Transpl Int (2000) 13: 372–378

ORIGINAL ARTICLE

Utz Settmacher
Barbara Stange
Roland Haase
Michael Heise
Thomas Steinmüller
Wolf Otto Bechstein
Peter Neuhaus

Arterial complications after liver transplantation

Received: 4 October 1999
Revised: 3 March 2000
Accepted: 23 May 2000

U. Settmacher (✉) · B. Stange · R. Haase
M. Heise · T. Steinmüller · W. O. Bechstein
P. Neuhaus
Department of Surgery, Charité,
Humboldt-University Berlin,
Augustenburger Platz 1, 13353 Berlin,
Germany
e-mail: utzsettmacher@charite.de
Fax: + 49-30-45052900
Tel.: + 49-30-45052001

Abstract From September 1988 through April 1998, 1000 liver transplantations were performed on 911 patients. During the postoperative control examinations of 837 patients, we found 23 (2.74%) with hepatic artery thromboses, 27 stenoses of the hepatic artery (3.22%), and 6 aneurysms of the graft artery. Seventeen patients underwent retransplantation because of arterial complications. Depending on the clinical symptoms, we treated both the local situation as well as the resulting complications of inadequate arterial graft flow. The aneurysms were primarily treated surgically. The first choice of treatment of stenoses was balloon angioplasty. Early postoperative artery thromboses were also treated surgically by thrombectomy in selected cases. For the resulting biliary and local septic complications we preferred endoscopic and drainage procedures. Our clinical experiences have led us to find pretransplantation angiography recommendable, especially in the case of splanchnic artery stenoses, for bypassing from the aorta for arterial perfusion of the graft.

Key words Liver transplantation · Arterial complications

Introduction

The adequate reconstruction of afferent vessels is a precondition for successful liver transplantation. Poor blood inflow and technical problems often lead to early postoperative organ failure and graft loss. Arterial complications prevail with an incidence of 2–25% in patients after liver transplantation of which 50% require retransplantation [4, 11]. Early portal vein occlusion is rare, occurring in 1–3% of transplantations.

Stenoses, occlusions, steal syndromes, and aneurysms can arise as complications in the arterial reconstruction after liver transplantation. Stenoses are found in the recipient artery, at the anastomosis, or in the graft artery and are situated extra- or intrahepatically. Preexistent stenoses of the celiac artery are hemodynamically relevant after transplantation and affect graft function. Stenoses at the anastomotic region are usually caused by technical errors. Postanastomotic stenoses result from the twisting and kinking of graft arteries that are too long. Immunologic and local ischemic damage of the vascular wall will be discussed further below. Early occlusions and thrombosis of the graft artery, respectively, are caused by technical error, preservation injury, or occur in marginal organs with high peripheral vascular perfusion resistance [10]. Late arterial occlusions may develop from early stenoses. Aneurysms of the liver artery after transplantation, if extrahepatic, are often mycotic aneurysms caused by a local infection (e.g., partial biliary insufficiency that induces erosion of the vascular wall or anastomotic suture). If aneurysms occur intrahepatically, they are often caused by liver punctures [2, 7, 16]. In the present paper we discuss the incidence, causes, and treatment of arterial complications in our liver transplant patients.

Patients and methods

Between September 1988 and April 1998, 1000 liver transplantations were performed on 911 patients at our institution. Thirty-four transplantations were performed on pediatric patients and were excluded from this study. The preoperative evaluation of transplant recipients included abdominal CT scan, angiography, and duplexsonography of the hepatic artery, vena cava, and portal vein. In a few patients with acute liver failure and/or severe coagulopathy, angiography was omitted. Organs were either harvested by surgeons from our institution, using simultaneous arterial and portal perfusion ($n = 649$), or were shipped from other institutions ($n = 351$).

