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ORIGINAL ARTICLE

Infrarenal versus supraceliac aorto-hepatic arterial revascularisation in adult liver transplantation: multicentre retrospective study

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Abstract

When the standard arterial reconstruction is not feasible during liver transplantation (LT), aorto-hepatic arterial reconstruction (AHAR) can be the only solution to save the graft. AHAR can be performed on the infrarenal (IR) or supraceliac (SC) tract of the aorta, but the possible effect on outcome of selecting SC versus IR reconstruction is still unclear. One hundred and twenty consecutive patients who underwent liver transplantation with AHAR in six European centres between January 2003 and December 2018 were retrospectively analysed to ascertain whether the incidence of hepatic artery thrombosis (HAT) was influenced by the type of AHAR (IR-AHAR vs. SC-AHAR). In 56/120 (46.6%) cases, an IR anastomosis was performed, always using an interposition arterial conduit. In the other 64/120 (53.4%) cases, an SC anastomosis was performed; an arterial conduit was used in 45/64 (70.3%) cases. Incidence of early (≤ 30 days) HAT was in 6.2% (4/64) in the SC-AHAR and 10.7% (6/56) IR-AHAR group ($p = 0.512$) whilst incidence of late HAT was significantly lower in the SC-AHAR group (4.7% (3/64) vs 19.6% (11/56) - $p = 0.024$). IR-AHAR was the only independent risk factor for HAT (exp[B] = 3.915; 95% CI 1.400–10.951; $p = 0.009$). When AHAR is necessary at liver transplantation, the use of the supraceliac aorta significantly reduces the incidence of hepatic artery thrombosis and should therefore be recommended whenever possible.

Keywords Liver transplantation · Hepatic artery · Aorto-hepatic arterial reconstruction · Hepatic artery thrombosis · Iliac conduit · Vessel graft

Abbreviations

AHAR	Aorto-Hepatic Arterial Reconstruction
SC	Supraceliac
IR	Infrarenal
HA	Hepatic Artery
HAT	Hepatic artery thrombosis
EAD	Early allograft dysfunction
ERC	Endoscopic retrograde cholangiography
ISGLS	International Study Group of Liver Surgery
LHA	Left hepatic artery
LT	Liver transplantation
PNF	Primary graft non-function

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Introduction

Liver transplantation (LT) is the treatment for several acute and chronic liver diseases, and its long-term benefits have been largely demonstrated [1]. Adequate arterial inflow to the liver graft is crucial for the success of LT. Nowadays a direct anastomosis between the hepatic artery (HA) of the graft and the recipient is the gold standard [2]. However, the recipient HA is not always suitable for effective revascularisation due to anatomical and technical reasons, such as different diameters of the donor and recipient HA, pronounced atherosclerosis, dissection or friability of the intima, stenosis or occlusion of the celiac axis, splenic artery steal syndrome, anatomical variants, damage due to pre-transplant locoregional cancer treatments (such as transarterial chemoembolisation) and the necessity to refashion the anastomosis at re-transplantation (re-LT) [3–7].

In the above-mentioned circumstances, aorto-hepatic arterial reconstruction (AHAR) using the infrarenal (IR) or supraceliac (SC) tract of the abdominal aorta with or without the interposition of an arterial conduit is most often the only alternative to the HA–HA anastomosis [5, 6, 8, 9]. In the case of anastomosis to the infrarenal aorta, the use of a free vessel jump graft is mandatory [10]. On the contrary, the SC region of the aorta can be frequently reached without the need for a supplementary interposition graft (Fig. 1).

With the aim of keeping the direction of the arterial flow to the allograft similar to that of the native HA, the anterior face of the SC aorta is theoretically the optimal site to perform the anastomosis in case of AHAR. However, this approach has not gained wide popularity within the LT community despite its haemodynamic advantage due to the more difficult surgical exposition of the SC aorta. Indeed, this region is located deep between the diaphragmatic pillars and it often contains a venous collateral network related to portal hypertension.

The IR aorta is more readily accessible, and so it is technically easier to perform the anastomosis at this site. However, this approach has three shortcomings: the distance between the IR aorta and the hilum of the allograft is wide, the use of an interposition conduit is necessary and finally, the blood flows upstream in these conduits because the liver is cranial to the infrarenal aorta.

Despite the importance of these technical issues, the effect of different modalities of aorto-hepatic revascularisation on LT outcome has not been clearly evaluated. The aim of the present study is to assess whether SC and IR-AHARs have an impact on the incidence of HAT after LT.

