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ORIGINAL ARTICLE

Liver transplantation and spontaneous neovascularization after arterial thrombosis: ''the neovascularized liver''

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Summary

The only arterial pathway available after liver transplantation is the hepatic artery. Therefore, hepatic artery thrombosis can result in graft loss necessitating re-transplantation. Herein, we present evidence of neovascularization at long-term follow-up in a series of transplant patients with hepatic artery thrombosis. We termed this phenomenon ''neovascularized liver''. Hepatic artery thrombosis was noted in 30/407 cases (7.37%), and occurred early in 13 patients (43.3%) and late (>30 days) in 17 (56.7%) patients. At the time of this study, 11 (36.7%) patients had a neovascularized liver. Those patients with neovascularized liver and normal liver function were closely followed. Of these patients, 10 (91%) showed evidence of neovascularized liver by imaging, and an echo-Doppler arterial signal was recorded in all patients. The mean interval between the diagnosis of hepatic artery thrombosis and neovascularized liver was 4.1 months (range of 3–5.5 months). Liver histology showed an arterial structure in 4 (36.4%) patients. Four factors were associated with development of neovascularized liver: late hepatic artery thrombosis, early hepatic artery stenosis, site of thrombosis, and Roux-en-Y anastomosis. The overall survival rate at 54 months was 90.9%. In conclusion, a late hepatic artery thrombosis may be quite uneventful and should not automatically lead to re-transplantation.

Introduction

Attributable to the complete dissection of the liver that occurs during hepatectomy, the only arterial supply for a liver graft is the hepatic artery (HA). Hepatic artery thrombosis (HAT) reportedly complicates 4–10% of liver transplantation (LT) cases and is generally more frequent after pediatric transplantation or in cases involving complex vascular reconstruction [1,2]. Considering that HAT can be the cause of graft loss and re-transplantation (re-LT), and in view of the ongoing scarcity of hepatic allografts, any strategy for preventing and managing patients with HAT should be considered [3]. The customary approach with a diagnosis of HAT is prompt surgical intervention with declotting and repair. Recently, a non-operative approach was proposed that uses angiography and percutaneous transluminal angioplasty (PTA) infusion [1,2]. The results of this approach in terms of graft salvage have not been optimal.

Very few cases of HAT and spontaneous arterial liver neovascularization (NV) have been reported since 1969 [4,5]. This phenomenon, still poorly understood, is believed to be an example of NV development through angiogenesis. The angiogenesis may involve the omentum, which is thought to have angiogenic potential and the ability to promote NV in chronically ischemic organs

[6–8]. Various hypotheses have been proposed to explain spontaneous arterial liver NV, but one of the most intriguing suggests that during LT the omentum and the mesentery are placed close to the graft (e.g., Roux-en-Y choledochojejunostomy). Surprisingly, however, in our series we observed hepatic NV in patients without a Roux-en-Y anastomosis [9,10]. There is evidence that the process of NV, leading to what we refer to herein as ''neovascularized liver'' (NL), is not rare. It is the purpose of our study to examine the evidence for NV in grafts in patients that have suffered HAT, the factors that may have contributed to NV, and the long-term outcome of these grafts.

Patients and methods

Using a prospectively collected transplantation database, we reviewed all adult LTs performed at the University of Montpellier School Of Medicine from 1998 to 2008. The study was reviewed and approved by the Institutional Review Board of the Office for the Protection of Research Subjects at Montpellier University Hospital. Data collected included recipient demographics, anastomotic techniques, pretransplantation TACE (trans-arterial chemo-embolization), timing and treatment of complications, and graft and patient survival. Management included surgical vascular revision or thrombectomy, re-transplantation, or no treatment. Diagnosis of HAT was based on liver function tests, the absence of intrahepatic arterial flow on echo-Doppler (D-US) analysis, clinical identification of HAT at exploration, or absence of hepatic arterial enhancement on computed tomography (CT)-angiogram or formal visceral angiogram. LT was performed using standard piggy-back techniques.

Immunosuppression included a regimen of tacrolimus (Prograf®; Astellas Pharma Europe, Inc. Staines, UK) as part of a dual or triple drug regimen with prednisone and mycophenolate mofetil (CellCept®; Hoffman-LaRoche, Inc. Basel, Switzerland) [11].

