TRANSPLANT INTERNATIONAL

Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Transcapsular arterial neovascularization of liver transplants increases the risk of intraoperative bleeding during retransplantation

Jochen Herrmann,[1] Uta Herden,[2] Rainer Ganschow,[3] Kay U. Petersen,[7] Felix Schmid,[4] Thorsten Derlin,[5] Andreas Koops,[5] Sven Peine,[6] Martina Sterneck,[2] Lutz Fischer[2] and Knut Helmke[1]

1 Department of Paediatric Radiology, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
2 Hepatobiliary and Transplant Surgery, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
3 Paediatric Hepatology and Liver Transplantation, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
4 Anaesthesiology, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
5 Diagnostic and Interventional Radiology, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
6 Transfusional Medicine, University Medical Centre Hamburg-Eppendorf, Hamburg, Germany
7 Department of Psychiatry and Psychotherapy, Section for Addiction Research and Therapy, University Hospital of Tübingen, Tübingen, Germany

Keywords
blood loss, children, doppler ultrasound, liver transplantation, neovascularization, transfusion.

Correspondence
Dr. Jochen Herrmann, Department of Paediatric Radiology, University Medical Centre Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany.
Tel.: +49 40 741052712;
fax: +49 40 741054964;
e-mail: j.herrmann@uke.de

Conflict of Interest
The authors have declared no conflicts of interest.

Received: 6 November 2012
Revision requested: 18 November 2012
Accepted: 23 December 2012
Published online: 25 January 2013

doi:10.1111/tri.12062

Summary

Arterial neovascularization of liver grafts can be a source of significant blood loss during retransplantation. This study evaluated the effect of transcapsular arterial neovascularization on intraoperative blood loss during retransplantation and long-term follow-up. Eleven consecutive patients with transcapsular arterial neovascularization (seven male, four female; nine children, two adults; mean age 12.3 ± 16.3 years) and the same number of matched control patients were analysed. Blood loss was calculated based on transfusion requirements. The volume of transfused units of red blood cells per kilogram bodyweight until hepatectomy and during the entire procedure was significantly higher in patients with neovascularization than in control patients (0.32 ± 0.21 vs. 0.14 ± 0.11, and 0.94 ± 0.83 vs. 0.36 ± 0.38 respectively; *P*-values 0.027). Neovascularization was associated with extensive intra-abdominal adhesions and a longer operating time until hepatectomy (175.6 ± 52.1 min vs. 124.3 ± 34.9 min, *P*-value 0.015). Postoperative revisions were performed more frequently in patients with neovessels. Graft survival did not differ between groups. Assessment for transcapsular arterial neovascularization should be included in preoperative Doppler ultrasound protocols to identify patients at risk of a complicated intra- and postoperative course in case of retransplantation.

Introduction

High-volume blood loss during liver transplantation (LTX) is a serious complication associated with increased mortality and morbidity [1–4]. Individual needs for blood transfusions are difficult to predict preoperatively and profuse bleeding can have multiple causes [5–9]. Among surgical causes, previous operation and retransplantation leading to intra-abdominal adhesions have been identified as substantial risk factors [10–13].

Development of atypical arterial collateral vessels is observed in some patients with chronic failure after liver transplantation. Transection of these vessels may be a direct cause of intraoperative blood loss during retransplantation in certain cases [11,14]. This phenomenon has been termed transcapsular arterial neovascularization and was sporadically described as angiographic findings in the context of hepatic artery thrombosis [15–19]. The possibility to use high-resolution Doppler ultrasound (US) for diagnosis of transcapsular arterial neovascularization was first reported

by Wachsberg *et al.* [19–21]. A recent follow-up study of our group noted this complication in 8.4% of all transplantations [20]. As arterial neovascularization was associated with a high incidence of subsequent retransplantation at a later stage, the prevalence of this finding in patients requiring re-LTX is probably underestimated. The purpose of this study was to determine whether transcapsular arterial neovascularization of the graft has an effect on intraoperative transfusion requirements and outcome in case of retransplantation.