Liver transplantation in adult patients was done following standard techniques and using a veno-venous bypass. The retrohepatic vena cava was resected, and an end-to-end interposition of the donor vena cava was performed. Reconstruction of the portal vein was done as end-to-end veno-venous anastomosis. The arterial anastomosis is routinely performed on the insertion of the gastroduodenal artery of the recipient hepatic artery. Depending on the preoperative angiography, the anastomoses were modified [13]. Patients with complex vascular reconstructions (reconstruction of accessoric arteries, multiple anastomoses) received low-dose heparinization during the early postoperative period. We continued anticoagulation only in patients with hypercoagulation disorders (Budd-Chiari syndrome etc.). Vascular patency was routinely checked by sonographic examination during hospitalization and upon presentation at our liver transplant outpatient clinic. In the case of pathologic findings (modification of systolic waveform and abnormal values for resistive index and systolic acceleration time) with clinical symptoms, angiographic control was ruled out. All patients received immunosuppressive therapy consisting of either cyclosporine- or tacrolimus-based regimens.

Retransplantation ($n = 89$) became necessary in 79 patients. The reasons for retransplantation were initial non-function of the graft ($n = 20$), recurrence of viral hepatitis ($n = 19$), chronic rejection ($n = 14$), acute hepatic artery thrombosis ($n = 13$), extrahepatic bile duct destruction ($n = 10$), acute rejection ($n = 6$), recurrence of Budd-Chiari syndrome ($n = 2$), occlusion of vena cava ($n = 2$), and combinations of the above ($n = 3$).

Results

Occlusions of the hepatic artery

We examined 837 of our adult transplant patients in the follow-up program for incidence of arterial complications. Occlusions of the hepatic artery were found in 23 patients (2.74%). These patients had undergone transplantation for posthepatitic cirrhosis ($n = 9$), postethylic cirrhosis ($n = 5$), PSC ($n = 2$), Budd-Chiari syndrome ($n = 1$), and other reasons ($n = 6$). The chronologic occurrence of the occlusion is shown in Fig. 1. Six of the 23 patients (26%) developed early occlusions (till day 30 after transplantation). Thirteen patients (57%) underwent retransplantation because of arterial occlusion (Fig. 1). Five patients died (22%) – two of them after retransplantation. Three deaths were not associated with arterial problems or retransplantation.

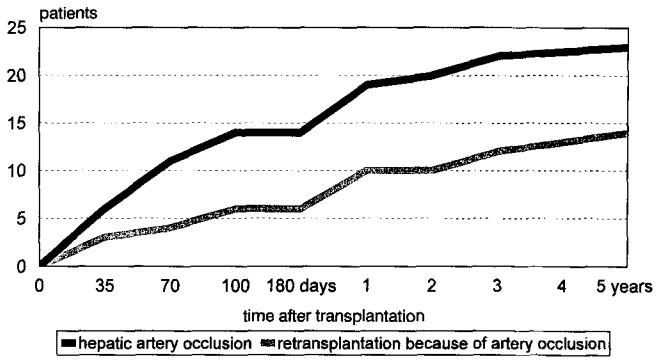

Fig. 1 Chronologic occurrence of hepatic artery occlusion after transplantation and incidence of retransplantation

All but two patients – receiving transplants for acute liver failure – underwent an angiography of the splanchnic arteries preoperatively, a routine procedure for patients before transplantation. At that time six stenoses of the celiac trunk were diagnosed (three caused by compression from the arcuate ligament), one aneurysm of the lienal artery, and one of the mesenteric artery.

Arterial reconstruction was performed as standard procedure (at the insertion of the gastroduodenal artery) using the celiac trunk of the donor in 17 patients. As a consequence of preoperative angiography, in one operation this was combined with a resection of the arcuate ligament. In five patients, a graft interposition (iliac artery) to the aorta was performed, of which one was infrarenal and four directly subdiaphragmatic. In another patient, the splenic artery insertion was used for the anastomosis.

Arterial occlusions occurred with an isolated increase of transaminases ($n = 1$) or in combination with colestasis ($n = 18$). Five patients developed cholangitis, and in seven an ischemic destruction of the biliary system was seen. Seven patients developed an abscess in the liver. Two patients showed clinical symptoms of an initially nonfunctioning organ. In one patient, the hepatic artery occlusion was diagnosed as an incidental finding. For all patients, the clinical and duplexsonographic suspicion of arterial occlusion was confirmed by angiography. In three patients, steal syndrome to the lienal artery was also diagnosed, and in one patient, a portal vein occlusion was found.