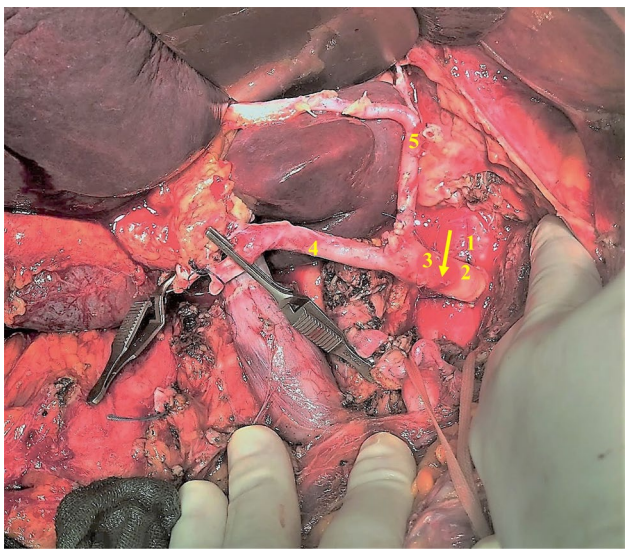


Fig. 1 Intra-operative view of SC-AHAR. An AHAR was performed using an interposition graft between the graft's celiac trunk and the supraceliac tract of the aorta. Supraceliac Aorta (1); Iliac conduit (2); Graft's Celiac Trunk (3); Graft's Gastroduodenal Artery (4); Aberrant Left Hepatic Artery originated from Left Gastric Artery (5); → Anastomosis between Iliac Conduit and Celiac Trunk

Materials and methods

The study included 120 consecutive adult (> 18 years) liver transplant recipients which had an AHAR during the period 2003–2018 in six different European centres (Azienda Opedaliera di Padova, Italy; Ospedali Riuniti Bergamo, Italy; Ospedali Riuniti, Ancona, Italy; Azienda Sanitaria Universitaria Integrata di Udine, Italy; Universitair Ziekenhuis Gent, Belgium; Saint-Luc University Hospitals, Brussels, Belgium). All the data collected were retrospectively analysed. Data from all donors and recipients were available (Tables 1 and 2).

Patients with IR and SC arterial reconstruction were compared, taking also into consideration the use of arterial interposition conduits.

Patients whose graft was obtained from a living or cardiac death donor were excluded.

The decision to perform an AHAR was based on the surgeon's intraoperative assessment of the native HA. Absent or poor arterial flow or an arterial wall that was severely compromised by plaques or intimal dissection was the reason to avoid the standard HA–HA reconstruction.

When an arterial graft was needed, AHAR was performed with the interposition of a free arterial conduit retrieved from the iliac arterial tree of the donor.

The decision on where to perform the AHAR was poorly detailed in the operatory reports; however, a survey amongst the surgeons involved in the present study revealed that the infrarenal site of the abdominal aorta was preferred for the AHAR as it was considered of easier access; presence of vascularised adhesions due to previous surgery or spontaneous

Table 1 Recipient preoperative and donor data

	Supraceliac anastomosis (64 pts)	Infrarenal anastomosis (56 pts)	*p*
Recipients			
Age	55(19–69.81)	51.5(27–68.07)	0.073
Sex (M)	45 (70.3%)	41 (73.2%)	0.882
BMI	24.16 ± 3.63	25.49 ± 4.90	0.149
LT indications			
Viral cirrhosis	32 (50%)	30 (53.6%)	0.847
Graft failure (Re-LT)	16 (25%)	14 (25%)	
Alcoholic cirrhosis	8 (12.5%)	6 (10.7%)	
NASH	5 (7.8%)	2 (3.6%)	
Others	3 (4.7%)	4 (7.1%)	
LT-Number			
1	48 (75%)	42 (75%)	> 0.99
> 1	16 (25%)	14 (25%)	
Re-LT indications			
HAT	3 (4.7%)	7 (12.5%)	0.205*
PNF	5 (7.8%)	2 (3.6%)	
Viral recurrence	3 (4.7%)	1 (1.8%)	
Rejection	2 (3.1%)	0 (0%)	
Others	3 (4.7%)	4 (7.1%)	
CLKT	1 (1.6%)	0 (0%)	> 0.99
Creatinine pre-transplant (mg/dl)	0.97(0.42–3.04)	1.11(0.5–4.56)	**0.041**
Split liver LT	2 (3.1%)	4 (7.1%)	0.416
HCC	23 (35.9%)	17 (30.4%)	0.651
HBV +	16 (25%)	18 (32.1%)	0.507
HCV +	26 (40.6%)	19 (33.9%)	0.571
MELD	20(7–44)	17(7–34)	0.067
TACE pre-transplant	13 (20.3%)	12 (21.4%)	> 0.99
Previous liver resection	1 (1.6%)	3 (5.4%)	0.338
Donors			
Age	60.5(14–87)	55.5(13–86)	0.170
Sex (M)	39(60.9%)	31(55.4%)	0.665
BMI	25.75(15.6–35.4)	24.9(17–39.5)	0.249
DRI	1.82 ± 0.42	1.67 ± 0.36	**0.040**
Hepatic artery variants			
Aberrant right hepatic artery	7 (10.9%)	9 (16.1%)	0.578
Aberrant left hepatic artery	9 (14.1%)	7 (12.5%)	> 0.99
Cause of death			
Cerebrovascular accident	41 (64.1%)	38 (67.9%)	0.501
Trauma	10 (15.6%)	12 (21.4%)	
Anoxia	9 (14.1%)	4 (7.1%)	
Other	4 (6.2%)	2 (3.6%)	

Bold values indicate the level of significance $p \leq 0.05$

BMI Body Mass Index, *HCC* Hepatocellular Carcinoma, *HBV+* hepatitis B virus, *HCV+* hepatitis C virus, *DRI* Donor Risk Index, *LT* Liver transplantation, *CLKT* Combined liver–kidney transplantation

*Analysed in the group of patients with Re-LT indication

bacterial peritonitis that made it hard to reach the infrarenal aorta was the main reason to choose the supraceliac aorta to perform the AHAR.