Patients and methods

This retrospective case–control study was approved by the local ethics committee with a waiver of informed consent. Eleven consecutive patients who developed transcapsular arterial neovascularization after LTX and who required retransplantation at our university hospital during the period from 01.01.2000 until 31.12.2008 were analysed retrospectively (11 patients, 7 male, 4 female; 9 children, 2 adults; mean age 12.3 ± 16.3 years, range 1.5–53 years). During this period, a total of 863 LTX had been performed in 721 patients at our institution; the retransplantation rate was 19.7% (142 of 721). Seven paediatric patients were part of one previous publication reporting prevalence of neovascularization and prognostic implications for the original graft [20]. In addition, the same number of control patients was selected by querying the local liver transplant database and applying the following criteria: (i) no evidence for transcapsular arterial neovascularization; (ii) same number of LTXs and an interval between the previous LTX of greater than 30 days; (iii) similar age (in case of paediatric patients, similar age group, 0–2 years, 3–6 years, 7–18 years); (iv) similar reason for initial transplantation (cholestatic or noncholestatic liver disease); (v) similar type of retransplanted graft (full graft, reduced graft, split graft - cadaveric or split graft living-related donor). The matching criteria were applied in descending order. If a control patient could not be identified with all criteria applied, divergence was tolerated with regard to the type of re-LTX and, in adults, the reason for transplantation. Data, including patient demographics, peri-operative findings, complications and outcomes, were extracted from the liver transplant database and from records of surgery and anaesthesia. Follow-up was performed until January 2011.

Arterial neovascularization

Diagnosis of transcapsular arterial neovascularization was based on colour Doppler ultrasound findings and defined as formation of vessels at the site of the hepatic capsule, with hepatopetal arterial flow from the periphery towards the centre of the liver [20]. The assessment of arterial neovascularization was part of a standardized Doppler US protocol applied in all patients and control subjects. Doppler US investigations were performed by a single, experienced senior radiologist (K.H.) using a commercial scanner (HDI® 5000 SonoCT®, Philips Medical Systems, The Netherlands) with an L10–5 MHz linear array transducer and a C7–4 MHz curved array transducer.

Replacement therapy

Intraoperative blood loss was evaluated based on transfusion requirements of red blood cells (RBCs) in units per kilogram of bodyweight until hepatectomy and until the end of surgery. In two patients with autologous transfusion using a red blood salvage procedure (Cell Saver®, Haemonetics, Braintree, MA, USA), the transfused red blood volume was calculated as follows: $Vt = Vh + Va/277 \times 0.5/0.59$, where Vt is the total amount of transfused blood, Vh is the quantity of transfused homologous RBCs, and Va is the transfused volume (ml) of autologous red blood [6]. Adjustment was based on an RBC volume of 277 ml and a haematocrit of 0.59; the haematocrit in autologous transfusion was 0.5.

Common criteria for intraoperative transfusion of blood and blood products were applied. Blood loss was compensated by blood transfusion to maintain a haematocrit between 25% and 30%. Platelets were administered to maintain a platelet count of 50 000/l or greater. Fresh frozen plasma (FFP) was given when the prothrombin time (expressed as the international normalized ratio, INR) was >3. Cryoprecipitates were given when the fibrinogen concentration was <80 mg/dl. Antifibrinolytics were not used.

Intraoperative and postoperative findings

Qualitative aspects of the surgical reports included the extent of adhesions and a description of bleeding during the hepatectomy. Extensive adhesions were diagnosed when substantial problems with adhesiolysis were noted in the reports. Bleeding was categorized as either diffuse or localized. Haemostatic methods were noted if mentioned in the reports. Outcome variables comprised days spent in the intensive care unit after re-LTX, surgical revisions required, surgical revisions required for intra-abdominal bleeding, deaths during follow-up, organ survival rate and organ survival time.

Statistical analysis

One-sided Student's *t*-tests were applied to test whether metric intra- and postoperative variables (including transfusion requirements, duration until hepatectomy, duration of anaesthesia, warm ischaemic time, cold ischaemic time and days in the intensive care unit) were higher in patients

Table 1. Pretransplantation clinical and laboratory data.

