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Risk factors associated with early hepatic artery thrombosis after orthotopic liver transplantation – univariable and multivariable analysis

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Summary

Hepatic artery thrombosis (HAT) is a serious complication in patients undergoing orthotopic liver transplantation (OLT). It is associated with a high graft loss and mortality rate. In this study, possible risk factors associated with early HAT (occurring within the first postoperative month) were evaluated using univariable and multivariable analyses. Nine-hundred-and-fourteen consecutive OLTs in our institution were examined by univariable and multivariable analyses. Early HAT occurred in 43 patients (4.7%). Graft number, abnormal donor arterial anatomy, bench arterial reconstruction, aortic conduit use, multiple anastomoses, reperfusion time (interval between portal vein reperfusion and restoration of arterial flow) and the number of units of blood received intraoperatively were significantly associated with early HAT in the univariable analysis($P < 0.1$). These variables were included in a multivariable regression model which showed that bench arterial reconstruction was associated with a fourfold risk of early HAT($P < 0.0001$), whereas each additional 10 min delay in reperfusion was associated with a 27% increase in the risk of early HAT ($P < 0.04$). The main risk factors associated with early HAT are abnormal arterial anatomy in the graft requiring bench reconstruction and a delay in arterial reperfusion. Early recognition of these factors, strict surveillance protocols with arterial Doppler and selective anticoagulation for patients at risk need to be evaluated prospectively.

Introduction

While transplantation is the most effective treatment for acute and chronic end-stage liver disease, it is also a procedure with significant morbidity and mortality, particularly in the early postoperative period. This crucial time can encompass several complications, the most significant being primary graft nonfunction and hepatic artery thrombosis (HAT). HAT after orthotopic liver transplantation (OLT) is a serious complication with a high mortality rate. The incidence of HAT reported in the literature varies widely, ranging from 2.5% [1] to 9% [2].

Hepatic artery thrombosis can be subdivided into early (occurring in less than 1 month post-OLT) or late (occurring later than 1 month post-OLT) HAT [3–5]. This is a useful classification as the risk factors, clinical presentation and the treatment of these two separate entities varies considerably. Early HAT is associated with an aggressive course, a higher rate of allograft loss and increased patient mortality in comparison to late HAT, which follows a more benign course [6].

The incidence of early HAT is between 1.2% and 6% [4,7]. It can present as fulminant hepatic necrosis and graft failure, sepsis and liver abscesses or with worsening

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graft function related to ischaemic bile duct injury leading to cholangitis, bile leak, and biliary strictures. Laboratory tests show leucocytosis, transaminitis, elevated bilirubin and an altered coagulation profile [1,3,8]. Diagnosis is made using Doppler ultrasound, microbubble ultrasound [9], contrast enhanced computed tomography (CT) and selective coeliac angiography [10]. Treatment is mainly surgical, with the majority of patients requiring re-transplantation. When recipients are mildly symptomatic, operative exploration with thrombectomy and arterial reconstruction (revision of anastomosis or interposition of an iliac conduit) can give good results [11,12]. In patients with minimal symptoms, nonsurgical options such as intra-arterial thrombolysis with or without angioplasty or stenting can also be attempted [13–15]. Despite these measures, the mortality rate of early HAT is between 11% and 56%, with a re-transplantation rate as high as 83% [1,10]. Late HAT, on the other hand, pursues a milder clinical course and presents with fever, jaundice, hepatic abscesses, ischaemic cholangiopathy and bile leaks [5]. Biliary tract complications are more frequent with late HAT [1]. Late HAT is treated with broad spectrum antibiotics, drainage of liver abscesses and re-transplantation after sepsis is controlled [5]. In the study of Stange *et al.* the mortality of late HAT from HAT-related complications was 0% (vs. 29% for early HAT) [1].

Early HAT was traditionally thought to be a result of solely surgical factors. However, more recently, nonsurgical factors such as donors being elderly, hypercoagulable state, rejection episodes, and cytomegalovirus (CMV) infection have also been implicated [10,12,16–19].