Arterial reconstruction was performed after portal vein revascularisation in all cases. The time interval between the portal and arterial revascularisation was recorded and defined as arterial ischaemia time.

Table 2 Intra- and postoperative data

	Supraceliac anastomosis (64 pts)	Infrarenal anastomosis (56 pts)	*p*
Intraoperative			
Surgical time (min)	470(170–825)	498.5(240–960)	0.196
Arterial conduit (Yes)	45 (70.3%)	56 (100%)	**< 0.001**
Caval anastomosis			
Piggyback	48 (75%)	34 (60.7%)	**0.048**
Conventional technique	15 (23.4%)	14 (25%)	
Latero-lateral	0 (0%)	5 (8.9%)	
End to side	1 (1.6%)	3 (5.4%)	
Portal anastomosis			
Termino-terminal	63 (98.4%)	54 (96.4%)	0.559
Jump graft	0 (0%)	1 (1.8%)	
Cavo-portal hemitransposition	1 (1.6%)	1 (1.8%)	
Biliary reconstruction			
Duct to duct	51 (79.7%)	42 (75%)	0.822
Roux-en-Y	9 (14.1%)	10 (17.9%)	
External biliary drainage	4 (6.2%)	4 (7.1%)	
Veno-venous Bypass	2 (3.1%)	1 (1.8%)	> 0.99
Homologous PRBCs (cc)	1325(0–6250)	1500(0–6750)	0.689
Autologous PRBCs (cc)	0(0–9062)	0(0–11,000)	0.821
Total PRBCs (cc)	1750(0–14,812)	2000(0–11,950)	0.421
Cold ischaemia time (min)	490(235–697)	477.50(245–989)	0.761
Warm ischaemia time (min)	31(15–195)	40(20–120)	**< 0.001**
Total ischaemia time (min)	535(266–793)	510(305–1054)	0.552
Arterial ischaemia time (min)	55(4–280)	125(19–386)	**< 0.001**
Postoperative			
PNF	1 (1.6%)	0 (0%)	> 0.99
EAD	18 (28.1%)	14 (25%)	0.858
Acute rejection	9 (14.1%)	11 (19.6%)	0.567
HAT	7 (10.9%)	17 (30.4%)	**0.015**
Timing (months)	0.1 (0–3.6)	2 (0.1–147.6)	**0.019**
Early	4 (6.2%)	6 (10.7%)	0.512
Late	3 (4.7%)	11 (19.6%)	**0.024**
Portal vein thrombosis	2 (3.1%)	7 (12.5%)	0.080
Biliary leak	2 (3.1%)	7 (12.5%)	0.080
Biliary stricture	18 (28.1%)	15 (26.8%)	> 0.99
Anastomotic	14 (21.9%)	13 (23.2%)	> 0.99
Non-anastomotic	4 (6.2%)	3 (5.4%)	> 0.99
Re-LT	5 (7.8%)	9 (16.1%)	0.262
Hospital stay (days)	21 (8–90)	21 (8–132)	0.866
Follow-up (months)	47.53 ± 38.32	62.5 ± 58.23	0.432

Bold values indicate the level of significance $p \leq 0.05$

PRBC packed red blood cells, *PNF* Primary Non-Function, *EAD* Early Allograft Dysfunction, *HAT* Hepatic artery thrombosis, *LT* Liver Transplantation

Other postoperative parameters compared between the two groups were biliary strictures and leaks, acute rejection, primary non-function (PNF), early allograft dysfunction (EAD), re-LT, postoperative hospitalisation, and patient and graft survival at 1, 3 and 5 years.

The primary endpoint of the study was HAT as a time-dependent variable. To assess whether the surgical experience influenced the incidence of HAT following AHAR a time trend analysis was carried out in the whole population. The study period was divided into three "eras", namely

2003–2007, 2008–2012 and 2013–2018 and the incidence of HAT in the three different eras was analysed. Thrombosis-free survival was defined as the time between LT and the event or the last follow-up. Univariate and multivariate analyses of the risk factors of HAT were performed on the entire patient cohort.

In all liver recipients with AHAR, a similar prophylactic anti-platelet treatment was used: this consisted of acetylsalicylic acid 100 mg once daily administered since the early postoperative whenever platelet count was above 50.000/μL and no coagulopathy or active bleeding was present. Prophylaxis was maintained in the long term in all patients.