Types of arterial and biliary reconstruction

In 356 (87.5%) of 407 recipients, the arterial anastomosis was fashioned with a running 7–0 polypropylene suture (®Prolene suture; Ethicon Inc., Johnson & Johnson, Sommerville, NJ, USA) between the celiac or common hepatic artery of the graft and the junction between the hepatic and gastroduodenal arteries. In the remaining 51 (12.5%) patients, vascular reconstruction was performed during the back-table phase (accessory right hepatic artery anastomized to the gastroduodenal or the splenic artery with a running 7–0 polypropylene suture). A bile duct-to-duct anastomosis without T-tube with a 5-0 interrupted suture (353 patients, 86.7%) or a hepatico-jejunostomy (54 patients, 13.3%) was routinely performed. In case of high diameter difference between the graft/recipient bile ducts, re-transplantation or primary sclerosing cholangitis a Roux en Y reconstruction was preferred. During these phases a magnification with x3.5 surgical loupes was utilized.

Follow-up of the patients with HAT

All patients with HAT with a normal liver function underwent a radiological follow-up: D-US twice weekly for the first month immediately after HAT and then weekly during the first 3 months. Measurements included the angle-corrected peak systolic and end-diastolic velocities and the resistive index (RI). A qualitative assessment of the hepatic arterial upstroke was made. In addition, CT-scan was routinely performed at the time of the HAT, 1 week later and then monthly during the first 3 months in case of normal liver function. Thereafter, patients with HAT were followed by monthly repeated echo D-US and three-monthly CT-scan. After the first year the NL patients were followed by an echo-D-US four times per year and a CT-scan three times per year. When signs of biliary complications (ischemic cholangitis and/or bile duct necrosis) were detected at CT-scan, a cholangio-MRI (magnetic resonance imaging) and liver biopsies were performed to evaluate the degree of the biliary injury. Periodical blood tests (liver function tests, alkaline phosphatase (ALP), gamma glutamyl transpeptidase (γ-GT), prothrombin time (PT), international normalized ration (INR) were performed during the entire follow-up.

Definition of a NL

Grafts with normal liver function and imaging evidence (CT-scan and/or Doppler) of NV after documented (early or late) HAT, and/or failed re-vascularization assay (radiological and/or surgical) were arbitrarily defined as NL.

Routine management and anticoagulant therapy

All patients underwent D-US once daily for the first two weeks immediately after transplantation and then twice weekly. After the first 3 months, normal liver function and bile duct complications in patients with NL were closely followed by liver biopsy and repeated D-US (twice per month) and CT-scan (four times per year). Patients with abnormal D-US and clinical findings received an angio CT-scan.

Patients with back-table arterial reconstruction were not routinely placed on anti-platelet therapy unless the additional anastomosis involved vessels with a diameter

<5 mm. Patients undergoing arterial thrombectomy were routinely placed on aspirin (100 mg p.o. daily) during the post-transplantation period once the allograft showed signs of good function and there was no evidence of bleeding. All NLs received antiplatelet prophylaxis with aspirin (100 mg per day).

In case of HAT during the first month the patient underwent surgical revascularization because of the fragility of the anastomosis and the risks related to an angiographic maneuver. As per general policy after the first month, a radiological procedure was the preferred method. Surgical or radiological revascularization was performed immediately after HAT diagnosis.

Statistical analysis

Parametric and nonparametric data were expressed as the mean ± standard deviation and median (range), respectively. Primary end points included both patient and graft survival. Statistical analysis was performed according to the methods of Kaplan and Meier, and resulting curves were compared using the log-rank test. Univariate analysis was performed to identify factors associated with the incidence of NV. A difference was considered significant when $P < 0.05$. All statistical analyses were performed using the SPSS statistical package.

Results

Study population

From January 1998 to December 2008, 407 LTs were performed at our institution. The overall 5-year patient survival rate was 82%. All transplants involved whole organ grafts and adult patients (Fig. 1).