Apart from retransplantation ($n = 13$) as treatment of the arterial occlusion in three patients, a hepatico-jejunostomy was performed to aid biliary drainage because of extrahepatic biliary duct destruction. One patient diagnosed with acute postoperative thrombosis was immediately re-operated and thrombectomized with an additional resection of the arcuate ligament and banding of the splenic artery. During retransplantation, four patients underwent standard arterial reconstruction at the insertion of the gastroduodenal artery

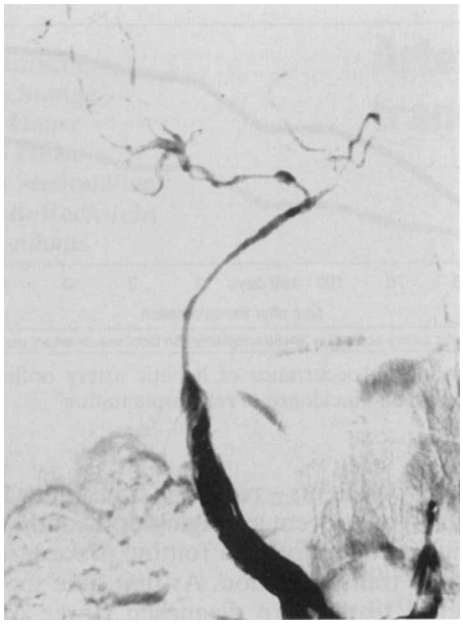

Fig. 2 Hepatic artery thrombosis after local incomplete lysis of the infrarenal aortic graft

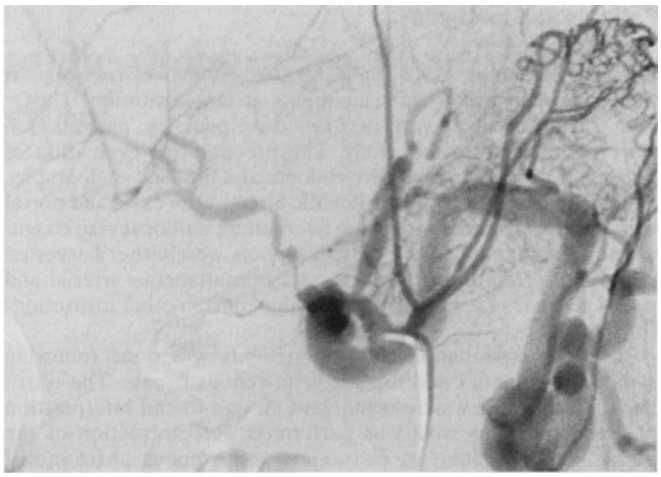

Fig. 3 Long distant stenosis of the graft artery after liver transplantation

Table 1 Anatomical localization of arterial stenoses after liver transplantation

	Preanastomotic	Stenosis in the anastomosis	Postanastomotic
With steal	2	3[a]	4
Without steal	4	9	5
Total	6	12	9

[a] One time steal over the gastroduodenal artery

and five patients at the insertion of the splenic artery. In four cases, an interposition to the aorta was performed (one infrarenal and three subdiaphragmatic). One occlusion reoccurred after retransplantation. A lysis therapy with rt-PA failed (Fig. 2). The patient also suffered from extrahepatic biliary destruction and underwent a new retransplantation. Another patient developed a symptomatic hepatic artery stenosis after retransplantation, and a coiling of the splenic artery was done because of a steal syndrome in the lienal artery.

Arterial stenoses

Twenty-seven stenoses of the transplant artery (3.22%) were diagnosed during the follow-up examination. All patients but one underwent a pretransplantation angiography, during which four patients showed a functional stenosis of the celiac trunk caused by compression of the arcuate ligament. Two of these were classified as hemodynamically relevant. In another patient, an organic stenosis of the celiac trunk was diagnosed. A further patient showed a stenosis of the superior mesenteric artery, and in three patients an aneurysm of the splenic artery was detected. In eight patients for liver transplantation, nonrelevant arterial variants were noticed. The arterial reconstruction in 21 patients was performed in the "standard" manner (at the insertion of the gastroduodenal artery) and modified six times (four times at the insertion of the splenic artery, once directly to the aorta, and in one patient by iliac artery graft interposition to the subdiaphragmatic aorta). In addition, a "banding" of the splenic artery and one splenectomy were performed twice because of a suspected steal to the splenic artery and hypersplenic myelodepression.