PNF was defined as graft failure that occurred without any obvious cause that led to re-transplantation (re-LT) or to death of the patient within the first postoperative week. EAD was diagnosed following the Olthoff criteria (presence of one or more of the following postoperative values: bilirubin ≥ 10 mg/dl on day 7, INR ≥ 1.6 on day 7 or ALT or AST > 2,000 IU/L within the first 7 days) [11].

Acute rejection was defined as an increase in the biochemical parameters of hepatic enzymes from 5 days to 6 weeks postoperatively, confirmed by corresponding pathology findings [12].

HAT was defined as a thrombotic occlusion of the HA; according to the most commonly used categorisation it was classified as "early" when it occurred within 1 month and as "late" when it occurred over 1 month after LT [3, 13–17]. We also carried out a further categorisation considering those HATs which occurred after 1 year from the time of transplantation that were defined as "very late".

Doppler ultrasound (DUS) was performed daily during the first post-LT week, twice weekly during hospitalisation and once monthly during the first post-LT year in all the patients who performed an AHAR. Computed tomography and/or selective angiography of the celiac trunk was performed to confirm any suspicion of HAT.

Biliary strictures were defined as an abnormal narrowing of the common bile duct that required invasive treatment, such as endoscopic retrograde cholangiography (ERC), percutaneous transhepatic drainage or re-do surgery. Biliary strictures were divided into "anastomotic" and "non-anastomotic". Anastomotic was defined as a segmental narrowing at the site of anastomosis, and non-anastomotic were lesions that occurred at any location in the biliary tree other than the anastomotic region [18].

In accordance with the International Study Group of Liver Surgery (ISGLS), bile leakage was defined as fluid with an increased bilirubin concentration (3 times greater than the serum bilirubin concentration measured at the same time) in the abdominal drain or intra-abdominal fluid on or after postoperative day (POD) 3 or as needed for radiological intervention (i.e., drainage) due to biliary collections or re-laparotomy resulting from bile peritonitis [19]. The radiological diagnosis was performed using T-tube, percutaneous transhepatic or endoscopic cholangiography or cholangio-magnetic resonance imaging.

In cases of T-tube positioning, cholangiography was routinely performed 1 week after the LT and after 3–6 months at the time of T-tube removal.

The ethical committee of the Regione Marche approved the study (number 2018–677).

Statistical analysis

Continuous data are reported as the mean ± SD and were compared using a two-sided Student's *t* test for normally distributed parameters. Continuous data that were not normally distributed are described as the medians (range) and compared using the Wilcoxon–Mann–Whitney test. The optimal cut-off for continuous variables was obtained from analyses of receiver operating characteristic (ROC) curves [20]. Comparisons between groups for categorical variables were performed using the Chi-squared test with Yates' correction or Fisher's exact test, when appropriate. To identify variables that were independent predictors of outcome, a logistic regression analysis with backward stepwise selection was constructed using variables with a significance level of $p < 0.1$. Patient survival was evaluated with the Kaplan–Meier method and compared with the log-rank test. Statistical significance was set at $p < 0.05$. The statistical analysis was performed using IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, NY, USA).

Results

During the time period of the study, 4255 LTs were performed in the centres involved. AHAR was needed in 120 (2.8%) of these cases.

LT was performed with preservation of the recipient vena cava in 91 (75.8%) cases using the piggy-back technique in 82 (68.3%), the latero-lateral cavo-caval anastomosis in 5 (4.2%) and the end-to-side cavo-caval anastomosis techniques in 4 (3.3%) cases. Conventional LT procedure with substitution of the recipient's infrahepatic inferior vena cava was performed in 29 cases (24.2%).

The graft was vascularised through the portal vein using anatomical reconstruction in 117 (97.5%) LTs; two (1.7%) patients needed a cavo-portal hemitransposition and one a venous jump graft to the superior mesenteric vein. Arterial interposition conduits were used in 101 (84.2%) patients who had AHAR. In all of these cases, fresh donor iliac or axillary conduits were used. Cryopreserved conduits were never used. Allograft arterialisation consisted of aorto-hepatic SC anastomosis in 64 (53%) and aorto-hepatic IR anastomosis in 56 (47%) recipients, respectively. An arterial interposition

conduit was used in 45 (70.3%) of the cases of SC-AHAR and 56 (100%) of the cases of IR-AHAR ($p < 0.001$). Biliary reconstruction consisted of a choledocho-choledocostomy in 93 (77.5%) cases, Roux-en-Y hepatico-jejunostomy in 19 (15.8%) cases, and external biliary drainage in 8 (6.7%) cases. External biliary drainage was performed in cases where satisfactory haemostasis was not achieved and packing was performed at the end of LT; the biliary reconstruction was therefore postponed to the time of the re-operation when packing was removed.

The preoperative demographic data of recipients and donors of the both study groups are displayed in Table 1.