Parameter	Arterial neovascularization (n = 11)	Controls (n = 11)	P value
Age (years)	12.3 ± 16.3	12.0 ± 17.66	0.968
Children (n = 9)	5.48 ± 4.03 (1.2–12.2)	5.11 ± 3.96 (1.1–12.2)	0.848
Adult patients (n = 2)	33, 53	25, 61	
Sex (M/F)	7/4	5/6	0.335
Weight (kg)	24.45 ± 19.76	29.21 ± 27.23	0.644
Height (cm)	113.27 ± 37.6	115.09 ± 43.65	0.918
Primary diagnosis			
Biliary atresia	6	8	
PFIC	1	0	
Alagille syndrome	1	0	
Haemochromatosis	1	0	
Crigler-Najjar syndrome	0	1	
Alcoholic cirrhosis	1	0	
Hepatitis C cirrhosis	0	1	
PSC	1	0	
Fulminant hepatitis	0	1	
No. of re-LTX			1.0
First	7	7	
Second	2	2	
Third	2	2	
Time since previous LTX (days)	822 (234–3216)	521 (132–3711)	0.869
Type of explanted graft			
Orthotopic LTX, full graft	2	2	
Reduced graft	1	1	
Split, cadaveric	4	6	
Split, living-related donor	4	2	
Type of implanted graft			
Orthotopic LTX, full graft	3	1	
Reduced graft	3	1	
Split, cadaveric	4	7	
Split, living-related donor	1	2	
Preoperative patient status (no.)			0.476
High-urgency	2	0	
Chronic disease	9	11	
Immediately pre re-LTX			
MELD Score	16.1 ± 7.7	14.0 ± 6.8	0.546
Haemoglobin (mg/dl)	9.5 ± 1.9	9.9 ± 1.9	0.648
C-reactive protein (mg/l)	22.6 ± 32.44	19.7 ± 22.8	0.839
INR	1.02 ± 0.31	1.37 ± 0.75	0.159
Platelet count ($\times 10^9$/l)	248 ± 181	207 ± 66	0.540

Data are given as means and standard deviations, unless otherwise indicated. For the time since previous LTX, median and range are provided. Preoperative patient status was defined according to the Eurotransplant liver allocation system, differentiating high-urgency listing from chronic disease (elective). PSC – primary sclerosing cholangitis; PFIC – progressive familial intrahepatic cholestasis; INR – international normalized ratio.

with neovascularization than in control subjects. Metric preoperative variables were compared using two-sided t-tests. Chi-square-tests were used to compare the frequency of occurrence of nonmetric variables. A failure time analysis was performed to assess the relation between arterial neovascularization and graft survival time after retransplantation. The Tarone–Ware test was used to compare graft survival functions in patients with and without neovascularization. P-values <0.05 were considered statistically significant. Statistical tests were carried out using IBM SPSS statistics, version 20.0.0.

Results

Patients

Eleven patients with transcapsular arterial neovascularization were retransplanted during the period 2000–2008, including nine children and two adult patients. The control group comprised the same number of children and adults with the same number of previous transplantations. The indication for retransplantation was chronic transplant failure in all cases. In patients with neovascularization, transplant failure was attributed to parenchymal damage

induced in eight cases by hepatic artery thrombosis, even though the hepatic artery thrombosis was surgically revised immediately in six of those eight patients. Less frequent causes of transplant failure were hepatitis B cirrhosis (one patient), chronic rejection (one patient) and portal vein thrombosis combined with hepatic artery occlusion (one patient). In the controls, the main reason for transplant failure was chronic rejection (8/11 patients). Less frequent causes were chronic portal vein thrombosis (one patient) and chronic hepatic artery thrombosis (two patients). Pretransplant clinical and laboratory data are summarized in Table 1.

Arterial neovascularization

The sites of transcapsular arterial neovascularization as detected using Doppler US were the diaphragmatic and abdominal wall attachments. In most patients, multiple arterial neovessels were detected (mean, 3; range, 1–6). The mean diameter of the vessels was 2.14 mm (range, 0.6–3.9 mm), and the mean length was 9.95 mm (range from 2.1 to 19.7 mm). Transcapsular vessels displayed an arterial Doppler spectrum, with a mean maximum systolic velocity of 29.3 cm/s (range, 9.9–48.9 cm/s) and a mean resistance index of 0.61 (range, 0.49–0.7). The flow direction was reversed and directed towards the centre of the liver (hepatopetal) (Fig. 1a, Fig. 1b, Fig. 1c).

Intraoperative findings

Extensive intra-abdominal adhesions causing difficulties during hepatectomy were associated with a preoperative diagnosis of arterial neovascularization and noted in 8/11 patients (72.7%) compared with 3/11 controls (27.3%, *P*-value 0.033). During the dissection, bowel perforation and rupture of the portal vein occurred in two patients with neovessels. The time required until hepatectomy was longer in patients with neovascularization than in the controls (175.6 ± 52.1 min vs. 124.3 ± 34.9 min, *P*-value 0.015) (Table 2).