Liver transplantation was complicated by HAT in 30 patients (7.37%). Indications for transplantation included alcoholic cirrhosis (12, 40%), hepatocellular carcinoma (10, 33.3%), hepatitis C (3, 10%), re-transplantation (2, 6.7%), hepatitis B (2, 6.7%), and sclerosing cholangitis (1, 3.3%). Fourteen (46.7%) out of the 30 patients with HAT had had vascular reconstruction during the back-table and eight (26.7%) patients underwent a preoperative TACE. Hepatic artery thrombosis was detected within the first 30 days after LT (early HAT) in 13 (43.3%) patients and diagnosed later (late HAT) in 17 (56.7%) patients. Eleven patients (36.7%) developing a NL constituted the subject population of this study.

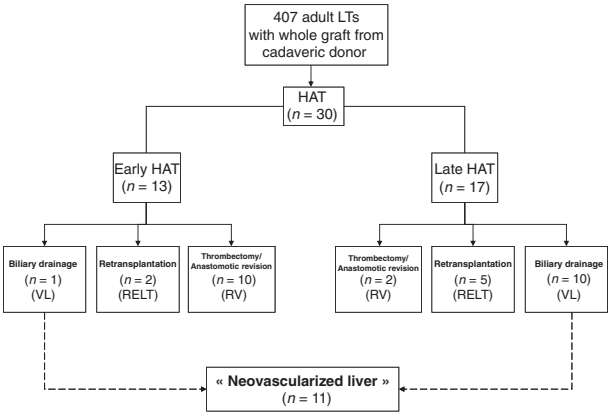

Figure 1 Distribution of early and late hepatic artery thrombosis according to the treatments performed.

Outcomes of early and late HAT

Initial treatment approaches for the entire cohort of patients and their outcomes are summarized in Table 1. Early HAT required surgical revision in 10 of 13 recipients (77%) and re-LT in two cases (15.4%). Of the 10 patients that required surgical revision, thrombectomy was performed in eight patients and hepatic artery anastomotic revision in two. The graft salvage rate for this group was 80% (eight grafts). Two patients underwent re-LT, with one of these patients dying owing to sepsis and multiple organ failure. Only one patient developed a NL after early HAT, but he/she died as a result of cerebral abscess and sepsis.

Late HAT developed in 17 patients (56.7%). In this group, surgical revision of the arterial anastomosis was performed in two patients, and in both cases the graft was rescued. Five patients underwent re-LT, and three of these patients died. A total of 11 patients developed a NL (10 patients developed a NL after a late HAT and one after an early HAT). These patients underwent repeated bile duct drainage procedures (endoscopic and/or radiological). The overall graft salvage rate was 100% (Table 1). The survival rate of these patients is reported in Fig. 2. Univariate analysis revealed that late HAT (>30 days), early hepatic artery stenosis (HAS), thrombosis at the anastomotic site, and Roux-en-Y hepaticojejunal anastomosis were significantly associated ($P < 0.05$) with development of NV (Table 2).

Outcomes of patients with NL

Among the 11 (36.7%) patients with NL, the Child-Pugh score at the time of transplantation was A in one patient, B in four patients, and C in six patients. Four (3.64%) patients underwent TACE attributable to hepatocellular carcinoma (HCC). At the routine CT-scan performed at post operative day (POD) 15, a hepatic anastomotic stenosis [12] was revealed in eight (72.7%) of these patients, while the remaining three (27.3%) patients had normal arterial images. Two (18.9%) of these patients developed

Table 1. Treatments and HAT salvage rate.

	Early HAT (n = 13)				Late HAT (n = 17)			
			Salvage rate				Salvage rate	
Management	n	%	n	%	n	%	n	%
Thrombectomy/Anastomotic revision	10	76.9	8	80	2	11.8	2	100
Retransplantation	2*	15.4	1	50	5**	29.4	2	40
Other treatment (NL)	1†	7.7	0	0	10†	58.8	10	100

*One patient in the early HAT group and **three in the late HAT group died owing to sepsis and multiorgan failure, respectively. HAT, hepatic artery thrombosis; NL, neovascularized livers. †Include patients undergoing biliary drainage (the patient in the early group died as a result of cerebral abscess and sepsis).

