Trans Int (2003) 16: 15–20
DOI 10.1007/s00147-002-0505-y

ORIGINAL ARTICLE

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Outcome of patients with pre-existing portal vein thrombosis undergoing arterialization of the portal vein during liver transplantation

Received: 8 October 2001
Revised: 9 August 2002
Accepted: 27 September 2002
Published online: 10 December 2002

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Abstract Arterialization of the portal vein is being propagated as a technical possibility in liver transplant recipients with pre-existing portal vein thrombosis. In our own small series, portal vein arterialization (PVA) was carried out in four patients undergoing orthotopic liver transplantation. In three of these cases, the portal vein was anastomosed to the aorta via an interposed iliac artery, and in one case, directly to the hepatic artery. After PVA, all transplants showed regular initial function. Two patients died postoperatively after 19 and 50 days, of intra-abdominal haemorrhage and liver necrosis with thrombosis of the portal vein, respectively. A further patient had previously developed fibrosis of the liver, which led to the death of the patient 11 months after PVA. In the remaining patient, chronic rejection requiring re-transplantation developed 24 months after PVA had been performed. These unfavourable results prompt the conclusion that PVA cannot be recommended as a standard clinical procedure.

Keywords Portal vein arterialization · Liver transplantation · Portal vein thrombosis

Introduction

In many centres, non-recanalizable portal vein thrombosis (PVT) is considered a contra-indication for liver transplantation [10, 14]. Such a situation always requires complicated vascular reconstruction, and is associated with a considerably increased peri-operative risk [15]. Aimed, nevertheless, at achieving adequate perfusion of the transplant even in such a situation, complete arterialization of the portal vein (PVA) has recently been propagated as a technically relatively simple procedure [2, 4, 5, 6, 14]. Some authors have also reported that PVA can also be employed in auxiliary liver transplantations [4, 6, 13]. Experience with the few patients that have undergone transplantation by this technique has been interpreted as a demonstration of both the technical feasibility of PVA and the regular initial function of the transplant [2, 3, 4, 5, 6, 7, 14]. However, the long-term effects of this unphysiological vascular reconstruction, in particular possible morphological changes in the transplant, have not yet been adequately investigated. The present report describes our experience with PVA in four patients undergoing orthotopic liver transplantation.

Patients and methods

Patients

In a series of 215 liver-transplanted patients, five (2%) had non-recanalizable PVT. In four cases (mean age 52 years), the portal vein was re-vascularized by complete PVA; in the fifth patient, a portocaval transposition was carried out [13]. In three of the arterialized patients, the PVT had been diagnosed before transplantation by means of duplex-ultrasonography and/or angiography. One patient underwent elective transplantation (patient 3), while three underwent urgent surgery (UNOS medical urgency status 1). Prior to surgery, all these patients were already in the ICU, two being on dialysis for renal failure.

Patient 1 had undergone elective transplantation 5 weeks previously, and the donor portal vein was anastomosed to the superior mesenteric vein by a jump graft. To deal with inadequate flow in the portal vein resulting in thrombosis, an arterioportal fistula (interposed great saphenous vein) was first created between the aorta and the portal vein. When this fistula occluded, resulting in renewed PVT, a re-transplantation with PVA was carried out. In the second patient, (patient 2), an emergency transplantation had been performed 8 weeks earlier to treat hepatitis B cirrhosis with acute deterioration. Already in the early postoperative phase, the portal anastomosis showed a high-grade stenosis that led to a complete thrombosis of the portal vein, requiring emergency re-transplantation. Thrombectomy failed to achieve adequate portal flow, and PVA was also performed. In one other patient, (patient 4) who had undergone emergency transplantation and whose status was extremely poor due to a fulminant hepatitis B infection, a PVT was first discovered intraoperatively (Table 1).

Surgical technique

In three patients, we effected arterialization by interposing a segment of the donor iliac artery between the recipient aorta (2 × suprarenal, 1× infrarenal) and portal vein. In these cases, the donor hepatic artery was anastomosed to the point of origin of the recipient gastroduodenal artery. In one case, the portal vein was connected directly to a large-calibre recipient hepatic artery (Fig. 1). In this case, the donor hepatic artery was anastomosed to the aorta via an interposed iliac artery. In none of the cases was intra-operative measurement of pressure or flow carried out, nor were blood flow-reducing measures undertaken. For prevention of thrombosis due to turbulent flow resulting from calibre mismatch of the anastomosed vessels, the patients, in whom plasma coagulation parameters had returned to normal, received anticoagulation treatment, first with heparin and then, on discharge, with phenprocoumon (Marcumar).