Depending on the location on the arterial tree of the stenosis, a cause may be hypothesized. We found symptomatic stenoses located at the anastomosis as well as in the recipient artery (Fig. 3). Furthermore, we observed the appearance of clinical symptoms of stenoses seen in preoperative angiography that had been classified preoperatively as hemodynamically nonrelevant (celiac trunk, Table 1). At the time of diagnosis of the hepatic artery stenosis, a steal of the splenic artery in eight patients and one of the gastroduodenal artery were found (Table 1). The steal was defined angiographically and consisted of an increased diameter of the splenic artery, which was visualized prior to the hepatic artery in patients with signs of hypersplenism and transplant dysfunction [5].

The clinical symptoms of liver artery stenoses appeared immediately after transplantation and developed mostly within the first 6 months. In two patients clinical signs appeared only 3 years after transplantation. A singular increase of transaminases and cholestat-

Table 2 Arterial aneurysms after liver transplantation (*AGD* anastomosis at the insertion of the gastroduodenal artery, *AL* anastomosis at the insertion of the splenic artery)

Patient no.	Arterial reconstruction	Bile duct anastomosis	Localization of the aneurysm	Clinical signs (appearance after transplantation)	Therapy
1 (283)	AGD with banding of AL	Side-side	Intrahepatic, left lobe	Gastrointestinal hemorrhage (11 months)	Retransplantation
2 (336)	AL	Side-side	Anastomosis	Abdominal hemorrhage (3 weeks)	Reconstruction by saphena vein interposition
3 (345)	AGD	Choledoch-oduodenostomy	Anastomosis	Gastrointestinal hemorrhage (8 weeks)	Reconstruction by saphena vein interposition
4 (463)	AL	Side-side	Celiac trunk	Cardial decompensation by arterio-venous fistula (3 years)	Ligation of the celiac trunc
5 (751)	AGD	Side-side	Anastomosis	Gastrointestinal hemorrhage (6 weeks)	Only resection (reconstruction impossible)
6 (975)	AGD	Choledoch-oduodenostomy	Distal of the anastomosis	Gastrointesti nal hemorrhage (7 months)	Only resection, reconstruction not necessary

ic enzymes were found in four and two patients, respectively. Seventeen patients showed cholestasis and an increase in serum levels for transaminases. Three patients suffered episodes of cholangitis, and in five we found endoscopic ischemic biliary duct lesions. Two of those patients developed hepatic abscesses. Seven patients showed no clinical signs, and in these cases the duplex-sonographic diagnosis of hepatic artery stenosis was not verified by angiography.

In seven patients diagnosed with hepatic artery stenosis, a "steal" of the splenic artery, was also diagnosed which was treated by coil embolization. Two of the latter patients had to be splenectomized because of septic complications. In one case a celiac artery stenosis was treated after transplantation by resection of the arcuate ligament. One stenosis of an iliac artery graft was dilated by balloon angioplasty. Later, the ischemic complications of stenoses were treated. Liver abscesses were drained. In one case biliary ducts were drained by hepatico-jejunostomy; in another, the patient underwent a dilatation of the biliary duct stenosis and stent application. Because of progredient biliary duct destruction, three patients were underwent retransplantation. In eight patients no treatment was necessary. Three patients died; two after embolization of the splenic artery and septic complications, the third after septic complications and multi-organ failure.

