Treatment of early hepatic artery complications after adult liver transplantation: A single center experience

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Abstract: *Introduction:* Hepatic artery complication represents recognized sequel of liver transplantation that carries significant morbidity and mortality. Besides retransplantation, hepatic artery recanalization is provided surgically, or by percutaneous angioplasty and stent placement. This study provides an analysis of a single center experience comparing surgical and interventional treatments in cases of early hepatic artery complications. *Methods:* In this retrospective single center study, 25 of 365 liver transplant recipients were enrolled who developed early hepatic artery complication after transplantation. Percutaneous intervention was performed in 10 cases, while surgical therapy in 15 cases. Mean follow-up time was not different between the groups (505 ± 377 vs. 706 ± 940 days, respectively). *Results:* 6 patients in the Intervention Group and 10 patients in the Surgery Group are alive. The retransplantation rate (1 and 3) was lower after interventional procedures, while the development of biliary complications was higher. The mortality rate was higher after operative treatment (2 and 5). *Conclusion:* Interventional therapy is a feasible and safe technique for treatment of early hepatic artery complication after transplantation. Being less invasive it is an invaluable alternative treatment having results comparable to surgical methods.

Keywords: arterial complication, liver transplantation, percutaneous transluminal angioplasty, surgical thrombectomy

Introduction

Liver transplantation (LTX) is a routine and effective treatment for patients with end stage liver disease caused by virus infection, alcoholic liver disease, etc. [1]. One of the serious complications is arterial stenosis or thrombosis, which is associated with a high risk of liver graft dysfunction. The rate of hepatic artery thrombosis (HAT) and stenosis (HAS), is 2–12% in liver transplant patients [2, 3]. In a recent study, Vivarelli et al. [4] analyzed the predisposing factors retrospectively. Besides surgical technical failures, donor age and back table arterial reconstruction caused frequently early HAT. Cerebrovascular cause of donor death and use of an iliac conduit were independent risk factors in cases of late HAT. HAS developed more frequently after retransplantation and Cytomegalo Virus (CMV) infection. HAT and HAS might be fatal in the early postoperative period [5, 6], requiring urgent treatment: the most invasive approach is repeated transplantation, with difficulties due to shortage of donor organs. Early surgical revascularization is a widely used option with the disadvantage of operative stress to the patients. The reported survival rate is inferior in both groups compared to the population without hepatic artery complications, or primarily chosen iliac conduit reconstruction [7–9]. Minimally invasive techniques have been widely used in pre- and post-transplantation [10] management, including endovascular management in the treatment of hepatic artery complications for years. Percutaneous transluminal balloon angioplasty (PTA), stent or stent-graft placement, thrombus aspiration and fibrinolysis are reported to be a tolerable therapeutic choice producing good results [11–15].

The aim of this retrospective study was to analyze our follow-up data of early arterial complications treated by surgical or interventional methods focusing on hepatic artery patency, biliary complication, patient survival and especially on graft loss (avoiding the need for retransplantation).

Methods

Patients: The clinical data of patients are presented in *Table I.* 365 patients after cadaver or living donor liver transplantation was examined and retrospectively searched as part of our single center transplantation pro-

Table I Demographic data of patients with early arterial complications

Age (in years)	Recipients	Donors
Mean (St.dev.)	41.28 (10.77)	38.57 (10.94)
Gender	Nr	%
Female	10	40
Male	15	60
Indications for LTX	Nr	%
Acut	1	4
ALD	5	20
Autoimmune	3	12
Cryptogenic	1	4
HCV	7	28
HCV/ALD	2	8
HCV/HCC	3	12
PSC	2	8
Adenomatosis	1	4
Types of complications	Nr	%
HAS	8	32
HAT	12	48
HAT + HAS	5	20

Abbreviations: ALD: alcoholic liver disease, HAS: hepatic artery stenosis, HAT: hepatic artery thrombosis, HCC: hepatocellular carcinoma, HCV: cirrhosis related to Hepatitis C virus infection, LTX: liver transplantation, PSC: primery sclerotising cholangitis

gram. In this retrospective study, we report on all 25 (7%) liver transplant recipients who developed early (within 30 days) hepatic artery complication after transplantation. In these patients 17 HAT, 13 HAS were diagnosed; four patients had HAS with a subsequent HAT. Hepatic artery complication was treated by PTA/stenting and fibrinolysis procedures in 10 patients (Interventional Group), and by surgical revascularization/retransplantation in 15 patients (Surgery Group).