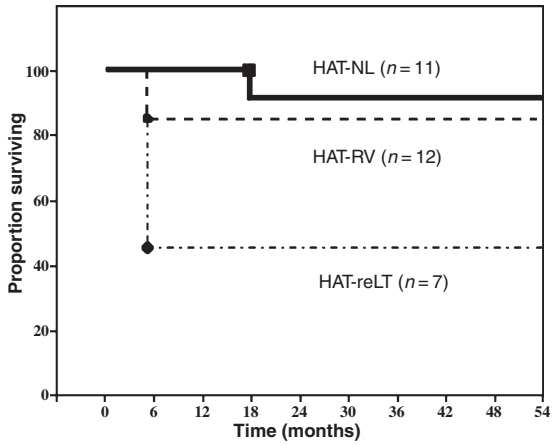

Figure 2 Kaplan–Meier survival curves for patients with hepatic artery thrombosis (HAT) and neovascularized liver (NL), HAT and revascularization (RV), and HAT with retransplantation (reLT). The overall survival rate of the NL patients was 90.9% at 54 months.

Table 2. Univariate analysis of factors associated with arterial neovascularization.

Factors	Odds ratio	P Value
Late HAT (>30 days)	4.12	0.001
Early HA stenosis	3.66	0.002
Site of HAT (anastomosis)	2.38	0.022
Roux en Y anastomosis	1.98	0.037

Univariate analysis revealed that late HAT (>30 days), early hepatic artery stenosis, thrombosis at the anastomotic site, and Roux-en-Y hepatico-jejunal anastomosis are significantly associated ($P < 0.05$) with development of NV. HAT, Hepatic artery thrombosis; HA, hepatic artery.

mycotic pseudoaneurisms requiring urgent treatment by arterial ligature at POD 35 and 60, respectively (Table 3). All patients developed an anastomotic bile duct stenosis (nine choledoco-choledoco and two hepatico-jejunostomy), three of which were associated with an intrahepatic ischemic cholangitis, and one was associated with a bile leakage. The mean interval time between arterial thrombosis and bile duct complication was 3.5 months (range of 2–5 months). Seven (63.6%) patients underwent biliary reconstruction with a Roux en Y hepatico-jejunostomy (the initial two hepatico-jejunostomy were re-performed owing to a recurrent anastomotic stenosis). The average number of bile duct treatments (endoscopic ± radiologic) was 2.45 (0-9). The values for total bilirubin (n.v. 5–17 μmol/l), γ-GT (n.v. 7–40 UI/L), ALP (n.v. 40–100 UI/L), and PT (n.v. 70–100%) at the time of the last follow-up were 14.4 μmol/l (range 10–21 μmol/l), 97.8 UI/L (range 31–365 UI/L), 183.1 UI/L (range 98–488 UI/L), and 85.3% (range 68–100%), respectively. Demographic data for this series of patients with NL are summarized in Table 3.

During the postoperative follow-up, the recipient common hepatic artery was visualized in 7 (63.6%) of 11 patients on CT-scan (Fig. 3), while the graft HA was visualized in only 1 patient (9.1%), and the HAT was localized at the anastomotic level. The site of the HAT was the anastomosis in seven (63.6%) patients, the celiac trunk in two (18.2%) patients, the ostium of the common HA in one (9.1%) patient, and the common HA in one (9.1%) patient. The intrahepatic right hepatic artery was visualized in 9 (81.8%) patients, and the left hepatic artery was visualized in 10 (90.9%) patients. The origin of the arterial NV was the Roux-en-Y hepatic-jejunum anastomosis in four (36.4%) patients (Fig. 4a), the collaterals of the hepatic pedicle in three (27.3%) patients, the collaterals of the left gastric artery in two (18.2%) patients (Fig. 4b and c), the collaterals of the internal mammary artery in one (9.1%) patient, and was undetermined in one (9.1%) patient. In three (27.3%) of these patients, the origin of the arterialization was multiple. Upon further review and analysis of images (CT-scan) for these patients by an independent expert, echo-color-Doppler signals for both the right and left hepatic arteries were

Table 3. Demographic data for patients with venous liver and neovascularization.

