 1. Intra-operative view and angiography of hepatic allograft revascularization using the fold-over technique in case of triple arterial allograft supply. *SMA with right HA (RHA); °CA with middle (MHA) and left HA (LHA).

Methods and materials

From March 1, 1980 through December 31, 1984, 177 adults and 136 children received a primary OLT in the Colorado-Pittsburgh series under the cyclosporine-low dose steroid regimen. Eighty-two retransplantations (re-OLT) were carried out in 70 patients. 12 patients had three transplants [9].

The donor hepatectomy is part of a previously described multiple organ procurement procedure [10]. Vascular anomalies of the liver are frequent, their identification is the initial step of every donor operation [11]. The HA is always removed with the coeliac axis (CA) and a patch of aortic wall. In case of anatomical variations, the procurement technique has to be adapted. A left hepatic artery (LHA), arising from the left gastric artery (LGA) will be found in the upper part of the gastro-hepatic ligament. The LHA is preserved in continuity with the main LGA and CA.

a b

Fig. 2. Intra-operative view and angiography of iliac vessel graft. This graft is anastomosed to the donor hepatic artery (↓), passed behind the neck of the pancreas (*) and anastomosed to the infrarenal abdominal aorta of recipient. PV = portal vein; BD = donor bile duct.

Hepatic artery arising from the superior mesenteric artery (SMA) is the most frequent anomaly. A right as well as a common hepatic artery coming off from the SMA are almost always located posteriorly to the portal vein (PV). A HA arising from SMA is preserved by dissecting out the artery to its origin at the SMA. The SMA is freed from its aortic origin several centimeters distal to the anomalous HA. In case of a double or triple hepatic arterial supply arising from the SMA and CA, the origins of these two vessels can be folded together and anastomosed in order to create a single trunk [1] (Fig. 1). The existence of uncommon anomalies of the hepatic arterial supply e.g. preduodenal HA or HA directly arising from the aorta should be kept in mind during every organ procurement.

Every donor operation ends up with removal of iliac arteries to be used as arterial grafts. In very small pediatric donors abdominal and/or thoracic aorta (AA and/or TA) are preserved in continuity with the hepatic arterial supply to serve as arterial conducts [9] (Fig. 2). If the thoracic aorta is taken out in continuity with the CA; the graft is cut off proximal to the CA and anastomosed again to the distal side of the aortic cylinder containing the CA. The upper end of the cylinder is closed by running sutures [10]. Cleaning of the hepatic arterial supply is done at the back table during the recipient operation.

Arterial reconstruction of the allograft usually consists of an end-to-end anastomosis between donor CA and recipient HA or CA. If the recipient vessels are diseased or unappropriate for vascular suturing the donor artery is anastomosed to an arterial graft (AG). This graft is passed through a retropancreatic tunnel and is sewn into the infrarenal recipient AA (Fig. 2a–b). A tunnel running behind the head of the pancreas and exiting to the right of the portal vein is usually preferred [10]. In case of aortic conduit-use in children the same technique is used [8]. The 'growth factor technique' allows a maximal expansion of all running 6 or 7/0 prolene vascular sutures [8].

Fig. 3. Angiography and CT-scan: showing massive gangrene of the allograft due to HAT; one can see the gazbubbles in the right hypochonder.

Ninety of the 393 (22.9%) allografts had a complex vascular reconstruction consisting of the use of an iliac graft (39×), a fold-over technique (26×), an abdominal (14×) and thoracic (8×) aortic conduit. In three patients the use of an iliac graft was combined with the fold-over technique (Table 1).

As clinical signs of hepatic arterial complications are often non-specific pulsed doppler ultrasound, is routinely performed during the early postoperative period to allow evaluation of both hepatic allograft artery and parenchyma. Angiography is realized in case of abnormal or unclear doppler findings [5].

Results

Twenty-seven grafts (6.8%) in 25 patients (7.9%) presented with an *hepatic artery thrombosis* (HAT). Three adults and three children, experienced a *massive hepatic necrosis* leading to a rapid fatal outcome due to sepsis and liver failure (Fig. 3). The average time of presentation was 8 days ± 7 (1 to 21 days post-OLT). Sudden and sharp rises in the serum transaminase levels (more than 100-fold over normal) were always present. All 6 patients died despite re-OLT in three of them (Table 2).