Results

Initial transplant function and postoperative course

The portal vein flow, measured on the first postoperative day by duplex-ultrasonography, varied between 0.42 and 2.80 m/s. All liver grafts showed regular initial function. The transaminase peak was reached within the first 2 postoperative days at levels between 108 and 779 U/l for AST, and subsequently decreased to the normal range in all four patients. Patient 3, a woman who had undergone elective transplantation, had a complication-free course and was discharged home with normal liver parameters on the 33rd postoperative day. In all three patients undergoing urgent transplantation with PVA, however, the in-hospital course was protracted. In one case (patient 2), re-laparotomy became necessary on the 12th postoperative day, due to leakage of the choledochojejunostomy. Subsequently, the arterialized portal vein became obstructed by a thrombus, and the patient died of hepatic failure on postoperative day 50. The second patient, (patient 2), developed severe right heart failure with recurrent pleural and pericardiac effusions, together with persistent renal failure, and recovered only very slowly from the transplantation operation. This patient was discharged home 4 months after the operation with completely normal liver function. In the last patient (patient 4), who had persistent portal hypertension, bleeding from retroperitoneal collaterals developed in the 3rd postoperative week. This could not be managed surgically, which finally led to the death of the patient.

Long-term results

Patient 2 developed re-infection of the transplant with the hepatic B virus, which, however, responded positively to treatment with lamivudine. Ten months after PVA, biopsy material revealed veno-occlusive disease and marked peri-cellular and peri-sinusoidal fibrosis of the liver, which was rapidly progressive and led to terminal transplant failure 1 month later. Patient 3 developed a chronic rejection reaction 3 months after orthotopic liver transplantation (OLT). During biopsy of the arterialized liver, a severe intra-abdominal haemorrhage occurred, requiring laparotomy and repeated abdominal tamponade. This patient developed multi-organ failure, from which she finally recovered after several months of intensive care. Her initially severe cholestasis was reversible under increased immunosuppression, with serum bilirubin decreasing from 60 mg/dl to 2 mg/dl. Two years after OLT, an irreversible ductopenic chronic rejection reaction made re-transplantation necessary, on the occasion of which the portal vein was anastomosed to a large suprapancreatic collateral vein. This patient was suffering from type 2 diabetes, and a pancreas transplantation was carried out at the same time. At present, this patient is still alive with a normally functioning transplant 3 years postoperatively.

Discussion

PVA is current practice, but has rarely been applied in liver transplantation. In the literature, this technique has

Table 1 Indications, technique, clinical course, and outcome of patients undergoing arterialization of the portal vein during liver transplantation (*PV* portal vein, *HA* hepatic artery, *PTx* pancreatic transplantation)

Patient	Primary indication	Age (years)	Urgency	Vascular reconstruction	Portal blood flow (m/sec)		Peak AST (U/l)	Early postoperative complications	Discharge (days after OLT)	Long-term complications	Outcome
					Maximum	Mean					
1	Alcoholic cirrhosis	35	Urgent Re-OLT	PV to recipient infrarenal aorta via iliac artery graft interposition, HA to HA	0.42	0.29	254	Leakage of biliary anastomosis, recurrent bleeding from abdominal wall, thrombosis of the arterialized portal vein	–	–	Died of liver necrosis 50 days after OLT
2	Hepatitis B cirrhosis	57	Urgent Re-OLT	PV to recipient infra-diaphragmatic aorta via iliac artery graft interposition, HA to HA	2.82	0.80	779	Right heart failure, pleural effusions, renal failure	117	Chronic renal failure, recurrence of hepatitis B, stenosis of arterioportal anastomosis, liver fibrosis	Died of liver fibrosis 11 months after re-OLT
3	Hepatitis B cirrhosis	54	Elective	PV to recipient HA, HA to infra-diaphragmatic aorta via iliac artery graft interposition	0.64	0.29	491	None	33	Chronic rejection, intra-abdominal bleeding after liver biopsy at 4 months, transient renal failure, new-onset diabetes	Alive, re-OLT (+ PTx) because of chronic rejection 2 years after primary transplant
4	Hepatitis B cirrhosis	68	Urgent	PV to recipient infra-diaphragmatic aorta via iliac artery graft interposition, HA to HA	2.50	0.99	108	Right heart failure, severe ascites and pleural effusions, recurrent bleeding from persisting retroperitoneal collaterals	–	–	Died 18 days after OLT because of intra-abdominal haemorrhage