Intraoperative bleeding and transfusions requirements

Diffuse bleeding was noted in three patients during the hepatectomy. Circumscribed bleeding from multiple arterial neovessels at the sites of abdominal attachments occurred in two patients, and selective suturing was needed to achieve haemostasis. Chemical haemostatic agents were not used and the surgical haemostasis was complete at the end of all procedures. The requirement of intraoperative transfusions varied widely between patients, with large standard deviations and ranges. Until completion of hepatectomy and during the entire procedure, the mean quantity of transfused RBCs (in units per kg body weight) was

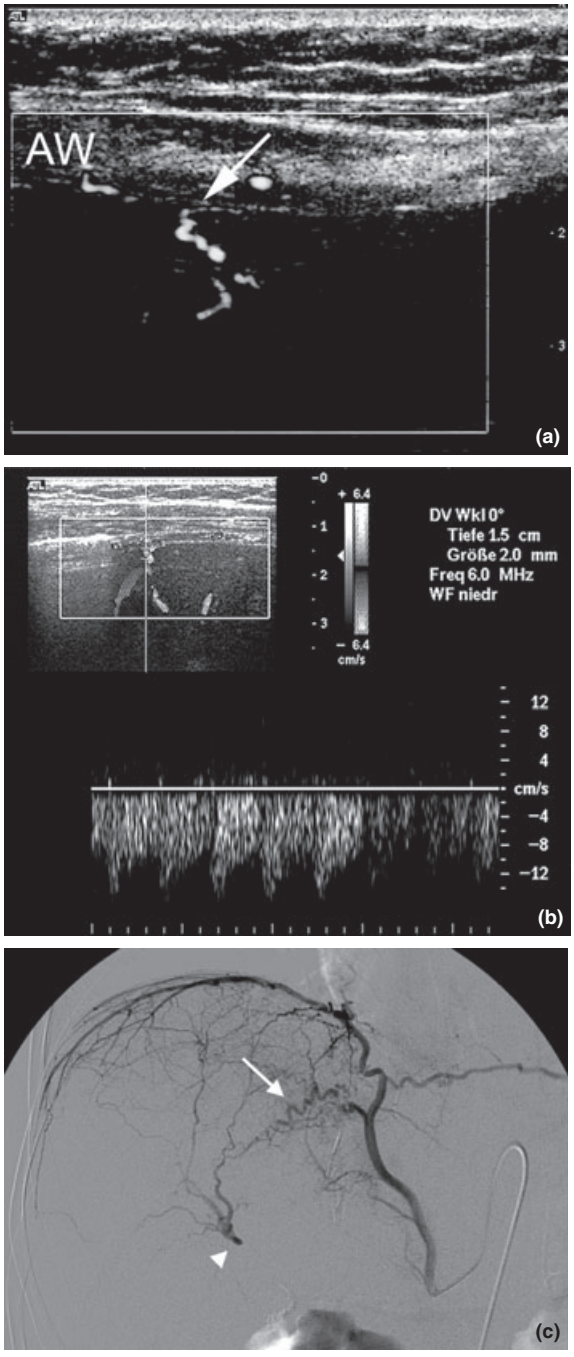

Figure 1 Data from a 33-year old patient after LTX and hepatic artery thrombosis (patient no. 11, Table 3). Doppler ultrasound examination with a 10–5 MHz linear array at the abdominal wall (AW) adhesion demonstrates an atypical vessel at the liver capsule. The corkscrew appearance of the collateral artery can be seen in power angio mode (Fig. 1a, arrow). An arterial flow pattern with flow directed towards the centre of the liver is shown (Fig. 1b). Conventional angiography after selective catheterization of the right main phrenic artery confirms multiple arterial collaterals with the typical corkscrew appearance (Fig. 1c, arrow). A parenchymal connection to the main hepatic artery can be seen. The common hepatic artery is occluded (arrowhead).

Table 2. Duration of surgery and blood products transfused until hepatectomy and during entire LTX.