Pt	LT indications	Child-Pugh score	Date LT	CT-scan (POD 15)	Date HAT(POD)	Type of bile complications	Roux en Y	N† treatments	Last total bilirubin, **γ-GT, ALP, PT	Survival
1	*Cirrhosis ETOH, HCV, HCC	A5	Jul 2005	stenosis	120	Anastomotic stenosis	no	1	10, 62, 98, 93	Yes
2	Cirrhosis HCV	C10	Sept 2005	Stenosis	60	Anastomotic stenosi, ischemic cholangitis, Roux en Y stenosis	Yes	1	11, 31, 184, 100	Yes
3	Cirrhosis ETOH, HBV	B8	Apr 2002	Stenosis	1	Roux en Y stenosis	Yes	1	15, 106, 122, 68	Not (£)
4	Cirrhosis ETOH, HCC	B7	Dec 2003	Stenosis	362	Anastomotic stenosis	No	4	10, 67, 488, 75	Yes
5	Cirrhosis ETOH	C10	Mar 2007	Normal	60 (+)	Bile duct leakage, anastomotic stenosis	No	3	18, 365, 243, 84	Yes
6	Cirrhosis ETOH	C10	Nov 2002	Stenosis	60	Anastomotic stenosis	No	9	16, 238, 155, 94	Yes
7	Cirrhosis ETOH	C10	Jul 2008	Stenosis	30	Anastomotic stenosis	Yes	2	18, 20, 170, 84	Yes
8	Cirrhosis HCV, HCC	C10	Oct 2007	Stenosis	32	Anastomotic stenosis	Yes	0	21, 23, 138, 85	Yes
9	Cirrhosis ETOH	B9	Feb 2005	Stenosis	45	Anastomotic stenosis recurrence, ischemic cholangitis	Yes†	2	13, 114, 115, 100	Yes
10	Cirrhosis HBV, HCC	B8	Jul 2005	Normal	35+	Anastomotic stenosis, ischemic cholangitis,	Yes	3	15, 67, 134, 86	Yes
11	Cirrhosis ETOH	C10	Jun 2006	Normal	60	Anastomotic stenosis recurrence	Yes†	3	11, 48, 167, 79	Yes

*Cirrhosis ETOH, ethanol; HCV, hepatitis c virus; HCC, hepato cellular carcinome; HBV, hepatitis B virus. Child Pugh score (A:5–6, B:7–9, C10–15). POD, post operative day; HA, hepatic artery.
**γ-GT, gamma glutamyl transpeptidase; ALP, alkaline phosphatase; PT, prothrombin time %.
(+) arterial ligature as a result of mycotic pseudoaneurysm rupture. Number of treatments (number of endoscopic or percutaneous drainage procedures).
(£) patient died on October 2004 owing to sepsis and cerebral abcess.
(†) The initial Roux en Y anastomosis were re-performed as a result of a recurrent stenosis (in the other five cases the Roux en Y was performed after an initial duct-to-duct anastomosis).

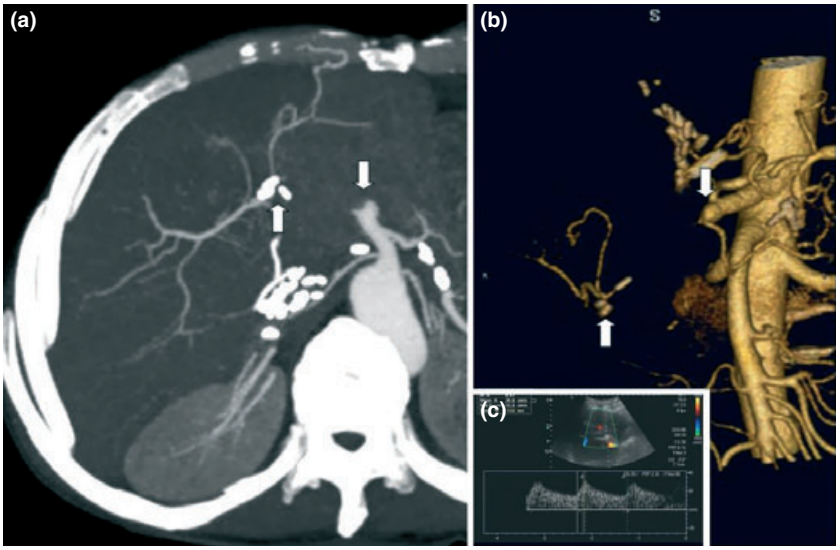

Figure 3 CT-scan and the three-dimensional vascular reconstruction of patient 1. (a and b): arrows indicate the complete common hepatic artery occlusion (⇓) and the new parenchyma neovascularization (NV) originating from the right internal mammary artery (⇑). (c): Hepatic echo-color-Doppler at 5-year post-hepatic artery (HA) ligature follow-up: presence of intrahepatic right artery signal with a resistive index (RI) of 0.47.