Intraoperative and postoperative imaging: Since 2003, intraoperative Color Doppler Ultrasound (IOP CDUS) [16] has been performed at the end of liver transplantation by one of the radiologists. Bedside Color Doppler Ultrasound (CDUS) examination was performed to monitor adequate liver perfusion in every case postoperatively being aware of the fact, that the changes of Doppler signal in an artery precede the abnormal laboratory values [17]. Postoperative CDUS was performed in every 24–48 hours during the first week by one of the radiologists. The CDUS diagnosis of arterial complication was based on the following criteria: pulse-wave Doppler imaging signs (peak systolic velocity > 2 m/sec); absence of intraparenchymal arterial signal; "parvus tardus" intraparenchymal arterial signal (systolic velocity < 30 cm/s; resistive index (RI) < 0.5; acceleration time > 0.1 s) or direct visualization of the lesion [18, 19].

If the suspicion of arterial complication emerged, Computed Tomography Angiography (CTA) with 3-Dimensional (3D) reconstruction *(Figs 1–2)* and/or Catheter-angiography (DSA) was performed. In the Interventional group, 4 patients had CTA and 6 had DSA after the CDUS examination. In the Surgery group, 3 patients were treated after the diagnosis of CDUS alone; CTA was performed in 8 and DSA in 5 cases. In both groups, DSA was performed in equivocal cases after CDUS, or, when initially endovascular therapy was planned.

Interventional radiology technique: For percutaneous therapy in one case brachial and in seven cases femoral ap-

Fig. 1. CTA volume rendered reconstruction shows complete occlusion of the hepatic artery (arrow) in a 42-year-old liver transplant recipient 7 days after transplantation

Fig. 2. Sagittal CTA maximum intensity projection reconstruction shows patent infrarenal conduit (arrows) in a 52-year-old liver transplant recipient 28 days after transplantation