	Arterial neovascularization (n = 11)	Controls (n = 11)	P value
Duration of anaesthesia (min)	513.3 ± 41.2	495.5 ± 99.9	0.622
Duration until hepatectomy (min)	175.6 ± 52.1	124.3 ± 34.9	0.015
Warm ischaemic time (min)	35.6 ± 10.4	32.3 ± 7.9	0.421
Cold ischaemic time (min)	603.6 ± 177	576 ± 171.2	0.714
Until hepatectomy			
Platelets transfused RBCs transfused (units/kg BW)	0.32 ± 0.21 (0.07–0.65)	0.14 ± 0.11 (0.02–0.19)	0.027
Platelets transfused FFP transfused (units/kg BW)	0.53 ± 0.37 (0.12–1.05)	0.27 ± 0.29 (0.11–1.1)	0.053
Platelets transfused Platelets transfused (units/kg BW)	0.04 ± 0.06 (0–0.11)	0.003 ± 0.01 (0–0.02)	0.024
During entire LTX			
RBCs transfused (units/kg BW)	0.94 ± 0.83 (0.12–2.6)	0.36 ± 0.38 (0.05–1.4)	0.027
FFP transfused (units/kg BW)	1.32 ± 1.01 (0.16–3.52)	0.65 ± 0.66 (0.22–2.5)	0.042
Platelets transfused (units/kg BW)	0.12 ± 0.1 (0–0.28)	0.04 ± 0.07 (0–0.2)	0.039

Numbers are means, standard deviations and ranges.
RBCs – Red Blood Cells; FFP – Fresh Frozen Plasma. All blood components are reported in units per kilogram (kg) body weight (BW).

significantly higher in patients with arterial neovascularization than in the control group (P-value 0.027, Table 2). In 4/9 children with neovessels, massive transfusions of more than 10 units of RBCs were required during the transplantation (mean 43 units, range 13–76 units) compared with 1/9 control patients (14 units). Individual details regarding patients with neovessels and control subjects are presented in Table 3 and Table 4. There was no correlation between the transfusion requirement and the number or maximum diameter of arterial neovessels as detected using Doppler US.

Postoperative events and follow-up

Within 4 weeks of retransplantation, 8/11 patients with previous neovascularization (63.63%) and 3/11 controls (18.18%) needed reoperation (P-value 0.033). A relaparotomy for intra-abdominal bleeding was performed in 4/11 patients with neovessels and in 2/11 controls. The mean stay in the intensive care unit after re-LTX tended to be longer in patients with neovascularization (11.91 ± 13.9 days vs. 5.64 ± 4.39 days; P-value 0.075). Patient and organ survival were not different between groups (Table 5).

Discussion

This study investigated the impact of transcapsular arterial neovascularization on liver retransplantation in terms of intraoperative transfusion requirements, complications and outcome. The phenomenon is characterized by the formation of bridging communications between the abdominal attachments, adjacent organs and the liver parenchyma [20,21]. During hepatectomy and mobilization of the graft, these vascular structures are highly vulnerable and can be a source of high-volume intraoperative bleeding, which may be difficult for the surgeon to control [11,14]. In accordance with these case reports, we found that the need for blood transfusions was substantially higher in patients with arterial neovascularization than in control subjects. The mean volume of transfused RBCs until hepatectomy was more than twice as high as in the control group. In our series, 4 of 11 patients required massive transfusions to compensate for intraoperative bleeding (>10 units per LTX; mean transfused RBCs 42 units, range 13–76 units). Larger vessels needed selective suturing to achieve haemostasis.

In our study, the number of arterial neovessels, vessel diameter and maximum flow velocity were not associated with intraoperative transfusion requirements. One explanation is that the preoperative Doppler ultrasound may underestimate the true extent of arterial neovascularization, as deeper areas of the hepatic capsule may be obscured by superimposition of bowel loops and other structures. Another explanation could be that intraoperative bleeding is not caused solely by transection of collateral vessels, but may also be a consequence of associated pathology.

Neovascularization is necessarily associated with the formation of intra-abdominal adhesions, and the proliferation of vascular structures is a precondition for the fibrous bands to develop [22,23]. Both processes are based on a fibrin matrix initiated by peritoneal injury after surgery, and are reinforced by inflammatory and ischaemic processes [24]. In our study, preoperative diagnosis of arterial neovascularization was associated with extensive intra-abdominal adhesions noted during surgery. Difficulties during dissection of adhesions contributed to a significantly longer time needed for the recipient's hepatectomy. Major complications directly attributable to extensive adhesions were rupture of the portal vein during dissection and bowel perforation, noted in two patients.