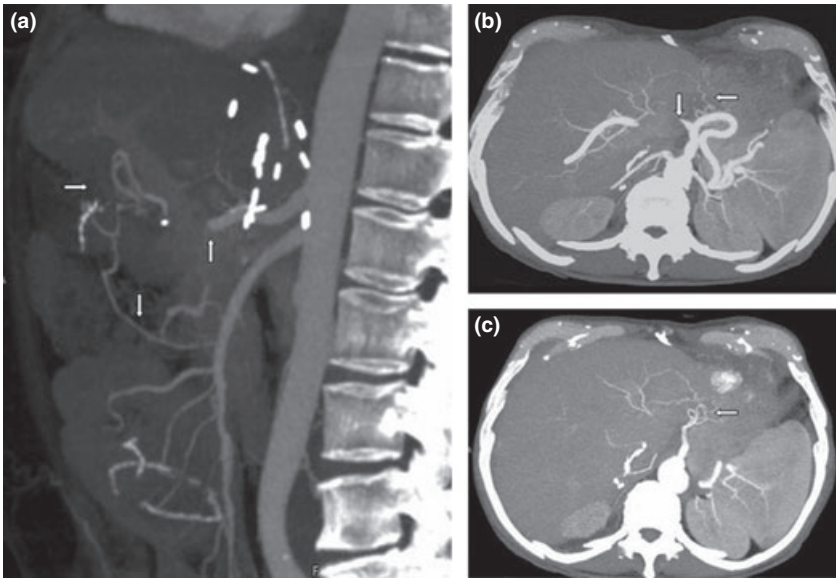

Figure 4 Angio CT-scan of patient 2 (lateral view). (a): arrows denote complete common hepatic artery thrombosis (⇑) and liver parenchyma arterial neovascularization (⇒) from the first jejunal artery originating from the superior mesenteric artery (⇓) in the case of Roux-en-Y anastomosis. (b and c): CT-scan of patient 8. Arrows indicate complete common hepatic artery occlusion (⇓) and new parenchyma neovascularization (NV) originating from the left gastric artery (⇐).

found in 9 (81.8%) of 11 patients. In one patient (9.1%) only the left hepatic artery was revealed, while in another patient the entire arterial flow was not detected (but was detected by CT-scan). The mean RI detected in the right HA was 0.47 for both the right and left arteries. The mean time between the diagnosis of HAT and the development of NV recognized by CT-scan and D-US was 4.1 months (range: 3–5.5 months). Demographic data for the NL patients are summarized in Table 4. Liver histology performed during the follow-up for various reasons (suspicion of rejection, organ dysfunction, persistent cholestasis, etc.) revealed an arterial structure in 4 (36.4%) of the 11 patients sampled. Histological analysis of the biopsied livers revealed distinct angiogenesis (presence of arterial structure in the portal space) with mild lymphocytic infiltration in these four patients (Fig. 5).

Discussion

Our results show that patients who develop a venous liver secondary to late HAT have a good prognosis in terms of survival if arterial NV is present. Our analyses identified late HAT (>30 days), early HAS, thrombosis at the anastomotic site, and a Roux-en-Y hepatico-jejunal anastomosis as possible factors associated with development of NV. We also noticed that despite the

Table 4. The origin of neovascularization in neovascularized liver as determined by CT-scan and echo-Doppler examination.