The donor risk index (DRI) was greater in the SC-AHAR group compared to the IR-AHAR group (1.82 ± 0.42 vs. 1.67 ± 0.36; $p = 0.04$). A higher prevalence of piggy-back caval anastomosis was also observed in the SC group (75% vs. 60.7% of the cases; $p = 0.048$). Warm and arterial ischaemia times were lower in the SC-AHAR group (31 vs. 40 min and 55 vs. 125 min, respectively: $p = 0.001$). Operative time, blood transfusion, warm and total ischaemia times were similar in the two groups.

HAT occurred in 7 (10.9%) LTs in the SC-AHAR group and 17 (30.4%) LTs in the IR-AHAR group ($p = 0.015$).

One IR-AHAR patient had simultaneous HA and portal vein thrombosis.

HAT developed at a median time of 2 months after IR-AHAR and at a median time of 0.1 month after SC-AHAR ($p = 0.019$). Whilst the incidence of early HAT (≤ 30 days after LT) was similar in the 2 groups [10.7% (6/56) and 6.2% (4/64) after IR and SC-AHAR respectively; $p = 0.512$], late HAT (≥ 30 days) had a significantly higher incidence in the IR-AHAR group [19.6% (11/56) vs. 4.7% (3/64); $p = 0.024$].

Very late HAT (beyond 1 year from LT) was observed in 4 of 56 (7.1%) patients with IR-AHAR whilst no case was observed in the SC-AHAR group ($p = 0.030$).

Of the 24 patients who experienced HAT, 9 lost their graft: eight were re-transplanted, and one died awaiting re-LT. In the remaining 15 patients, HAT was managed conservatively (Table 3). Five of these latter 15 patients had surgical (3 cases) or interventional radiological procedures (2 cases) to revascularise the graft after early HAT: revascularisation was successful in 3 of these 5 patients whilst 2 died of sepsis. Of the 10 patients with late HAT who were managed conservatively, 6 had revascularisation achieved with interventional radiological procedures (these were successful in 3 cases, whilst 3 other patients died of chronic ischaemic liver damage), 3 had no specific treatment as the graft function remained stable and another 1 underwent a left hepatectomy.

Median patient and graft survival of the 15 patients with HAT who were treated conservatively were of 48 (0.2–91) months.

Univariate analysis revealed that the only prognostic factor of HAT was the AHAR performed on the infrarenal aorta (Tables 4 and 5). This finding was confirmed in the multivariate analysis, in which the IR hepatic anastomosis was the only independent risk factor for HAT (exp[B] = 3.915; 95% CI 1.400–10.951; $p = 0.009$).

HAT-free survival was also statistically lower in the IR-AHAR group ($p = 0.018$, Fig. 2). After a mean follow-up of 47.53 ± 38.32 and 62.5 ± 58.23 months for the SC-AHAR and IR-AHAR groups, respectively, graft and patient survival were higher in the SC-AHAR group ($p = 0.061$; $p = 0.129$ respectively; Fig. 3) but this results barely failed to attain statistical significance.

No significant differences were found between the study groups in the incidence of PNF, EAD, biliary strictures, acute rejection, re-LT, and length of postoperative stay.

Although a trend towards a higher incidence of biliary leaks was observed in the IR-AHAR group (7/56–12.5% vs. 2/64–3.1%; $p = 0.08$), this difference was not statistical significant.

To assess whether the surgical experience influenced the incidence of HAT, a time trend analysis was carried out. The incidence of HA thrombosis after AHAR was 22.9 (8/35), 17.1 (7/41) and 20.5% (9/44) respectively in the three "eras" considered (Fig. 4). The rate of HAT after AHAR was comparable between the centres (range 13.8–20.9%, $p = 0.482$). The volume of the Centre was not associated with a lower incidence of HAT after AHAR either; indeed, the highest

Table 3 Treatments of hepatic artery thrombosis related to the time of onset

Treatments	Supraceliac anastomosis (7/64 pts)		Infrarenal anastomosis (17/56 pts)	
	EARLY-HAT	LATE-HAT	EARLY-HAT	LATE-HAT
Interventional radiology	0	1/7(14.3%)	2/17(11.7%)	5/17(29.4%)
Re-LT	1/7(14.3%)	2/7(28.6%)	4/17(23.5%)	1/17(5.9%)
Surgical revascularisation	3/7(42.8%)	0	0	0
No therapy	0	0	0	3/17(17.6%)
Liver resection	0	0	0	1/17(5.9%)
Dead on wait-list	0	0	0	1/17(5.9%)