Postoperative revisions were needed in the majority of patients with arterial neovascularization (7/11 patients, 63.3%), which was significantly more frequent than in the control group. The reasons for relaparotomy varied;

Table 3. Individual details of patients with transcapsular arterial neovascularization and liver retransplantation.

Patient No./ Age/ Sex	Reason for chronic transplant failure and Re-LTX	Type of failing graft/ No. of LTX/ Days to previous LTX	Intraoperative findings	RBC transfusion in units (units/kg BW)	Postoperative course
1/1.5/m	HAT, cholangitis	SPLIT-CAD/2nd LTX/249 days	Adhesions, diffuse bleeding	7 (0.78)	Uncomplicated
2/8.7/f	HAT, liver abscess	OLT/4th LTX/822 days	Extensive adhesions, multiple neovessels requiring ligation, portal vein rupture	36 (1.80)	Laparotomy for large perihepatic haematoma, no origin visible (day 2)
3/10.1/f	Hepatitis B cirrhosis	SPLIT-LR/2nd LTX/3216 days	Extensive adhesions, massive diffuse bleeding	76 (2.62)	Laparotomy for bleeding from multiple small sites (day 1); sepsis; biliary dilatation, percutaneous drainage
4/2.3/m	HAT, cholangitis	RED/2nd LTX/751 days	Extensive adhesions, bowel perforation, peritonitis	5 (0.56)	Laparotomy, small bowel perforation (day 14).
5/1.2/m	Chronic rejection, recurrent cholangitis	SPLIT-LR/2nd LTX/234 days	Extensive adhesions	5 (0.63)	Laparotomy, revision hepatic artery (day 1)
6/4.9/m	HAT, cholangitis	SPLIT-LR/2nd LTX/1448 days	Adhesions	2 (0.13)	Laparotomy for malperfusion (day 2)
7/2.6/m	HAT, cholangitis	SPLIT-LR/2nd LTX/756 days	Adhesions	3 (0.25)	Blood loss, replacement therapy (day 1)
8/12.2/m	HAT, liver abscess	SPLIT-CAD/3rd LTX/517 days	Extensive adhesions, diffuse bleeding	50.3 (2.01)	Laparotomy, perihepatic haematoma, no origin visible (day 1)
9/5.8/f	Portal vein thrombosis	SPLIT-CAD/2nd LTX/1860 days	Extensive adhesions, no hepatic artery	15.3 (0.85)	Blood loss, replacement therapy (until day 6)
10/53/f	HAT, liver abscess	SPLIT-CAD/3rd LTX/1452 days	Extensive adhesions, combined transplantation liver and kidney	8 (0.13)	Blood loss, replacement therapy (day 1); sepsis; laparotomy, revision of biliary anastomosis (day 7)
11/33/m	HAT, liver abscess	OLT/4th LTX/925 days	Extensive adhesions, multiple neovessels requiring ligation, massive bleeding	37 (0.62)	Laparotomy for perihepatic haemorrhage, origin from the abdominal attachments (day 1)

HAT– hepatic artery thrombosis; SPLIT-CAD – Split, cadaveric; SPLIT-LR – Split, living-related; RED – reduced graft; No. – number; RBC – red blood cell transfusion intraoperatively, provided in units and in units per kilogram (kg) bodyweight (BW).

Table 4. Individual details of matched control patients limited to cases with a complicated postoperative course.

Patient No./ Age/ Sex	Reason for chronic transplant failure and Re-LTX	Type of failing graft/ No of LTX/ Days to previous LTX	Intraoperative findings	RBC trans-fusion in units (units/kg BW)	Postoperative course
1/1.5/f	Chronic rejection	SPLIT-LR/2nd LTX/361 days	Adhesions	14 (1.4)	Laparotomy for perihepatic haematoma, no origin visible (day 2)
4/4.8/f	Chronic rejection	SPLIT-CAD/2nd LTX/469 days		9 (0.6)	Laparotomy for diffuse bleeding from split area (day 1 + 3)
10/61/m	Chronic HAT	OLT/3rd LTX/321 days		11 (0.12)	Laparotomy for infected perihepatic seroma (day 12)

Provided are only control matched control patients with a complicated intra or postoperative course requiring surgical intervention. HAT– hepatic artery thrombosis; SPLIT-CAD – Split, cadaveric; SPLIT-LR – Split, living-related; OLT – full graft; No. – number; RBC – red blood cell transfusion intraoperatively, in units and in units per kilogram (kg) bodyweight (BW).