The aim of this study was to analyse donor-related, recipient-related, surgical and postoperative factors in order to identify the risk factors associated with early HAT after OLT in a single institution. The identification of risk factors could improve prompt diagnosis of early HAT by concentrating on those at risk and allow appropriate trials of prophylactic therapy.

Materials and methods

Data were obtained from a prospectively collected database of all OLTs performed at the Royal Free Hospital in London, UK. Information stored on the database includes demographic and clinical status pretransplant, as well as both peri- and postoperative transplant factors and outcome. For the analyses reported in this article, we extracted data on 914 consecutive deceased donor liver transplantations (including re-transplants) performed between October 1988, the start of our programme, and October 2005.

Hepatic artery thrombosis was classified as early (within the first month post-transplant) or late HAT (beyond the first month post-transplant).

Operative details

Allografts were preserved with University of Wisconsin (UW) solution. In the vast majority of cases, a caval replacement OLT was performed. Venovenous bypass was performed selectively in 30% of patients. The graft was reperfused following completion of the caval and portal venous anastomoses. Arterial anastomosis was usually performed between the donor hepatic artery and the recipient common hepatic artery at the junction with the gastroduodenal artery or the proper hepatic artery at its division into right and left hepatic arteries. In cases with insufficient arterial flow in the coeliac trunk or a small diameter of the recipient hepatic artery, arterial reconstruction was performed by using a segment of the donor iliac artery as a conduit between the infrarenal aorta and the donor hepatic artery.

For the purpose of this analysis, donor- and recipient anatomy were classified as normal or abnormal. Abnormal anatomy encompasses the presence of an accessory right, accessory left or accessory right and left hepatic arteries. When necessary, bench arterial reconstruction of an accessory right hepatic artery was performed with an end-to-end anastomosis to the gastroduodenal or splenic artery, or anastomosing the superior mesenteric artery patch to the coeliac artery. In cases in which the accessory left hepatic artery had been inadvertently divided during graft recovery, it was reconstructed to the left gastric artery or the splenic artery. For the purpose of the analysis, arterial anastomoses were classified as single (when donor anatomy was normal and there was sufficient arterial flow) or multiple (when donor anatomy was abnormal and bench arterial reconstruction or the use of an iliac conduit was required).

Intraoperative thromboelastograms (TEGs) were performed to monitor patients clotting status. Wherever the potential risk of HAT was considered to be high, either because of a complicated reconstruction or because of small vessel size, epoprosterol was used postoperatively.

Postoperative management

A Doppler was performed the morning after surgery as routine and whenever clinically indicated, such as following a rise in the serum transaminases or continued impaired synthetic hepatic function. If the Doppler evaluation suggested HAT, a contrast-enhanced triple-phase abdominal CT and when required, angiography was performed to confirm the diagnosis.

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Immunosuppression consisted of monotherapy with tacrolimus or cyclosporine or triple therapy with tacrolimus/cyclosporine, azathioprine and prednisolone either in a randomized trial [20–22] or tailored to the individual. Rejection episodes were treated with steroids (1 g of methylprednisolone for 3 days) in the first instance. If rejection was not adequately treated following two cycles of methylprednisolone, OKT3 was administered.

All patients underwent prospective screening for CMV three times per week for up to 6 weeks, initially by detection of early antigen fluorescent foci testing, then by polymerase chain reaction (PCR). CMV infection was diagnosed when two consecutive blood tests were positive and was treated with intravenous gancyclovir and more recently oral valganciclovir until the CMV test results were negative on two consecutive occasions.