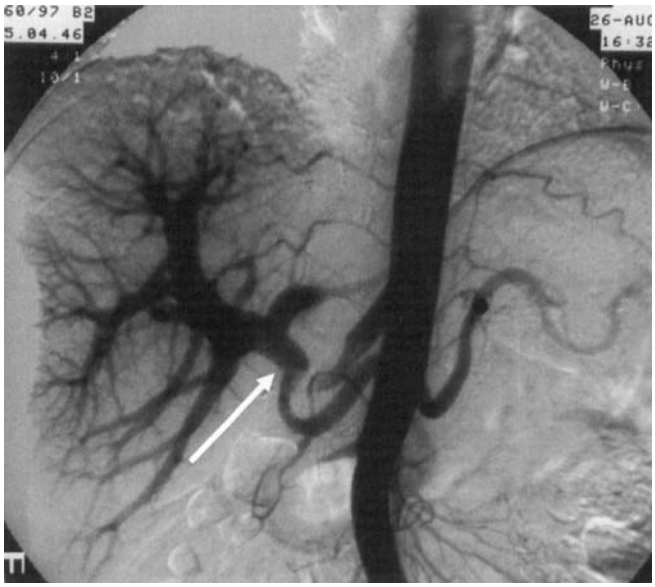

Fig. 1 Angiography of the arterialized portal vein. Anastomosis of the donor portal vein to the recipient hepatic artery

been described in a total of only seven cases of orthotopic, and four of auxiliary transplantation (Table 2) [2, 3, 4, 5, 6, 14]. The authors describe regular initial function of the arterialized transplant, as was the case in our own group of patients. From this we may conclude that fears of elevated pressure in the portal vein leading to necrosis of the liver parenchyma are unfounded [9]. Rather, shearing forces acting on the endothelium even appear to have a stimulating effect on liver regeneration [12].

For OLT – in contrast to auxiliary liver transplantation (ALT) – the long-term effects of PVA are of great importance, since the graft is meant to be permanent. Here, however, our experience is sparse. The first cases were described by Erhard in a small series of only three transplantations (of which one was a split graft), with the donor portal vein being connected to the infrarenal aorta by an interposed iliac artery segment [3, 5]. In two of the cases, PVA was done primarily during the transplantation, and in one, on the first postoperative day after a week portal return had led to a PVT. All grafts initially showed regular function. At the time of the last follow-up (6, 10 and 12 months after OLT), the portal vein was freely perfused, and there were no clinical or bioptic signs of graft dysfunction [3, 5]. Stange et al. reported similar results in a series of three transplantations with PVA [14]. Here, arterialization was effected either by connection via an interposed vessel segment to the aorta, or directly to the recipient hepatic artery. Here too, all grafts showed regular function. Follow-up at 6, 12, and 24 months showed the patient to be in good clinical condition. Biopsy material obtained 6 and 12 months after the operation showed no pathological changes [14]. In all of these six cases, the arterioportal shunt had been banded to reduce portal vein pressure and flow. A further case was reported by Aspinall et al. [2], in which, 1 day after re-transplantation had been necessitated by a PVT, PVA was carried out because of re-thrombosis caused by insufficient portal flow. Although levels of transaminases and bilirubin decreased postoperatively, the patient developed a severe (grade IV) encephalopathy, and died of sepsis 5 weeks later [2] (Table 2).