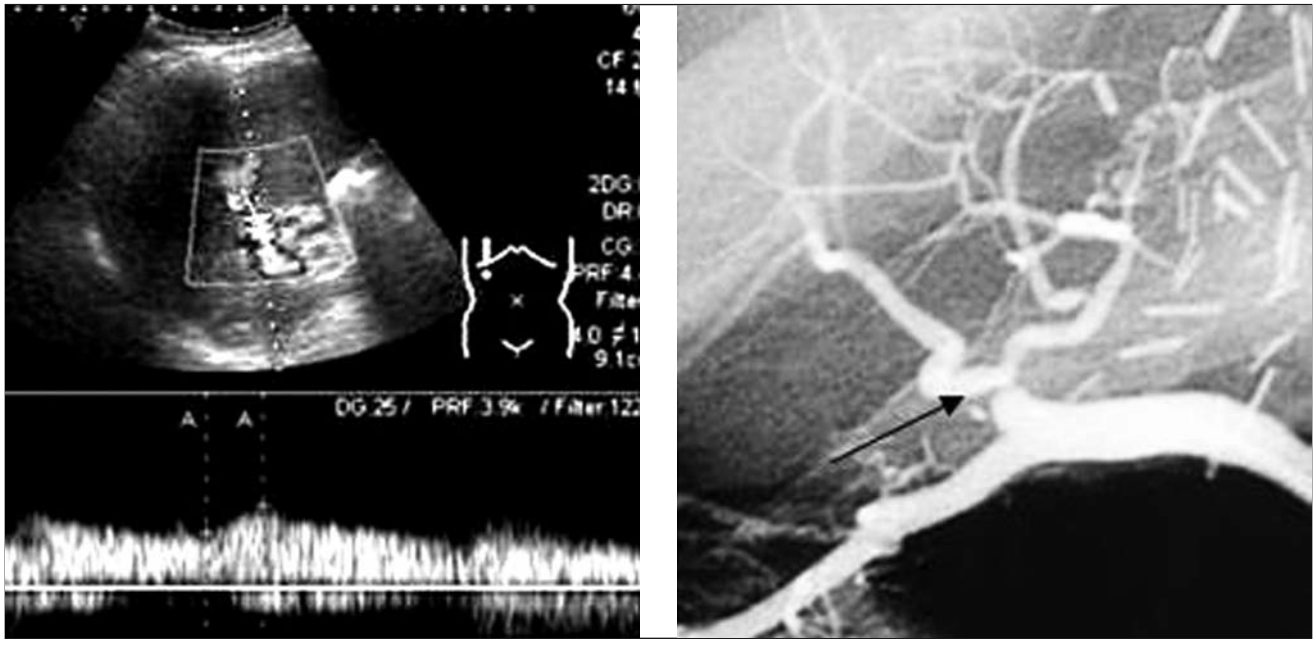

Fig. 3a. CDUS (left panel) and DSA (right panel) imaging in a 23-year-old liver transplant recipient with hepatic artery stenosis before intervention. CDUS examination shows resistance index of 0.33 in the poststenotic hepatic artery. DSA shows a short anastomotic stenosis on the hepatic artery

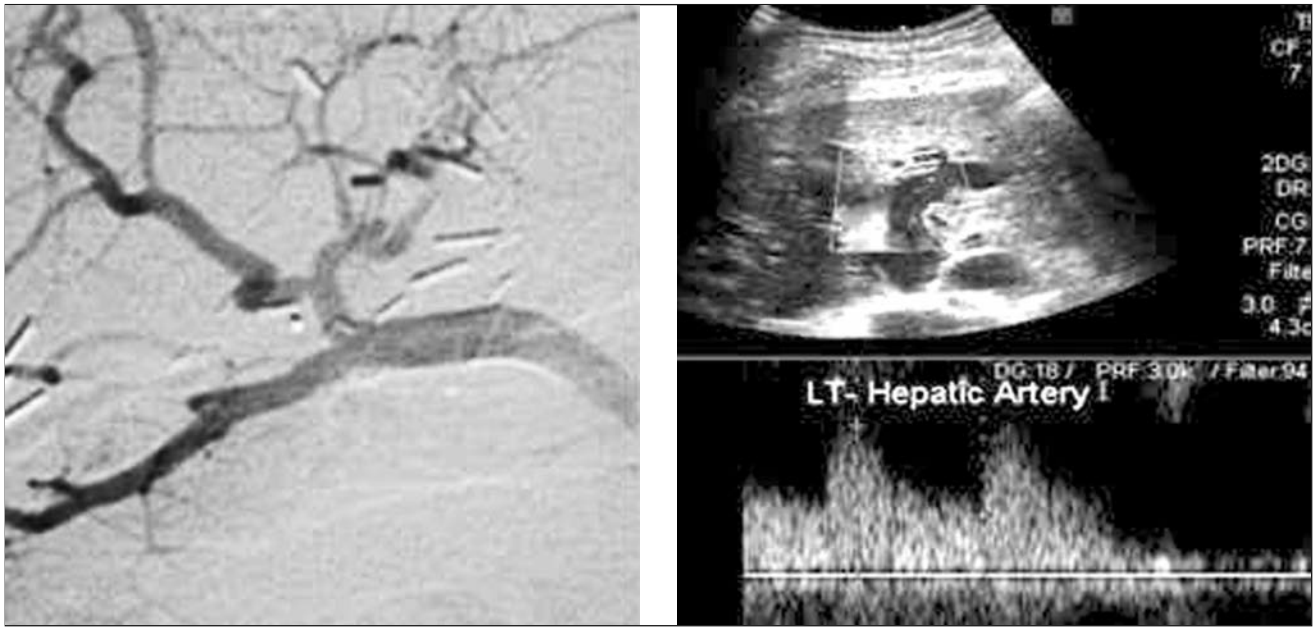

Fig. 3b. CDUS (left panel) and DSA (right panel) imaging in the same patient after intervention. Control CDUS shows improved arterial flow with a resistance index of 0.60. Control DSA shows patent hepatic artery after stent placement

proach were used, with Seldinger technique. After selective catheterization of the common hepatic artery, multiple projection digital angiographies were performed. The length of the stenosis was measured carefully, and after crossing the stenosis, an appropriate sized balloon catheter and/or stent was chosen. All PTA was performed with 0.018" systems (Johnson and Johnson Medical, Belgium), or percutaneous transluminal coronary angioplasty (PTCA) balloons (Abbot Vascular Devices, Medlines, Hungary). Palmaz stent (Johnson and Johnson Medical, Belgium) of 4 mm diameter on a 0.018" delivery system and a coronary stent (Boston Scientific, Hungary) of 3.5 mm diameter were applied. In the third case a self-expandable nitinol stent 8 mm in diameter, 60 mm in length (Johnson and Johnson, Cordis, Hungary) was implanted into the iliac conduit. For control and backup 6F guiding catheters or 5F long sheathes (Johnson and Johnson Medical, Belgium) were used. For fibrinolysis, recombinant tissue plasminogen activator (rTPA) (Boehringer Ingelheim GmbH, Germany) was used in a dose of 13–30