Aneurysms of the hepatic artery

We diagnosed 6 (0.7%) aneurysms (Tab. 2). The clinical signs developed 4 weeks to 3 years after liver transplantation. Four patients underwent arterial reconstruction by insertion of the gastroduodenal artery and the other two patients by insertion of the splenic artery. In two patients who underwent transplantation because of primary sclerosing cholangitis with extrahepatic bile duct destruction, biliary reconstruction was performed as choledocho-duodenostomy. The other patients underwent a choledocho-choledochostomy as side-to-side anastomosis. We found one intrahepatic aneurysm after liver punction and five extrahepatic aneurysms. In four patients, these were mycotic aneurysms. For three patients the treatment consisted of resection of the aneurysm and ligation of the artery. In two patients, vascular continuity was established by saphenous vein interposition. The patient with the intrahepatic false aneurysm suffered severe gastrointestinal bleeding from the aneurysm 11 months after transplantation via the biliary ducts of the left lobe. He underwent retransplantation, but later died as a result of multi-organ failure. In another patient, we discovered an aneurysmatic celiac trunk before transplantation. Because of severe portal hypertension, a Linton-shunt was inserted before transplantation. Three years after transplantation, he developed a massive arterio-venous fistula from the celiac trunk with a latent cardiac decompensation. After central ligation of the celiac trunc, the cardiac symptomatology improved. In three patients, the aneurysm was diagnosed 4–6 weeks after transplantation. The clinical symptomatology developed as a massive gastrointestinal hemorrhage and bleeding over the T-tube. In two patients, the arteria was reconstructed by saphenous vein interposition (Fig. 4). Both of these patients died: the first, 3 years after transplantation due to a Klatskin's tumor and the other at 6 months after transplantation. Here the cause of death was not determinable. In the third patient, reconstruction of the arteries in the graft for anastomosis of a potential interposition was not possible. He was treated by hepatico-jejunostomy at the time of resection of the aneurysm. To date he is free of symptoms.

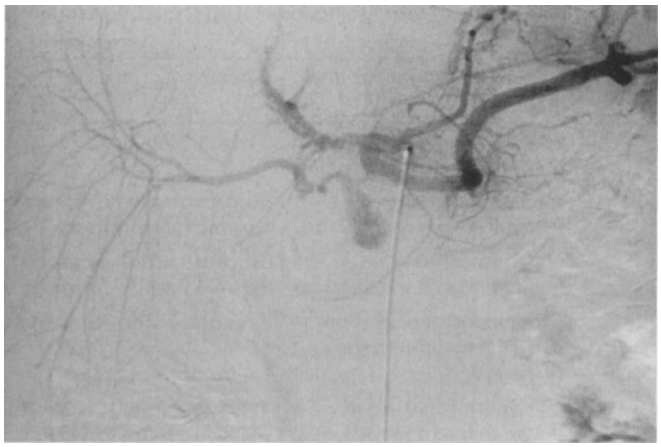

Fig. 4 Hepatic artery aneurysm of the graft artery

The last patient was urgently readmitted 7 months after transplantation with severe gastrointestinal hemorrhage. We found a mycotic aneurysm near the choledocho-duodenostomy, which developed in a branch of the graft artery. The aneurysm was resected and the branch ligated with preservation of the liver artery. To date he is free of symptoms.

Discussion

From September 1988 through April 1998, 1000 liver transplantations were performed on 911 patients. Of these, 837 transplantations on adult patients were analyzed for the incidence of arterial complications. These findings are presented in this paper. The complications were: occlusions of the liver graft artery, 2.74% ($n = 23$); stenoses, 3.22% ($n = 27$); and aneurysms, 0.7% ($n = 6$). The incidence of liver graft artery occlusions varies in the literature from 2 to 25% [4, 11]. Early hepatic artery thrombosis develops more dramatically than later artery occlusions. The diagnosis is made after duplexsonography and angiography in symptomatic patients and confirmed during relaparotomy, retransplantation, or by pathological examination [6]. The sensitivity of duplexsonographic examination is 92% [3, 9]. Nevertheless, in most transplantation units the hepatic artery occlusion will be confirmed by angiography. Aside from liver parenchymal necrosis with secondary infection, which has a mortality rate of up to 75%, without retransplantation after arterial occlusion, ischemic bile duct destruction can result [6]. This can range from strictures and leaks to total bile duct necrosis and secondary infections. Another clinical manifestation of graft artery occlusion is septicemia. Rarely does the graft artery occlusion develop without clinical symptoms. Nevertheless, late occlusions generally have the better prognosis, causing graft organ loss of 10% [14].