Eight patients with 9 grafts, developed a *delayed bile leak*. The average time of biliary leak presentation has been 15.4 days ± 5.8 (4 to 21 days post-OLT). Six

Table 1. Type of arterial reconstruction in 393 OLT

Hepatic artery (HA)	- HA	295	
Graft	- HA	61	90 (23.4%)
iliac graft		39	
abdominal aorta		14	
thoracic		8	
Fold over	- HA	26	
Fold overgraft	- HA	3	

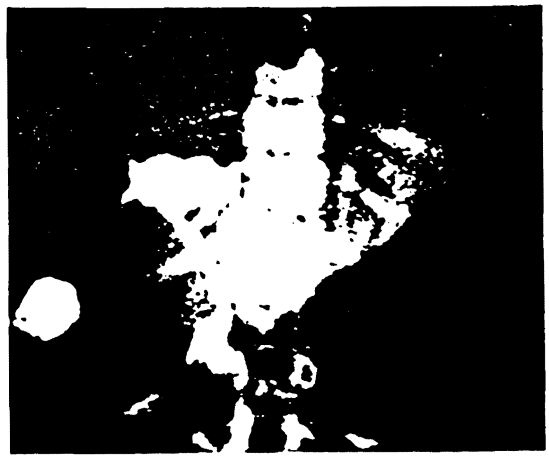
Table 2. Hepatic artery thrombosis (HAT) in OLT-clinical expression

	Grafts	Outcome	
		Retransplantation	Death
Fulminant failure	6	3	6
Biliary leak	9[xx]	7	5ø●
stricture	1[o]		
Relapsing bacteremia	12[xo]	9	5
		19/27 grafts 70%	16/25 recip. 64%

[xx] same patients
ø death due to primary non-function of second graft
● death due to late rupture of mycotic aneurysm

patients of this group were children. One young boy presented 3 times with an HAT, twice manifested as a bile leakage, once as bacteremia. All patients had a persistant fever together with deterioration of the liver function tests (LFT), not responding to enhanced immunosuppression. Bloodculture showed gramnegative germs in 6 patients. A 'biloma' was diagnosed on CT-scan in 5 patients (Fig. 4). Three of the six retransplanted patients recovered, three died. One patient died of a primary non-function (PNF) of the graft another of a late rupture of a mycotic aneurysm of the iliac graft. As both non-regrafted patients died of septicemia, 5 of the 8 patients in this group died.

Eight pediatric and 3 adult patients presented with 'unexplained' *relapsing bacteremia*. The onset of the repeated episodes of bacteremia, usually associated with normal or subnormal liver function tests, averaged about 2 months after transplantation (61,5 days ± 90,5 with extremes from 9 to 330 days). The bacteremia was mostly controlled with appropriate antibiotics. Five of 9 retransplantations were successfull. One patient died of PNF of the new graft. At relaparotomy 2 patients had bile duct necrosis without biliary soilage. Two of



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b

Fig. 4. Percutaneous transcutaneous cholangiography (PTC) and CT-scan: showing intrahepatic 'biloma' formation secondary to HAT.

the 3 non-retransplanted patients survived; one of them, a child, developed a stricture of the choledochojejunostomy (Fig. 5), treated be repeated percutaneous transhepatic baloon dilatation (PBD). A retransplantation will become necessary in a near future because of the problems related with the permanently indwelling catheter in the biliary tract. Diagnosis of HAT was based on clinical presentation, CT-scan and ultrasound (11 pat.) percutaneous and/or retrograde cholangiography (3 pat.) and angiography (9 case). In 2 cases of fulminant liver necrosis gasbubbles were demonstrated on the plain film of the abdomen. Four times the diagnosis was made at retransplantation. A specific cause of the HAT was identified in 7 of the 25 patients (28%): medial necrosis and intramural hemorrhage of the CA, 180° turning-over of the donor thoracic aortic graft.