Pt	Recipient hepatic artery	Graft hepatic artery	Site Hepatic artery thrombosis	Right Intrahepatic artery visualization	Left intrahepatic artery visualization	Arterial neovascularization origin	Last echo-doppler
1	No	No	Ostium	Yes	Yes	Internal mammary artery	Right and left HA signals (RI: 0.45, 0.36) (*)
2	Yes	No	Anastomosis	Yes	No	Roux en Y	Right HA (RI: 0.35–0.40)
3	Yes	No	Anastomosis	Yes	Yes	Left gastric artery	Low bilateral arterial flow (RI: not reported), pedicle collaterals
4	Yes	No	Anastomosis	Yes	Yes	*Undetermined	Low bilateral arterial flow (RI: not reported), absence arterial flow at the hepatic pedicle
5	Yes	No	Anastomosis	Yes	Yes	Hepatic pedicle	Arterial flow not detected
6	Yes	Yes	Anastomosis	Yes	Yes	Hepatic pedicle	Right and left arterial flow (RI: 0.5)
7	Yes	No	Anastomosis	Yes	Yes	Left gastric artery and Hepatic pedicle	Intrahepatic right and left arterial flow (RI: 0.5)
8	No	No	Common HA	No	Yes	Left gastric artery	Right and left arterial flow (RI: 0.47)
9	Yes	No	Anastomosis	Yes	Yes	Roux en Y	Left intrahepatic artery (RI: 0.72), right HA (RI: 0.42)
10	No	No	Celiac trunk	Yes	Yes	Left diaphragmatic artery, left gastric artery, Roux en Y	Left hepatic artery normal. Right HA (RI: 0.47)
11	No	No	Celiac trunk	No	Yes	Left gastric artery, Roux en Y	Left hepatic artery (RI: 0.59). Right HA absent

*In this patient the NV was confirmed by CT-scan and echo-Doppler but its origin is undetermined. RI, arterial resistance index. *Echo-color-Doppler signal (Fig. 3c). HA, hepatic artery.

numerous interventions, patients who develop a NL have a relatively low morbidity rate and a chance for long-term survival similar to the other patients.

The HA plays a vital physiological role after LT, providing blood supply for both the liver parenchyma and bile duct system. Hepatic artery stenosis is an insidious vascular complication occurring after LT. The most common complications seen in patients with HAS are anastomotic and/or nonanastomotic biliary strictures, which are seen in ≤49% of patients at cholangiography. When these strictures progress toward complete HAT, an ischemic cholangitis that severely impacts graft survival is the most common complication [13]. HAS usually occurs at or near the anastomosis site as a result of operative technique or vascular clamp injury. Surgical revision has traditionally been the therapy of choice for HAS, but recently endovascular techniques, including PTA and stenting have been suggested as alternative therapeutic options [14]. At the present time there is no consensus regarding the optimal treatment of HAS and HAT (angioplasty, surgical revision, retransplantation, no treatment) [12,15], and until 2008 there was no consensus within our institution regarding percutaneous angiographic intervention in HAS cases. Therefore, in patients with NL associated with normal or near normal liver function (modest elevation of γ-GT and ALP) and a demonstrable NV on CT-scan and/or echo-Doppler, we adopted a ''wait and see'' policy (Fig. 6). In the other patients, when HAS or HAT caused clinically significant liver dysfunction the strategy followed was surgical re-exploration with the aim of performing a thrombectomy and/or anastomotic revision. In those cases in which revascularization failed, a re-LT was performed. Re-transplantation was required in 22.6% of HAT patients, with no encouraging outcomes.

An interesting question that arises from our study is: what are the factors that could induce NV in a NL? Our investigation indicated that the only factors promoting NV in such a case are late HAT appearing after HAS, HAT occurring at the site of the arterial anastomosis, and a Roux-en-Y hepatico-jejunum anastomosis performed soon after the diagnosis of HAT. It is remarkable how NV can be induced in patients who develop a late HAT after HA stenosis. In fact, it has been reported that by inducing a chronic parenchymal ischemia, arterial stenosis