The causes and risk factors for hepatic artery occlusion are:

1 Body weight of less than 10 kg
2 Long cold ischemic time
3 Insufficient inflow, especially in the case of celiac trunk stenosis and stenosis of the superior mesenteric artery (causes bad portal inflow)
4 Small diameter (less than 3 mm) of the recipient artery
5 Technique of reconstruction (anatomical variants, expansive reconstruction especially in children, iatrogenic arterial wall dissections etc.) [8, 11].

Aside from retransplantation for arterial occlusions, the following therapeutical options exist:

1 Local surgical revision and thrombectomy in the case of early hepatic artery thrombosis with or without modification of reconstruction (e.g., interposition to the aorta) [11]
2 Local lysis and balloon dilatation if necessary, this procedure was indicated in the middle postoperative interval after transplantation, an occluded small vessel periphery can benefit from lysis
3 Palliative therapy of the complication (bile duct strictures and leaks, liver abscesses).

The primary attempt of recanalization is generally accepted. Thereby, the rate of retransplantation may be reduced and therapeutical options exist for patients who cannot undergo transplantation (because of septic complications) [11, 14]. Our experience with local lysis in surgical reconstruction of occlusions is limited to only a small number of patients.

Five patients with hepatic artery occlusion were preoperatively diagnosed as having celiac trunk stenosis, which was not treated at the time of transplantation. To prevent these complications, we now perform angiography before transplantation and also bypass middle-degree stenosis of the celiac trunk. Later, an increased flow in the splenic artery during conventional reconstruction upon insertion of the gastroduodenal artery may cause a steal phenomenon, leading to graft artery stenosis and occlusion. We observed the development of steal syndrome with stenosis of liver arteries in different areas and amplification of the clinical symptomatology of graft ischemia. Angiography can show suspicion of a steal, but clear evidence, as in a subclavian steal syndrome, is not possible. We did not observe an increased incidence of arterial complications after complex reconstruction in our adult patients. Patients with liver artery occlusions did not have a prolonged cold ischemia time in comparison to the others. Additional causes for he-

patic artery occlusion, apart from technical surgical problems, may be local immunologic reactions as well as coagulation disorders.

The incidence of hepatic artery stenoses after transplantation is 3–5% [10]. The resulting malperfusion of the graft, especially the bile ducts, leads to stenoses and eventually to the development of cholestasis. Almost two thirds of the patients with hepatic artery stenosis present a symptomatology that develops between 5 and 7 months after transplantation [10]. Hepatic artery stenosis can be diagnosed by duplexsonography with an accuracy of 85% [12]. Finally, the stenosis was evaluated angiographically. Two thirds of the hepatic artery stenoses are localized at the anastomosis. To characterize hepatic artery flow intraoperatively after reperfusion of the graft, the flow rate was measured. Here, with a flow of less than 350 ml/min compared to a median flow of 550 ml/min, a stenosis in the graft artery was suspected and the arterial reconstruction was modified [1]. Other definitive risk factors for the development of postoperative stenosis were not confirmed. Graft artery stenoses were treated by balloon dilatation as well as by surgical resection and direct reconstruction or saphenous vein interposition. After treatment of stenoses, patient and graft survival is comparable to that of patients without stenosis [1]. Of importance is the exclusion of stenoses in the recipient celiac artery. The hemodynamic relevance of these stenoses is often misjudged. Modification of splanchnic artery perfusion after transplantation is well known. This may also cause a change in relevance of pre-existent stenoses. Therefore, we often exclude celiac trunk stenosis, also caused by arcuate ligament, by using an iliac artery graft to the aorta for graft perfusion.

The incidence of hepatic artery aneurysm after transplantation is low. In most cases they are mycotic aneurysms caused by a local infection (partial bile duct insufficiency). They develop as anastomotic aneurysms or in stumps of ligated artery side branches [7, 15, 16]. In addition, the growth of known splenic artery aneurysms as well as the de novo development of splenic artery aneurysms after transplantation was described [2]. In the presence of a splenic artery aneurysm, the ligation of the splenic artery at the time of transplantation or a postoperative coil embolization of the splenic artery was recommended. Splenectomy is not necessary. The aneurysms may appear without clinical symptoms or, more often, develop with an acute clinical picture of a gastrointestinal hemorrhage. The therapeutical options are surgical resection of the aneursym and, if possible, reconstruction of arterial perfusion by saphena vein interposition. Failure of the reconstruction results in bile duct necrosis, and graft loss can result. In this situation we therefore performed a hepatico-jejunostomy simultaneously.