Analysis of risk factors

We considered whether any donor-related, recipient-related, surgical or postoperative factors were associated with early HAT after OLT. Donor factors considered were blood group and CMV status. Recipient factors were age (sub classified into <60 or >60 years), gender, ethnic group (Caucasian, Asian, other), blood group, aetiology (primary sclerosing cholangitis (PSC), primary biliary cirrhosis (PBC), hepatocellular carcinoma (HCC), alcoholic, hepatitis B or C, other) and CMV status. For aetiology, conditions associated with a prothrombotic state such as PSC, PBC and HCC were analysed individually, as well as together as a group, to determine their association with early HAT. In addition, donor–recipient CMV matching was also analysed as a separate covariate as previous reports have suggested a link between CMV and HAT [18]. Surgical factors analysed were graft number, donor- and recipient arterial anatomy (normal, abnormal), bench arterial reconstruction (present, absent), total number of anastomoses (single, multiple), the use of an aortic conduit, cold ischaemia time, reperfusion time, transfusion of blood, cryoprecipitate, fresh frozen plasma (FFP) and platelets. Cold ischaemia was defined as the time that the graft is stored in hypothermic hypoxic conditions. Reperfusion time was the time between portal vein reperfusion and restoration of arterial flow after completion of the arterial anastomosis.

For a reduced dataset of 552 consecutive patients, we also had detailed daily information on postoperative use of immunosuppression and inotropes as well as the number of rejection episodes and the treatment received by each patient.

Statistical analysis

Cox proportional hazards regression models were used to identify risk factors for the development of early HAT. For these analyses, patient follow-up was considered from the date of OLT until the date of onset of HAT, death or until 1 month after OLT, whichever occurred first (follow-up was censored at 1 month as patients were no longer at risk of developing early HAT after this time).

Factors that were associated with early HAT in the univariable regression models ($P < 0.1$) were then considered for inclusion in a multivariable regression model; variables that were no longer significant in this multivariable model were removed from the model using a backward selection procedure. All analyses were performed using the PHREG procedure in SAS version 9 (SAS Institute Inc., 100 SAS Campus Drive, Cary, NC, USA); P-values <0.05 were considered significant for these final analyses.

The model was repeated in the subset of patients with detailed information on postoperative immunosuppression, inotropes and rejection episodes. The model additionally incorporated the type of immunosuppressive regimen (mono- or triple-therapy), receipt of inotropes and number of confirmed rejection episodes as time-updated covariates.

Results

Nine-hundred-and-fourteen liver transplants (including re-transplants) were performed between 1998 and 2005. The characteristics of the patients included in the study are shown in Table 1. Of the 914 patients included in the study, 546 (59.7%) were male subjects. The median age was 49 years with 101 patients (11.1%) being over the age of 60 years. The median weight was 70 kg. ABO blood groups were identical between donor and recipient in 760 patients (83.2%), while 125 (13.7%) received a compatible blood group organ. Twenty-nine patients (3.2%) received an incompatible blood group graft.

Sixty-five patients developed HAT (7.1%), with 43 (4.7%) developing this within the first month post-transplant; 20 of the 43 (46.5%) died within 90 days post-OLT. Twenty-six patients (60.5%) were re-transplanted and out of them eight (30.8%) died within the first 3 months after the first OLT. Five patients underwent thrombectomies, with three (60%) surviving beyond 3 months post-OLT.

Neither donor (blood group, CMV status) nor recipient (age, gender, aetiology, ethnic group, blood group, CMV status) factors were identified as significant risk factors for early HAT in the univariable analyses. When all the aetiological factors associated with a prothrombotic state (PBC, PSC and HCC) were grouped together, this group was not significantly associated with early HAT ($P > 0.05$).