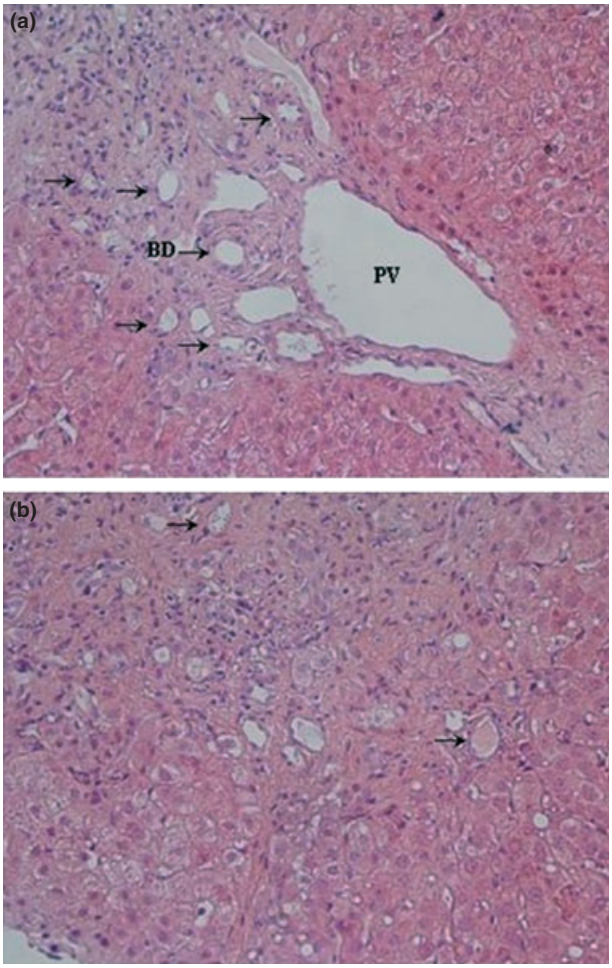

Figure 5 Representative observations of neovascularization in the portal space (H&E x100) in patient 1 (a) and patient 2 (b). Mild inflammatory cell infiltration and new blood-vessels (arrows) are indicated. BD, bile duct; PV, portal vein.

promotes the stimulation of NV through the production of cytokines such as vascular endothelial growth factor A (VEGF-A) [16,17].

The VEGF-A is a chemical signal that stimulates the growth of new blood vessels (angiogenesis). Other factors that may play a role in inducing NV include hypoxia-inducible factor-1alpha (HIF-1alpha), an oxygen-sensitive transcription factor which makes intralobular hepatic stellate cells (HSCs) more responsive to hypoxia. Furthermore, other pericytes play a key role in angiogenesis through their interaction with endothelial cells via platelet-derived growth factor (PGDF) and VEGF signaling [9]. The Roux-en-Y anastomosis brings small bowel mesentery and omentum into close association with the graft. Studies have proven that the omentum has angiogenic potential and the ability to promote NV in chronically ischemic organs. Moreover, the omental patch repair has been performed for perforated duodenal ulcers, inducing a vascular source from the omentum for the injured region. Why a HAT at the anastomotic level increases NV remains unexplained [10,15,18–25].

There are several limitations to this study. For instance, the study population comprised only a small number of patients and did not include a control group. In addition, the study involved a retrospective series, and we did not conduct any specific molecular neoangiogenetic analysis. However, despite these limitations, our data show that new blood-vessels were formed in the liver parenchyma of patients with late HAT who underwent LT, thereby delaying re-transplantation.

Authorship

FP, BG and FN: Designed research/study. FP, HB and JR: Performed research/study. FP, GP, PA and JD: Contrib-

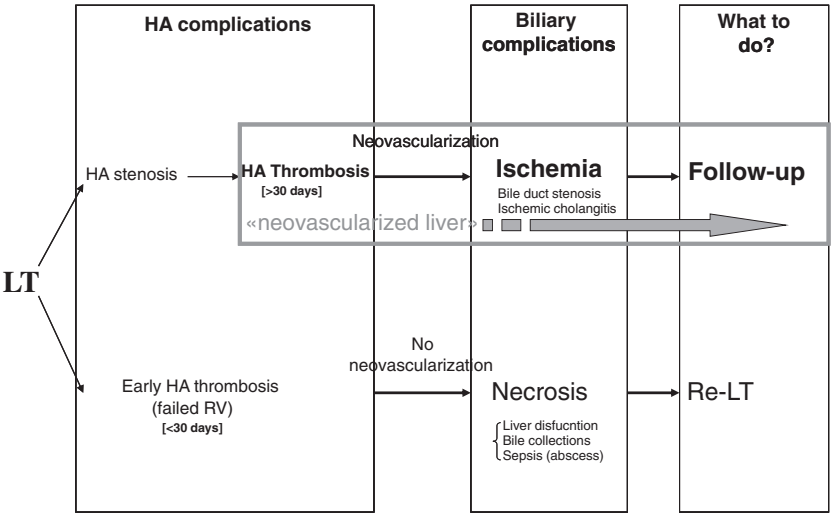

Figure 6 Flow-chart of the decision-making algorithm in cases of hepatic artery thrombosis following liver transplantation.

uted important reagents. FP and JPC: Collected data. FP and GT: Analyzed data. FP, BG and GT: Wrote the article.

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