Table 5. Post-transplantation course and follow-up of patients.

	Arterial neovascularization	Controls	*P* value
Post-LTX course			
Days in intensive care unit	11.91 ± 13.9	5.64 ± 4.39	0.075
Patients with reoperation	8/11	3/11	0.033
Patients with reoperation for bleeding	4/11	2/11	
Patients with abdominal infection	2	1	
Patients with hepatic artery thrombosis	0	0	
Follow-up			
Retransplantation	3	2	
Deaths	2	1	
Organ survival time (days)	2252 ± 265	1690 ± 381	0.271

abdominal bleeding and abdominal infection were the most common causes. The more complicated postoperative course in this group may be attributed to a significantly higher quantity of intraoperative blood transfusion, which has been shown to increase postoperative morbidity [1,2,4]. The presence of neovascularization before retransplantation had no impact on long term outcome.

Our study has the following limitations: (i) The study is a retrospective case–control study; such studies are prone to selection bias and depend on the quality of documentation; (ii) The number of patients included is relatively small, but represents the largest series of patients with arterial neovascularization and re-LTX reported to date; (iii) The requirement for blood transfusions is a recognized, but indirect measure of intraoperative blood loss. Transfusion quantity may also depend on the replacement criteria applied; these remained unchanged during the time of our single-centre study; (iv) Blood loss may result from different surgical and medical situations during the LTX. The transfusion requirement was recorded until hepatectomy to determine blood loss associated with adhesiolysis and transection of neovessels. Medical factors, such as the presence of coagulopathies, may also cause increased bleeding. To the best of our knowledge, no patients with coagulation defects were included in this series, and prior studies have shown that coagulation defects do not predict blood product use during LTX [3].

In conclusion, diagnosis of transcapsular arterial neovascularization identifies patients at risk of intra and postoperative complications in case of retransplantation. Bleeding from transection of an arterial collateral network can be

substantial. As bleeding complications represent a main factor for mortality and morbidity during LTX, awareness of arterial neovascularization can be important for the surgical and anaesthesia team and to ensure sufficient blood bank support. Neovascularization also identifies patients in whom extensive abdominal adhesions can be expected. As transcapsular arterial neovascularization can be detected using high-resolution ultrasound, preoperative evaluation of patients listed for retransplantation should be performed.

Authorship

All authors have approved this version of the manuscript. Individual contributions to this article were as follows: JH: conception and study design, data collection, drafting of manuscript. UH: conception and study design, data acquisition and matching, critical revision of manuscript. RG: data collection (paediatric data-bank), interpretation of data, critical revision of manuscript. KUP: data analysis, statistics, critical revision of manuscript. FS: acquisition of data (anaesthesiology), critical revision of manuscript. TD: interpretation of data, preparation and critical revision of manuscript. AK: acquisition of data (interventional, adults), critical revision of manuscript. SP: acquisition of data (blood bank, transfusion medicine), manuscript preparation. MS: acquisition of data (adults, clinical), manuscript preparation. LF: acquisition of data (surgery, intraoperative), data interpretation and critical revision. KH: doppler investigations, study design, manuscript preparation and revision.

Funding

The 'Hamburg macht Kinder gesund e.V.' and 'YAEL-Stiftung' organizations provided financial support for maintenance of the local liver transplant database. No other funding.

Acknowledgements

We thank the 'Hamburg macht Kinder gesund e.V.' and the 'YAEL-Stiftung foundations for giving financial support to maintain the local liver transplant database. We also thank Denise Obrecht for her assistance with retrieval of patient information from the database.