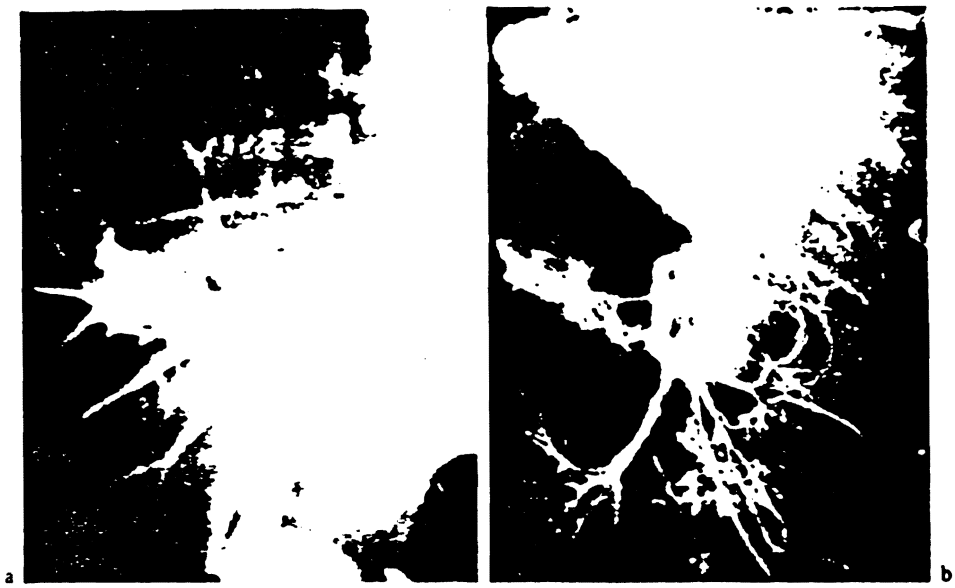


Fig. 5. PTC: biliary stricture of choledochojejunostomy secondary to HAT. The angiography shows a well collateralized allograft.

Table 3. Hepatic artery thrombosis in OLT

Relation to age group						
Age	0–2	3–6	7–11	11–18	years	Adult
	4	11	3	1		8
			19/177			8/216
			10.7%			3.7%

Relation to type of vascularization				
Type	fold-over graft	fold-over-HA	graft-HA	HA-HA
	0	5	10	12
		15/90		12/295
		16.6%		4%

inappropriate fold-over technique and intimal dissection of the donor iliac graft. Two of 8 reversed thoracic conduits thrombosed.

HAT was much more frequent in the pediatric age group and in the group of patients having a complex vascular reconstruction, although these were equally spread throughout the different age groups (Table 3).

Nineteen of 82 retransplantations in these series were realized, in 18 patients, because of an HAT (19/82 re-OLT: 23.2%). As already mentioned two

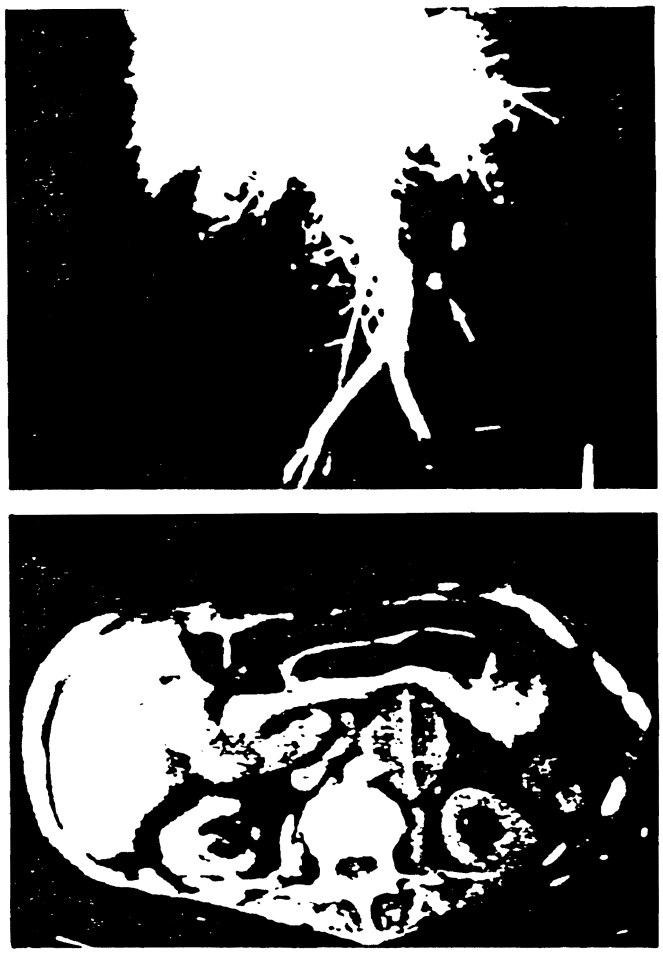
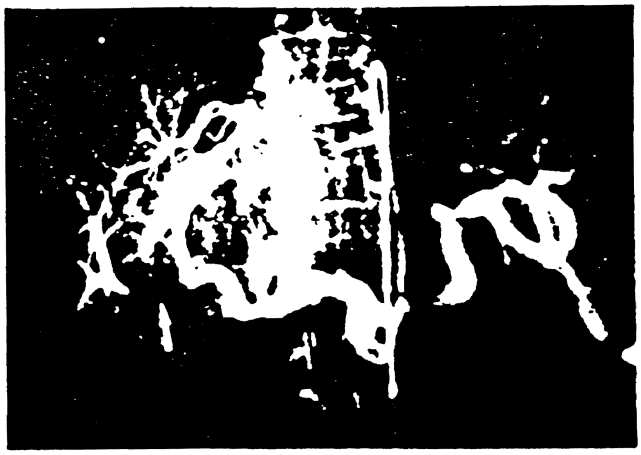