References

1. Abbasoglu O, Levy MF, Vodapally MS, Goldstein RM, Husberg BS, Gonwa TA, Klintmalm GB (1997) Hepatic artery stenosis after liver transplantation-incidence, presentation, treatment, and long-term outcome. Transplantation 63: 250–255
2. Ayalon A, Wiesner RH, Perkins JD, Tominaga S, Hayes DH, Krom RA (1988) Splenic artery aneurysms in liver transplant patients. Transplantation 45: 386–389
3. Flint EW, Sumkin JH, Zajko AB, Bowen A (1988) Duplex sonography of hepatic artery thrombosis after liver transplantation. AJR Am J Roentgenol 151: 481–483
4. Harms J, Chavan A, Ringe B, Galanski M, Pichlmayr R (1994) Vascular complications in adult patients after orthotopic liver transplantation: role of color duplex sonography in the diagnosis and management of vascular complications. Bildgebung 61: 14–19
5. Langer R, Langer M, Scholz A, Felix R, Neuhaus P, Keck H (1992) The splenic steal syndrome and the gastroduodenal steal syndrome in patients before and after liver transplantation. Aktuelle Radiol 2: 55–58
6. Langnas AN, Marujo W, Stratta RJ, Wood RP, Li SJ, Shaw BW (1991) Hepatic allograft rescue following arterial thrombosis. Role of urgent revascularization. Transplantation 51: 86–90
7. Madariaga J, Tzakis A, Zajko AB, Tzoracoleftherakis E, Tepetes K, Gordon R, Todo S, Starzl TE (1992) Hepatic artery pseudoaneurysm ligation after orthotopic liver transplantation – a report of 7 cases. Transplantation 54: 824–828
8. Mazzaferro V, Esquivel CO, Makowka L, Kahn D, Belle S, Kahn D, Scantlebury VP, Ferla G, Koneru B, Scotti FC, Foglieni CL (1989) Factors responsible for hepatic artery thrombosis after pediatric liver transplantation. Transplant Proc 21: 2466–2467
9. Nolten A, Sproat IA (1996) Hepatic artery thrombosis after liver transplantation: temporal accuracy of diagnosis with duplex US and the syndrome of impending thrombosis. Radiology 198: 553–559
10. Orons PD, Sheng R, Zajko AB (1995) Hepatic artery stenosis in liver transplant recipients: prevalence and cholangiographic appearance of associated biliary complications. AJR Am J Roentgenol 165: 1145–1149
11. Pinna AD, Smith CV, Furukawa H, Starzl TE, Fung JJ (1996) Urgent revascularization of liver allografts after early hepatic artery thrombosis. Transplantation 62: 1584–1587
12. Platt JF, Yutzy GG, Bude RO, Ellis JH, Rubin JM (1997) Use of Doppler sonography for revealing hepatic artery stenosis in liver transplant recipients. AJR Am J Roentgenol 168: 473–476
13. Settmacher U, Haase R, Heise M, Bechstein WO, Neuhaus-P (1999) Variations of surgical reconstruction in liver transplantation depending on vasculature. Langenbecks Arch Surg 384: 378–383

14. Valente JF, Alonso MH, Weber FL, Hanto DW (1996) Late hepatic artery thrombosis in liver allograft recipients is associated with intrahepatic biliary necrosis. Transplantation 61: 61–65

15. Zajko AB, Bradshaw JR, Marsh JW (1988) Mycotic pseudoaneurysm of the gastroduodenal artery – an unusual cause of lower gastrointestinal tract hemorrhage following liver transplantation. Transplantation 45: 990–991

16. Zajko AB, Tobben PJ, Esquivel CO, Starzl TE (1989) Pseudoaneurysms following orthotopic liver transplantation: clinical and radiologic manifestations. Transplant Proc 21: 2457–2459