Table II Clinical data of the treated patients

	Interventional group		(Days)					
	Type of complications	Primary treatment	Start of therapy	Follow-up	Results	HA patent	Liver failure / ReTx	Exit
1	HAS	PTA	1	1051	no symptoms	yes	no	no
2	HAS	STENT	7	603	BC/ReTx	no	yes	no
3	HAS	PTA	1	91	no symptoms	yes	no	no
4	HAS	PTA	3	998	no symptoms	yes	no	no
5	HAT + HAS	PTA + LY	17	25	sepsis/exit	yes	no	yes
6	HAS	PTA	2	529	treated BC	yes	no	no
7	HAT + HAS	STENT + LY	24	315	treated BC	no	no	no
8	HAT + HAS	PTA + LY	2	435	no symptoms	yes	no	no
9	HAT	PTA + LY	3	464	no symptoms	yes	no	no
10	HAT + HAS	STENT + LY	2	270	treated BC	yes	no	no
	Surgery group		(Days)					
11	HAT	revision	2	1063	treated BC	yes	no	no
12	HAT	revision	7	1325	ReTX	no	yes	no
13	HAT	revision	1	24	sepsis/exit	no	no	yes
14	HAT	revision	1	21	sepsis/exit	no	no	yes
15	HAT + HAS	revision	1	38	BC/sepsis/exit	no	no	yes
16	HAS	revision	2	2545	no symptoms	yes	no	no
17	HAT	revision	3	296	no symptoms	yes	no	no
18	HAS	revision	5	20	no symptoms	yes	no	no
19	HAT	revision	1	48	ReTx/sepsis	no	yes	yes
20	HAT	conduit	1	926	no symptoms	yes	no	no
21	HAT	conduit	1	336	no symptoms	yes	no	no
22	HAS	ReTx	20	2968	BC	yes	no	no
23	HAT	conduit	2	221	no symptoms	yes	no	no
24	HAT	ReTx	11	12	ReTX/sepsis	no	yes	yes
25	HAT	conduit	3	744	no symptoms	yes	no	no

Abbreviations: BC: biliary complications, conduit: iliac artery interpositum graft, HA: hepatic artery, HAS: hepatic artery stenosis, HAT: hepatic artery thrombosis, LY: thrombolysis, PTA: percutan transluminalis ballon angioplasty, ReTx: retransplatation

mg. During the treatments, additional intra-arterial heparin (5000 IU) was administered. In 10 patients 14 interventions were performed; 6 PTA alone, 3 primary stent implantations and 5 fibrinolysis *(Fig. 3a–b)*.

Surgical therapy: The liver transplant surgeons performed the surgical management of the arterial complications. The applied techniques were surgical thrombectomy with revision of the anastomosis (9 cases), grafting with an iliac artery segment from the donor (4 cases) and retransplantation (2 cases). In 15 patients, 15 surgical procedures were performed to re-establish arterial flow, or liver function.

Results

The results of the different treatments are shown in *Table II*.

Interventional radiology group: Two of 10 patients died, thus 5 of 8 alive are free of symptoms. One death occurred after recanalization due to septic complication. One patient died after a failed intervention resulting retransplantation for untreatable biliary strictures. In addition, 3 patients developed ischemic biliary complications; both treated successfully by percutaneous drainage, dilatation or metallic stent placement. Six of 8 patients had patent hepatic artery during follow-up, one hepatic artery reoccluded 4 months after successful initial treatment, without clinical signs, remained untreated. There was only one procedure related complication: after fibrinolysis a subhepatic hematoma developed, requiring surgical evacuation 3 days later.