HAT Hepatic artery thrombosis, *LT* Liver Transplantation

Table 4 Univariate analysis: recipient and donor risk factors of HAT

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*p*	Odds ratio (95% CI)	*p*
HAT risk factors				
Age (years) > 58	0.408 (0.110–1.934)	0.259		
Sex (M)	1.400 (0.436–4.496)	0.572		
BMI > 25	1.873 (0.626–5.603)	0.262		
Chronic liver disease				
Viral				
Re-LT	0.867 (0.121–6.500)	0.900		
Alcoholic	0.473 (0.111–4.083)	0.496		
NASH	1.300 (0.131–8.141)	0.823		
Others	0.636 (0.190–6.128)	0.305		
LT-number				
> 1	1.278 (0.331–4.926)	0.772		
Creatinine pre-transplant (mg/dl)	1.553 (0.622–3.878)	0.346		
HCC	1.723 (0.573–5.175)	0.333		
HBV +	3.033 (0.999–9.204)	**0.050**	0.807 (0.262–2.490)	0.710
HCV +	0.315 (0.111–1.191)	**0.089**	0.296 (0.083–1.058)	0.079
MELD > 17	1.203 (0.403–3.589)	0.740		
TACE	2.667 (0.845–8.412)	**0.094**	2.762 (0.879–8.682)	0.082
Donor				
Age > 63	2.705 (0.872–8.669)	**0.084**	1.112 (0.295–4.192)	0.876
Sex (M)	1.189 (0.392–3.605)	0.760		
BMI > 21	1.609 (0.914–1.230)	0.439		
DRI > 1.68	3.037 (0.804–11.468)	**0.099**	2.132 (0.533–8.530)	0.284
Hepatic artery variants				
Aberrant right hepatic artery	0.970 (0.196–4.804)	0.971		
Aberrant left hepatic artery	2.777 (0.753–10.246)	0.125		
Cause of death				
Cerebrovascular accident		0.739		
Trauma	0.682 (0.123–6.515)	0.856		
Anoxia	1.250 (0.112–13.924)	0.758		
Others	0.625 (0.031–12.401)			

Bold values indicate the level of significance $p \leq 0.05$

HAT Hepatic artery thrombosis, *BMI* Body Mass Index, *HCC* Hepatocellular Carcinoma, *HBV+* hepatitis B virus, *HCV+* hepatitis C virus, *TACE* trans-arterial chemoembolisation, *DRI* Donor Risk Index, *CLKT* combined liver–kidney transplantation

incidence of thrombosis was recorded in the Centre which had the largest number of LTs performed in the study period whilst the two Centres that had the lowest volume had the lowest incidence of HA thrombosis.

Discussion

The success of a liver transplantation procedure depends on adequate vascularisation of the graft. Poor or absent arterial inflow results in severe damage to the liver that often leads to allograft loss. Thrombosis of the hepatic artery is the most fearsome surgical complication of LT, and its incidence in adult LT ranges from 2 to 9% [21].

When the recipient's hepatic artery is not suitable for a direct anastomosis, the celiac axis or the splenic artery may be used as possible alternative anastomotic sites; however, these two latter vessels are frequently affected by the same anatomical abnormalities of the arterial wall that made it impossible to practise the HA [22–24].

In these circumstances, AHAR is the only possibility to arterialise the graft. However, there is some evidence that this type of reconstruction is associated with an increased risk of HAT when compared to the standard (HA to HA) arterial reconstruction [3, 25].

Table 5 Univariate analysis: intra- and postoperative risk factors of HAT

HAT risk factors	Univariate analysis		Multivariate analysis	
	Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Surgical time (min) > 470	2.419 (0.768–7.616)	0.131		
Hepatic artery anastomosis				
SC-AHAR				
IR-AHAR	5.048 (1.337–19.054	**0.017**	3.915 (1.400–10.951)	**0.009**
Arterial conduit	1.873 (0.626–5.603)	0.165		
Caval anastomosis				
Piggyback				
Conventional technique	1.693 (0.504–5.685)	0.394		
Latero-lateral	2.031 (0.201–8.675)	0.374		
End to side	4.063 (0.330–9.564)	0.548		
Portal anastomosis				
Termino-terminal				
Jump graft	1.000 (0.999–1.000)	> 0.999		
Cavo-portal hemitransposition	1.000 (0.999–1.001)	> 0.999		
Biliary reconstruction				
Duct to duct				
Roux-en-Y	0.535 (0.064–4.494)	0.564		
External biliary drainage	2.139 (0.386–11.850)	0.384		
Homologous PRBCs (cc)				
> 1850	1.959 (0.654–5.866)	0.229		
Autologous PRBCs (cc)				
≥ 250	0.440 (0.131–1.480)	0.221		
Total PRBCs (cc)				
> 450	0.765 (0.298–1.897)	0.187		
Cold ischaemia time (min)				
> 358	2.000 (0.611–6.544)	0.252		
Warm ischaemia time (min)				
> 34	1.217 (0.409–3.625)	0.724		
Total ischaemia time (min)				
> 605	3.302 (0.702–15.529)	0.131		
Arterial ischaemia time (min)				
> 65	1.127 (0.348–3.650)	0.843		

Bold values indicate the level of significance $p \leq 0.05$

IR-AHAR Infrarenal Aorto-Hepatic Arterial Reconstruction, *SC-AHAR* Supraceliac Aorto-Hepatic Arterial Reconstruction, *HAT* Hepatic artery thrombosis, *PRBC* packed red blood cells