Early HAT was shown to be primarily associated with surgical factors (Table 1). Eight hundred and twenty-seven (90.5%) of the transplants analysed were primary OLTs, whereas 79 (8.6%) were second and eight (0.9%)

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Table 1. Characteristics of 914 patients included in the study, and results from univariable proportional hazards regression analyses of factors associated with early HAT.

	n (%)	*n* (%) with early HAT	Relative hazard (95% CI)	*P*-value
Number of patients	914 (100.0)	43 (4.7)		
Gender				
Male	546 (59.7)	23 (4.2)	1	
Female	368 (40.3)	20 (5.4)	1.30 (0.72, 2.37)	0.39
Country of origin				
European	707 (77.4)	31 (4.4)	1	
Asian	131 (14.3)	10 (7.6)	1.82 (0.89, 3.71)	0.10
Other	76 (8.4)	2 (2.6)	0.59 (0.14, 2.45)	0.46
Age				
≤60	813 (88.9)	37 (4.7)	1	
>60	101 (11.1)	6 (5.9)	1.25 (0.53, 2.96)	0.62
Aetiology*				
PSC	75 (8.2)	3 (4.0)	0.83 (0.26, 2.69)	0.76
PBC	115 (12.6)	8 (7.0)	1.56 (0.72, 3.36)	0.26
HCC	111 (12.1)	5 (4.5)	0.93 (0.37, 2.36)	0.88
Alcoholic	165 (18.1)	5 (3.0)	0.57 (0.22, 1.44)	0.94
Hepatitis B/C	298 (32.6)	14 (4.7)	0.98 (0.52, 1.85)	0.23
Other	287 (31.4)	15 (5.2)	1.25 (0.67, 2.34)	0.48
Blood group				
Match	760 (83.2)	34 (4.5)	1	
Compatible	125 (13.7)	7 (5.6)	1.31 (0.58, 2.95)	0.52
Incompatible	29 (3.2)	2 (6.9)	1.82 (0.44, 7.60)	0.41
Graft number				
1	827 (90.5)	36 (4.4)	1	
2	79 (8.6)	6 (7.6)	1.90 (0.80, 4.51)	0.15
3	8 (0.9)	1 (12.5)	3.36 (0.46, 24.51)	0.23
Per graft			1.87 (0.96, 3.65)	0.07
Donor anatomy				
Normal	711 (77.8)	32 (4.5)	1	
Abnormal	195 (21.3)	11 (5.6)	2.79 (1.45, 5.37)	0.002
Not known	8 (0.9)	0 (–)	–	–
Recipient anatomy				
Normal	782 (85.6)	35 (4.5)	1	
Abnormal	124 (13.6)	8 (6.5)	1.56 (0.68, 3.55)	0.29
Not known	8 (0.9)	0 (–)	–	–
Bench arterial reconstruction				
None	754 (82.5)	25 (3.3)	1	
Present	152 (16.6)	18 (11.8)	3.68 (1.91, 7.10)	0.0001
Not known	8 (0.9)	0 (–)	–	–
Arterial conduit				
No		30 (4.4)		
Yes		13 (11.1)		0.02
Number of anastomoses				
Single	721 (78.9)	23 (3.2)	1	
Multiple	184 (20.1)	20 (10.9)	3.62 (1.90, 6.91)	0.0001
Not known	9 (1.0)	0 (–)	–	–
Cold ischaemia time (h)				
<12	573 (62.9)	29 (5.1)	1	
12–16	288 (31.6)	13 (4.5)	0.90 (0.47, 1.72)	0.74
>16	50 (5.4)	1 (2.0)	0.44 (0.06, 3.24)	0.42
Per hour			0.96 (0.87, 1.05)	0.34