References

1. Cacciarelli TV, Keeffe EB, Moore DH, *et al.* Effect of intraoperative blood transfusion on patient outcome in hepatic transplantation. *Arch Surg* 1999; **134**: 25.
2. Hendriks HG, van der Meer J, de Wolf JT, *et al.* Intraoperative blood transfusion requirement is the main determinant of early surgical re-intervention after orthotopic liver transplantation. *Transpl Int* 2005; **17**: 673.
3. Massicotte L, Beaulieu D, Thibeault L, *et al.* Coagulation defects do not predict blood product requirements during liver transplantation. *Transplantation* 2008; **85**: 956.
4. Ramos E, Dalmau A, Sabate A, *et al.* Intraoperative red blood cell transfusion in liver transplantation: influence on patient outcome, prediction of requirements, and measures to reduce them. *Liver Transpl* 2003; **9**: 1320.
5. Ozier Y, Pessione F, Samain E, Courtois F. Institutional variability in transfusion practice for liver transplantation. *Anesth Analg* 2003; **97**: 671.
6. Ozier YM, Le Cam B, Chatellier G, *et al.* Intraoperative blood loss in pediatric liver transplantation: analysis of preoperative risk factors. *Anesth Analg* 1995; **81**: 1142.
7. Brems JJ, Hiatt JR, Colonna JO 2nd, *et al.* Variables influencing the outcome following orthotopic liver transplantation. *Arch Surg* 1987; **122**: 1109.
8. Mor E, Jennings L, Gonwa TA, *et al.* The impact of operative bleeding on outcome in transplantation of the liver. *Surg Gynecol Obstet* 1993; **176**: 219.
9. Shaw BW Jr, Wood RP, Gordon RD, Iwatsuki S, Gillquist WP, Starzl TE. Influence of selected patient variables and operative blood loss on six-month survival following liver transplantation. *Semin Liver Dis* 1985; **5**: 385.
10. Cuervas-Mons V, Rimola A, Van Thiel DH, Gavaler JS, Schade RR, Starzl TE. Does previous abdominal surgery alter the outcome of pediatric patients subjected to orthotopic liver transplantation? *Gastroenterology* 1986; **90**: 853.
11. Shaw BW, Gordon RD, Iwatsuki S, Starzl TE. Hepatic Retransplantation. *Transplant Proc* 1985; **17**: 264.
12. Yang SC, Chen CL, Wang CH, *et al.* Intraoperative blood and fluid administration differences in primary liver transplantation versus liver retransplantation. *Acta Anaesthesiol Taiwan* 2011; **49**: 50.
13. Carlier M, Van Obbergh LJ, Veyckemans F, *et al.* Hemostasis in children undergoing liver transplantation. *Semin Thromb Hemost* 1993; **19**: 218.
14. Pariente D, Riou JY, Schmit P, *et al.* Variability of clinical presentation of hepatic artery thrombosis in pediatric liver transplantation: role of imaging modalities. *Pediatr Radiol* 1990; **20**: 253.
15. Flint EW, Sumkin JH, Zajko AB, Bowen A. Duplex sonography of hepatic artery thrombosis after liver transplantation. *AJR Am J Roentgenol* 1988; **151**: 481.
16. Hall TR, McDiarmid SV, Grant EG, Boechat MI, Busuttil RW. False-negative duplex Doppler studies in children with hepatic artery thrombosis after liver transplantation. *AJR Am J Roentgenol* 1990; **154**: 573.
17. Wozney P, Zajko AB, Bron KM, Point S, Starzl TE. Vascular complications after liver transplantation: a 5-year experience. *AJR Am J Roentgenol* 1986; **147**: 657.
18. Yedlicka JW Jr, Halloran J, Payne WD, *et al.* Angiogenesis after hepatic arterial occlusion in liver transplant patients. *J Vasc Interv Radiol* 1991; **2**: 235.
19. Horrow MM, Blumenthal BM, Reich DJ, Manzarbeitia C. Sonographic diagnosis and outcome of hepatic artery

thrombosis after orthotopic liver transplantation in adults. *AJR Am J Roentgenol* 2007; **189**: 346.
20. Herrmann J, Junge CM, Burdelski M, *et al.* Transcapsular arterial neovascularization after liver transplantation in pediatric patients indicates transplant failure. *Radiology* 2011; **261**: 566.
21. Wachsberg RH, Koneru B, Levine CD. Transcapsular arterial collateralization of a liver allograft after hepatic artery occlusion in an adult: color Doppler ultrasonographic diagnosis. *J Ultrasound Med* 1995; **14**: 859.
22. Duron JJ. Postoperative intraperitoneal adhesion pathophysiology. *Colorectal Dis* 2007; **9**: 14.
23. Thaler K, Mack JA, Berho M, Grotendorst G, Wexner SD, Abramson SR. Coincidence of connective tissue growth factor expression with fibrosis and angiogenesis in postoperative peritoneal adhesion formation. *Eur Surg Res* 2005; **37**: 235.
24. Arung W, Meurisse M, Detry O. Pathophysiology and prevention of postoperative peritoneal adhesions. *World J Gastroenterol* 2011; **17**: 4545.