Surgery group: 10 of the 15 patients are alive (1 had retransplantation, 5 had early surgical reanastomosis and 4 had iliac artery conduit interposition). Three of 15 patients developed biliary complications (in 2 patients after surgical revision); one of these patients was treated with percutaneous intervention, and one patient with retransplantation. In addition, one more patient had retransplantation. 9 hepatic arteries remained patent during fol-

low-up. Altogether 5 patients died after surgery for arterial complication, all of them due to sepsis.

In comparison, because of the arterial complication, 25% (2/8) of patients died after endovascular therapy and 33% (5/15) in the surgery group. The rate of retransplantation was 10% (1/10) and 20% (3/15), and the number of the biliary complication was 40% (4/10) and 20% (3/15), respectively. The successfully treated biliary complications were similar in both groups. The hepatic arteries remained patent during follow-up in 80% (Interventional Group) and in 60% (Surgery Group).

Discussion

Early diagnosis and treatment of the HAT and HAS is recognized being mandatory to both graft and patient survival [20–23]. HAT and HAS, especially in the early postoperative period causes deterioration of liver function leading to liver parenchyma or biliary necrosis. Fatal consequences require urgent retransplantation. However, limited availability of organs and higher mortality rate narrows this option [9, 24]. The challenge of diagnostic radiology is to check the patency of vascular anastomoses. The essential method is CDUS [25, 26], CTA or Magnetic Resonance Angiography (MRA) [27, 28]. DSA may be needed if these techniques are unable to make a definite diagnosis and preferably as an introduction to endovascular intervention [29]. Having the diagnosis of HAT or HAS urgent surgical revascularization, revision of anastomosis or iliac conduit interposition is required [30]. Interventional treatment by fibrinolysis and PTA represents a valid alternative to surgery in the management of arterial steno-obstructive lesions after liver transplantation [31–33]. Yang et al. in a recent study analyzed their experience in 25 patients, 5 HAT and 20 HAS. Approximately half of the HAS occurred in the early postoperative phase. Their experience with early HAT thrombolysis resulted in unfavorable outcome suggesting surgical repair or retransplantation. Our experience is somewhat different – in a multidisciplinary team approach the decision between the available treatment methods is individual and flexible. Radiologic intervention can be started and in certain points deciding further steps consultation is advisable [34].

In the Hungarian Liver Transplant Program, the operative and interventional methods were available to treat the complications from the beginning. The rate of arterial complications decreased during our learning curve. In this retrospective analysis early HAT and HAS cases were included outnumbering the sporadically noticed and usually clinically silent late arterial complications. The monitoring of early liver vascularization and treatment of complications is based on a protocol, containing regular postoperative CDUS (intraoperative, at the first post-transplantation day then every 24–48 hours during the first week, depending on the clinical situation, then weekly during hospitalization). In cases of diagnosed vascular complications, CTA is performed whenever the confirmation of diagnosis is required, or the acquired volumetric data seems to be helpful in planning the endovascular or surgical treatment. The decision between surgical and endovascular treatment is made by a multidisciplinary team consisting of liver transplant surgeons, anesthesiologists, hepatologists and interventional radiologists. However, the number of patients is still low precluding detailed statistical analysis, the presented results suggest that interventional techniques were valuable, providing good outcomes in terms of vessel patency, rate of retransplantation and death. The development of biliary complications was somewhat higher in this group, although two of three patients were treated successfully in both groups by means of interventional radiological techniques. Having the results of this analysis our policy concerning primary treatment of choice in early arterial complications remains individual preferring the less invasive interventional methods.

Abbreviations

ALD – alcoholic liver disease; BC – Biliary complications; CDUS – Color Doppler Ultrasound; CMV – Cytomegalo Virus; CTA – Computed Tomography Angiography; DSA – Catheter-angiography, Digital Subtraction Angiography; GL – Graft Loss; HA – Hepatic artery; HAS – Hepatic artery stenosis; HAT – Hepatic artery thrombosis; HCC – hepatocellular carcinoma; HCV – Hepatitis C viral infection/related cirrhosis; IOP CDUS – Intraoperative Color Doppler Ultrasound; LTX – Liver transplantation; LY – Thrombolysis; MELD – Model for End-Stage Liver Disease; MRA – Magnetic Resonance Angiography; PSC – primery sclerotising cholangitis; PTA – Percutaneous transluminal balloon angioplasty; PTCA – Percutaneous transluminal coronary angioplasty; ReTx – retransplantation

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