In a recent study that analysed several recipients' parameters, including the severity of liver disease and the presence of metabolic or cardiovascular disorders, Oberkofler et al. showed that the arterial reconstruction technique was the most important independent risk factor for the development of HAT [26]. This finding was confirmed by Hibi et al. who showed that AHAR with the use of arterial conduits was associated with an increased incidence of HAT and a lower graft survival [27]. In that study, 252 of the 267 (94.4%) cases of AHAR reported were IR-AHAR, the incidence of HAT was 6.4% following AHAR versus 2.4% following the standard end-to-end HA–HA anastomosis; a higher prevalence of late HAT was also observed in the AHAR group.

The present study confirms that the risk of HAT following AHAR is higher than that expected after HA–HA reconstruction. In our study, AHAR was used in 2.8% only of the LTs performed, a rate which is lower than that reported in several other series. This seems to indicate that all participating centres performed an AHAR only when strictly needed [28].

In cases where AHAR is required, IR-AHAR has been the most widely used technique. Although the access to the infrarenal aorta is easier, the IR-AHAR has potential drawbacks: the use of a long free vessel graft is unavoidable, and the conduit must be positioned in a caudo-cranial direction. Similarly to what is observed in visceral revascularisation

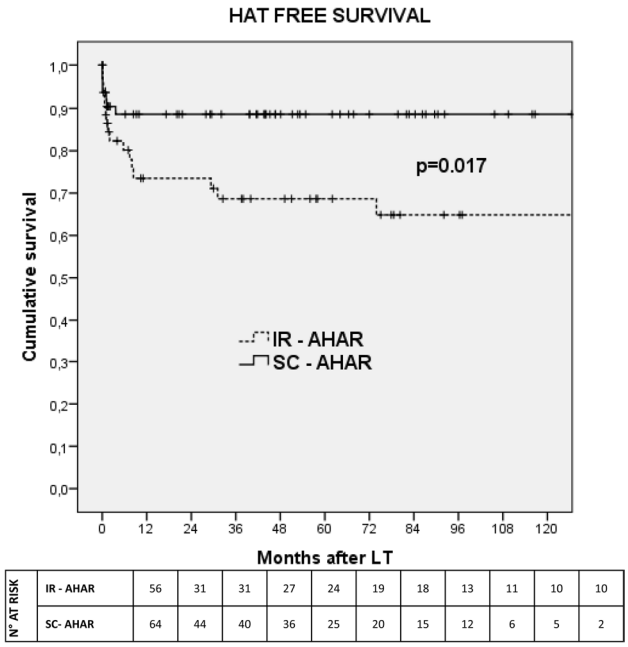


Fig. 2 HAT-free survival in the IR-AHAR group and the SC-AHAR group

procedures of vascular surgery, retrograde blood flow through the conduit is likely to induce turbulence and disturbed flow, which can hinder the patency of the vessel [29]. Vascular grafts in the LT setting are retrieved from donors whose age in most European countries is progressively increasing. The median age of the donors in the present series was 59 years, and 30% of donors were over 70 years. Vascular grafts retrieved from older donors are likely to carry significant atherosclerotic changes that can predispose to thrombosis. In the study of Hibi and colleagues the median age of the donors was 44 years, and no donor was over 57 years. This lower age may explain why the incidence of HA thrombosis after AHAR was lower in that series than in the present study.

The development of HAT at a median time of 2 months after LT in the IR-AHAR group in our series supports the hypothesis that the shear wall stress, which is a well-known risk factor for intimal hyperplasia, atherosclerosis and finally thrombosis, could affect suboptimal vessels that are anastomosed in unfavourable technical conditions [27, 30–32]. Indeed, in the IR-AHAR a sharp degree of angulation and caudal–cranial flow may contribute to the formation of complex flow patterns and areas of shear stress within the anastomosis which can eventually result in thrombosis [33]. In some of the cases of the present series, the HAT occurred several years after LT following IR-AHAR; in fact, "very late" HAT was observed only in the IR-AHAR group.

The SC-AHAR may be technically more challenging, particularly in patients with severe portal hypertension. Surprisingly, in the present study, the comparative analysis between the two techniques of AHAR showed that the arterial ischaemia time was significantly lower in the SC-AHAR group. This finding seems to indicate that, in the IR-AHAR, to complete the reconstruction of long-length arterial conduits and place them correctly may be time-consuming despite the easier access to the IR site of the aorta.

Nevertheless, SC-AHAR offers the possibility to create a much more physiological and haemodynamically advantageous allograft arterialisation. In SC-AHAR, the direction of the arterial flow is cranio-caudal, and depending on the length of the graft's artery, the use of an interposition conduit can sometimes be avoided.