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Table 1. continued

	n (%)	*n* (%) with early HAT	Relative hazard (95% CI)	*P*-value
Reperfusion time (min)				
<30	20 (2.2)	1 (5.0)	1	
30–60	831 (91.4)	36 (4.3)	1.06 (0.15, 7.73)	0.95
>60	58 (6.4)	6 (10.3)	2.74 (0.33, 22.75)	0.35
Per 10 min			1.32 (1.04, 1.68)	0.03
Platelets				
No	353 (38.6)	21 (6.1)	1	
Yes	561 (62.1)	22 (3.9)	0.65 (0.36–1.19)	0.16
Per five units			0.82 (0.59, 1.14)	0.24
Blood				
No	93 (10.2)	5 (6.0)	1	
Yes	821 (90.8)	38 (4.6)	0.80 (0.31–2.03)	0.64
Per five units			1.14 (1.00, 1.30)	0.05
Cryoprecipitate				
No	746 (81.6)	35 (4.8)	1	
Yes	168 (18.7)	8 (4.8)	1.06 (0.49–2.29)	0.88
Per five units			1.12 (0.87, 1.46)	0.38
Plasma				
No	136 (14.9)	7 (5.6)	1	
Yes	778 (86.1)	36 (4.6)	0.85 (0.38–1.92)	0.70
Per five units			1.02 (0.81, 1.28)	0.24
CMV status				
Donor				
Negative	414 (45.3)	20 (4.8)	1	
Positive	445 (48.7)	23 (5.2)	1.10 (0.60–2.00)	0.76
Not known	55 (6.0)	0 (–)	–	–
Recipient				
Negative	215 (23.5)	12 (5.6)	1	
Positive	600 (65.7)	30 (5.0)	0.89 (0.46–1.74)	0.74
Not known	99 (10.8)	1 (1.0)	0.18 (0.02, 1.41)	0.10
Matching				
No	347 (38.0)	18 (5.2)	1	
Yes	439 (48.0)	24 (5.5)	0.93 (0.50–1.71)	0.81
Not known	128 (14.0)	1 (0.8)	0.14 (0.02, 1.06)	0.06

*Some patients may have multiple aetiological factors, so the numbers with each aetiological factor will sum to more than the total sample size. Estimates from the regression analyses reflect the hazard rate in patients with each specific aetiological factor as compared with patients without that aetiological factor.

CMV, cytomegalovirus; HAT, hepatic artery thrombosis; HCC, hepatocellular carcinoma; PSC, primary sclerosing cholangitis; PBC, primary biliary cirrhosis.

were third transplants; the rate of HAT increased by 37% with each additional graft ($P = 0.07$). Abnormal donor anatomy ($P = 0.002$), the presence of bench arterial reconstruction ($P = 0.0001$), the use of arterial (iliac) conduit ($P = 0.02$) and multiple final anastomoses (0.0001) were also associated with early HAT in univariable analyses. Cold ischaemia time demonstrated no significant association with the development of early HAT ($P = 0.34$). In contrast, longer reperfusion time (median 43, range 19–117 min) was significantly associated with a higher rate of early HAT ($P = 0.03$). The transfusion requirement of blood was significantly associated with early HAT in univariable analyses ($P = 0.05$) but no associations were reported with transfusion requirements of cryoprecipitate, FFP or platelets.

Neither donor- nor recipient CMV status (nor CMV matching) correlated with the development of early HAT.

In the subgroup of 552 patients with detailed information concerning post-transplant immunosuppressive therapy and rejection episodes, there was no association between the use of mono- or triple-based immunosuppressive therapy and the development of early HAT (Table 2). Furthermore, neither the postoperative use of inotropes in ITU nor the number of confirmed rejection episodes were significantly associated with the development of early HAT.

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Table 2. Results from univariable analyses of postoperative factors associated with early hepatic artery thrombosis.

	Relative hazard (95% CI)	*P*-value
Immunosuppression		
None	0.86 (0.19, 3.83)	0.84
Mono	1	
≥2 drugs	0.80 (0.38, 1.68)	0.56
Use of inotropes	1.16 (0.19, 6.90)	0.87
Number of rejection episodes (per additional rejection)	1.31 (0.62, 2.77)	0.48

Table 3. Results from multiple proportional hazards regression analyses of factors independently associated with early hepatic artery thrombosis.