Fig. 6. Pseudoaneurysm at the anastomosis between donor and recipient aorta (↓) on angiography and CT-scan.

patients died because of a PNF-graft, one of an aneurysm. Only 2 (28%) of the 7 non-retransplanted patients survived. Despite the high retransplantation rate (19/27 grafts: 70%) the mortality of HAT was very high (64% = 16/25 patients).

Two *mycotic aneurysms* were lethal because of an early rupture. One patient had a simple graft supply, the other an aortic graft. Two *pseudoaneurysms* were located at the anastomosis between donor and recipient aorta. One could be successfully repaired, the other caused a lethal bleeding due to delayed aneurysmal rupture (Fig. 6). Three of the 4 aneurysms were lethal (75%).

An asymptomatic *stenosis of the H.A* was accidentally diagnosed in 4 patients. One patient presenting with persistant elevation of LFT had a well



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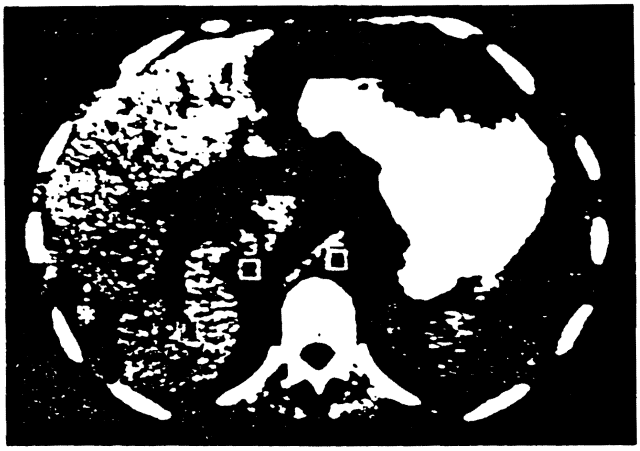

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Fig. 7. Limited liver allograft infarction (*) due to embolization (↓) of the posterolateral arterial branch of the graft.

defined hepatic infarction due to an occlusion of the right posterolateral arterial branch of the liver secondary to an *embolization* (Fig. 7). Liver function recovered following collaterization of this obstruction.

Discussion

Technical complications remain an important cause of morbidity and mortality after orthotopic liver transplantation (OLT). *Thrombosis of the hepatic artery (HAT)* is common and has three different clinical presentations: fulminant hepatic necrosis, delayed bile leakage and relapsing bacteremia [2, 4, 11].

Table 4. Differences between primary and secondary biliary complications (BTC) in liver transplantation

	Primary	Secondary BTC
Diagnosis	(T-tube, PT, ERCP) cholangiography	Doppler ultrasound, angiography, (PT) cholangiography
Success biliary redo surgery	high (25/27 pat.* = 92.5%)	low (1/5 pat. = 20%)
Retransplant rate	low (4/52 pat.)	high (6/8 pat. = 75%)
Mortality rate	low (5/52 pat. = 9.6%)	high (5/8 pat. = 62.5%)

* in CC-T and RYCJ-S biliary tract reconstructions
PT = percutaneous transhepatic cholangiography

HAT should be considered in all recipient presenting with fever and/or sepsis and with positive gramnegative bloodculture with or without increase in hepatic transaminases. Intra-abdominal abscess or other undetected sources of persistant infection must also be excluded. Arteriography and pulsed doppler-ultrasound are the decisive diagnostic procedures. Routine doppler-ultrasound investigation during the first postoperative days will allow a rapid diagnosis of HAT [5]. Differential diagnosis between primary and secondary biliary leakage is of utmost importance because of the completely different management an outcome [4]. Primary BTC can be managed successfully by conventional biliary repair techniques. In case of secondary BTC, reintervention on the biliary tract is doomed to fail because of the borderline or insufficient vascularization of donor bile duct (80% failure rate in 5 patients). Recurrent leakage exposes to prolonged localized or generalized sepsis and to a high mortality rate (62%) (Table 4).