To date, only four studies have investigated the possible effect on the LT outcome the two different AHAR

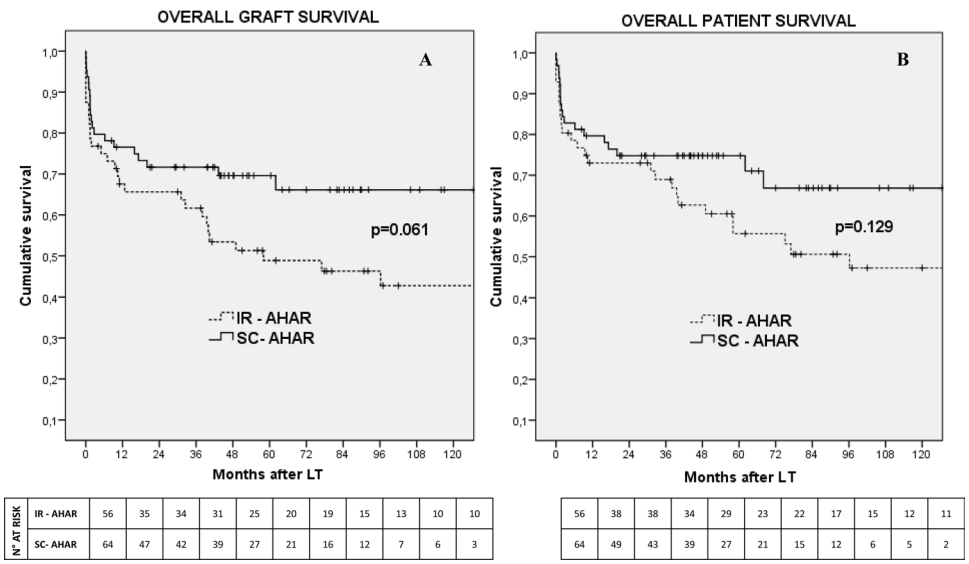


Fig. 3 Overall graft (**a**) and patient (**b**) survival in the IR-AHAR group and the SC-AHAR group

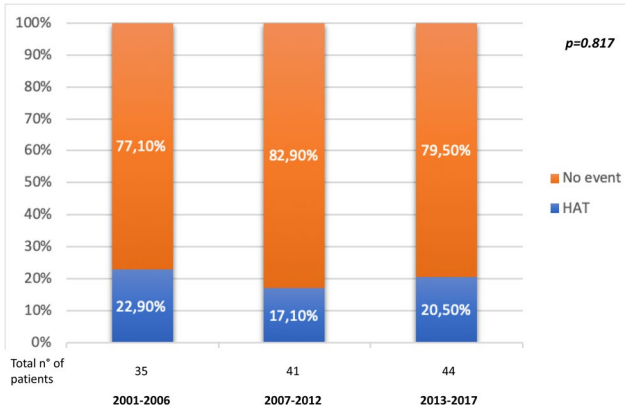


Fig. 4 Time trend bar chart of HAT after AHAR over different time periods ("eras") in the whole population

techniques. In 1991, Shaked et al. reported 45 SC-AHAR cases in adult LT with no postoperative HAT, whilst the incidence of HAT after IR-AHAR was 23% [6]. Hummels et al. reported 15 cases of AHAR, of which 7 were infrarenal and 8 supraceliac; in that series the authors found no difference between the two techniques in terms of HAT [6, 34]. More recently, Livingston et al. compared the outcome of 22 SC-AHARs to that of 82 IR-AHARs: although the incidence of HAT was slightly higher following IR-AHAR, there was no difference between the two techniques in terms of clinical outcome [35]. A recently published international multicentre cohort study analysed the outcome of 565 LT recipients whose graft was revascularised using an arterial conduit [36]. Although the overall results of the study were similar to those reported herein in terms of incidence of arterial occlusion, the type of AHAR (IR versus SC) did not influence arterial patency. However, the primary endpoint of that study was the 30-day conduit patency, whilst only few comments were reported about late occlusion. In the present study, it was precisely the incidence of late occlusion which significantly differed between the two types of AHAR, whilst the rate of early thrombosis was similar.

The above-mentioned study of Oberkofler et al. also found that the incidence of early HAT was higher in those LT recipients that did not receive antiaggregant prophylaxis [36]; in the present study, antiplatelet prophylaxis was administered to all patients and the effect of this potential risk factor was therefore not assessable.

The present study has some limitations, namely the retrospective design, the lack of randomisation and the long time span analysed. However, the incidence of complications did not vary in the different eras considered nor there was an association with the centres' volume.

In conclusion, our results indicate that SC-AHAR is associated with a lower incidence of late HAT in comparison with the IR-AHAR. Therefore, the supraceliac aorta should be preferred whenever possible over the infrarenal aorta in case of aorto-hepatic arterial revascularisation.

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Compliance with ethical standards

Conflict of interest None of the authors has a conflict to declare.

Research involving human participants and/or animals The ethical committee of the Regione Marche approved the study and the protocol (number of ethical committee approval 2018–677).

Informed consent Informed consent for this type of study is not required.

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