Table 2 Literature review; technique, complications, and outcome after PVA in liver transplantations (*ALF* acute liver failure)

Reference	Patient	Transplant technique	Site of arterioportal anastomosis	Complications	Outcome (follow-up)
[3, 5]	1	Orthotopic	Aorta (iliac artery graft)	Persisting portal hypertension: mesenterico-portal shunt 4 weeks after PVA	Alive and well at 12 months
	2	Auxiliary	Aorta (iliac artery graft)	–	Alive and well at 10 months
	3	Auxiliary	Aorta (iliac artery graft)	Small bowel perforation, peritonitis, multiple organ failure 11 days after transplant	Died with functioning graft, 17 days after ALT (sepsis)
	4	Auxiliary	Not stated	CMV disease	Died with functioning graft 3 months after ALT (CMV disease)
	5	Orthotopic	Not stated	–	Alive, auxiliary graft removed 6 weeks after ALT, 4 weeks later OLT due to ALF
	6	Orthotopic, split graft	Not stated	–	Alive and well
[2]	7	Orthotopic	Aorta (iliac artery graft)	Encephalopathy, septic shock	Died, 5 weeks after transplant (sepsis)
[4]	8	Auxiliary	Aorta (iliac artery graft)	Rejection, renal failure	Alive and well, 6 months, auxiliary graft removed 2.5 months after ALT
[12]	9	Orthotopic	Hepatic artery	–	Alive and well at 24 months
	10	Orthotopic	Hepatic artery	Recurrent right heart failure	Alive and well at 12 months
	11	Orthotopic	Aorta (iliac artery graft)	–	Alive and well at 6 months

In contrast to the mostly positive experience reported in the literature, the unfavourable outcomes seen in our own patients may, at least in part, have been caused by the PVA. While the chronic rejection reaction seen in one of our patients (with low portal vein flow) cannot definitively be causally related to the PVA, two of the deaths in our group might have been caused by "over-arterialization" of the liver. In these two cases, the portal vein had been anastomosed to the aorta via a large-calibre iliac artery with no banding, and maximal portal vein flows of more than 2 m/s were measured. Subsequent fibrosis developing in patients (patient 2) undergoing PVA with no pressure reduction has repeatedly been described by other investigators [1, 8, 9]. The right heart failure observed in two of our cases was probably also due to too large a shunt volume. This might be supported by Stange et al., who observed a regression of these cardiac symptoms on reducing portal vein flow (via embolization of the supplying artery) [14].

A major problem of PVA is that it leaves portal hypertension unchanged, although it wards off liver failure. As in the case of one of our patients (patient 4) who died of uncontrollable haemorrhage, this problem has also been reported by other authors.

In the series reported by Erhard et al. [5], a mesenterico-caval shunt had to be created in one patient undergoing PVA. Apart from the danger of a life-threatening haemorrhage occurring when obtaining a biopsy of the arterialized liver, we consider the discrepancy in calibre between portal vein and supplying arterial vessel to be another major problem associated with PVA. This results in flow turbulence leading to intravascular formation of thrombi together with the danger of micro-embolization in the peripheral portal vein tributaries, or even occlusion of the vessel by a thrombus (patient 1).

The above-mentioned problems associated with the unphysiological vascular reconstruction – in particular the persistence of portal hypertension – clearly show that PVA in OLT is an option that should be employed only in exceptional cases when no other re-vascularization options are available. In retrospect, it is possible that in our patients the indication for PVA was established too liberally, with too little consideration having been given to a more physiological vascular reconstruction (e.g. a jump graft to the superior mesenteric vein). Thus, in a female patient (number 3) undergoing re-transplantation after PVA, the portal vein was successfully anastomosed, long-term, to a suprapancreatic collateral vessel. Other authors have also recommended the mesenteric vein, the middle colic and the left renal vein, or cavoportal transposition as alternatives in PVT [11, 15]. In order to be able to plan such complex re-vascularization better, however, accurate imaging of the visceral vessels – preferentially, by means of angio-NMR or multiphase spiral CT with 3D reconstruction – should be done prior to transplantation.

In the last instance, the unfavourable results achieved in our group of patients may be explained (but not proven) on the basis of the problems associated with PVA described above, since the poor results were obtained exclusively from urgent transplantation in patients who were already in a very poor general state of health. Until long-term results are available, PVA should be employed only in carefully selected patients for whom no other vascular construction options are open. If it is carried out, appropriate limitation of pressure and flow should be applied [14].

Acknowledgements This study was supported by the Johannes and Frieda Marohn Foundation of the University of Erlangen-Nuremberg.

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