Interruption of the arterial blood supply of the liver graft is a devastating complication. The graft is at disadvantage compared with the native organ in that it lacks the collaterals that normally exist in the attachments of the liver and in that, the graft is subject to rejection with the consequent adverse effect on bloodflow [11]. These two findings render the graft ischemic and vulnerable to invasion by intestinal micro-organisms. As the bile duct is completely dependant for its blood supply on the donor hepatic artery, the principal injury of HAT is an ischemic necrosis of the intra- and/or extrahepatic bile ducts. This explains the high incidence of bile duct necrosis after HAT (8/25 pat. - 32%). If the intrahepatic ducts are involved, development of hepatic abscess is common [4, 11]. The necrosis of bile duct epithelium is followed by a dispersion of bile into the ischemic hepatic tissue corresponding to the 'biloma'-formation detected by CT-scan or US. Percutaneous or T-tube cholangiographies will confirm the connection of this cavity with the biliary tract. If the extrahepatic ducts

are involved, extrahepatic bile abscess or frank bile peritonitis occur which requires laparotomy for drainage and liver replacement. In milder cases, late biliary strictures can develop, which can be temporarily managed by percutaneous balloon dilatation.

Because of its dramatic consequences every effort should be undertaken to arterialize adequately the allograft and to prevent subsequent thrombosis. In small pediatric recipients and in patients requiring complex vascular reconstruction appropriate fluid administration, avoidance of aggressive correction of abnormal clotting parameters before allograft implantation and prophylactic administration of Dextran 40 (given at 20 cm^3 per hour) for the first 5 days are desirable. As soon as the patient is on oral intake aspirin (40 mg/day) is given daily.

Simplified methods of allograft arterialization should be aimed at. The bifurcation of the common hepatic and gastroduodenal arteries mostly provides an adequate cuff to be anastomosed with the donor hepatic artery [2, 9, 11]. In small children, the allograft artery is preferentially anastomosed to the native aorta. Ligation of the recipient splenic artery may enhance the hepatic blood flow by preventing a steal phenomenon in case of end-to-end anastomosis of the donor artery with recipient HA. Intraoperative blood flow measurements can identify technical anastomotic errors but will also assure the surgeon of a good allograft flow. Intraoperative flow measurements beneath 200 ml/min are mandatory for an immediate revision and correction of the arterial anastomosis [3]. The routine use of pulsed doppler ultrasound should be extended to the early postoperative period. These investigations enable a rapid diagnosis and treatment of these arterial complications.

Retransplantation represents the final solution for HAT [4, 9, 11]. Only in patients, presenting with a stable liver function and sepsis, controlled with antibiotics, a decision to delay the retransplantation may be considered. Children and adolescents tolerate HAT more readily than older patients, because they are better able to develop hepatopedal arterial collaterals [11]. Percutaneous transhepatic catheter manipulation can than be useful in temporary drainage of intrahepatic collections of dilation of biliary structures. The high mortality rate of HAT in these series, despite the high retransplantation rate, is explained by a major delay in diagnosis and in regrafting. HAT of the allograft is therefore an urgent indication for retransplantation.

Aneurysms of the arterial allograft supply have a high incidence of fatal rupture. Ultrasound examination of the grafted patient may be helpful in making a rapid diagnosis. As soon as diagnosed, the pseudoaneurysm should be repaired by conventional vascular techniques. Retransplantation is necessary in case of mycotic aneurysm formation although the chance to rescue these patients is poor because of the persisting systemic infection.

Arterial embolization is a minor complication of OLT one should think about in case of persistent unexplained and moderate liver dysfunction. Liver

function will be normalized by progressive collateralization of the ischemic liver segment.

Results of OLT can be further improved by reducing surgical technical problems and earlier recognition of these complications. As biliary and arterial complications represent the vast majority of postoperative surgical problems, adequate training in hepatobiliary and vascular surgery should be one or the prerequisites of the liver transplant surgeon.

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