Factor	Relative hazard (95% CI)	*P*-value
Benchwork present	3.55 (1.89, 6.66)	0.0001
Reperfusion time (per 10 min delay)	1.27 (1.02, 1.60)	0.04

Of the variables that were significantly associated with early HAT in the univariable analysis, only two (bench arterial reconstruction and reperfusion time) remained significant in the multivariable analysis (Table 3). In particular, the presence of bench arterial reconstruction was associated with an almost fourfold risk of early HAT, whereas each additional 10 min of reperfusion time was associated with a 27% increase in the risk of early HAT.

Discussion

The incidence of early HAT in our cohort was 4.7% while late HAT occurred in 2.4% of patients. As the risk factors, clinical presentation and treatment of early HAT is widely different from those of late HAT, it should be considered as a separate entity. In this study, we have only assessed factors potentially associated with early HAT, having previously evaluated factors associated with late HAT [5]. A range of donor-related, recipient-related, surgical and postoperative factors were analysed. In both our univariable and multivariable analyses, the factors significantly associated with early HAT were primarily surgical. In our univariable analysis, the significant associations were graft number, abnormal donor anatomy, bench arterial reconstruction, use of an aortic conduit, reperfusion time and the number of units of blood received during surgery. However, of these, only two factors were shown to be independently associated with early HAT: bench arterial reconstruction (fourfold risk of early HAT) and reperfusion time (every additional 10 min of reperfusion time was associated with a 27% increase in risk). As many of the univariable-associated factors are correlated, it is not surprising that only two remained significant in the multivariable analysis. Re-transplantation was not found to be significant in the multivariable analysis possibly because of its low numbers, or because it correlates with abnormal anatomy and increased reperfusion time.

Benchwork has previously been shown to significantly increase the risk of early HAT [12]. In this study by Vivarelli *et al.* the incidence of early HAT was 3.6% while bench arterial reconstruction significantly increased the incidence of early HAT (10.8% vs. 2.8% respectively, $P = 0.01$). This was also the case in our study (12.4% vs. 3.6%, respectively, $P = 0.0001$). This is, however, the first time that reperfusion time, analysed as a continuous covariate, has been shown to play an important role in the development of early HAT.

Del Gaudio *et al.* found that the use of jump grafts to the infrarenal aorta was associated with an increased risk of early HAT, while Stange *et al.* found that supracoeliac grafts increased the risk of HAT by almost sixfold [1,4]. In our analysis, the use of donor iliac interposition grafts to the infrarenal recipient aorta was associated with early HAT (11.1% vs. 4.4%, presence of arterial conduit versus no conduit, $P = 0.02$). Silva *et al.* had similar results to ours, in that aortic conduits were associated with early HAT ($P = 0.01$) but not independently so in the multivariable analysis [23]. Vivarelli *et al.* on the other hand, found that jump grafts were associated with late HAT [12].

Cytomegalovirus infection has been linked to HAT, as it has been shown in an *in vitro* system that CMV is able to infect endothelial cells and this leads to a rapid procoagulant response within 90 min [24,25]. While there seems to be a link between CMV and HAT, the link between CMV and early HAT remains debatable. Madalosso *et al.* and Oh *et al.* have shown that CMV-seronegative patients receiving a seropositive graft are at risk of early HAT [10,18]. Silva *et al.* found an association with HAT (without distinguishing early from late) in their univariable analysis but not in the multivariable analysis [23]. A previous study performed at our centre showed that CMV was associated with late HAT in our patients [5]. In the current study, we found that donor or recipient CMV status and CMV matching were not associated with early HAT. A possible explanation for the lack of association between early HAT with CMV viraemia is that our patients receive intensive monitoring with thrice-weekly PCR tests and treatment with appropriate antiviral therapy as soon as two consecutive blood tests are positive, even without clinical symptoms. Interestingly, this was also the practice of Vivarelli *et al.* [12], who did not

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demonstrate an association between CMV viraemia with early HAT, but did with late HAT. Pre-emptive CMV treatment may stop or delay the progression of endothelial damage by CMV and therefore explain the lack of association.

As primary sclerosing cholangitis, primary biliary cirrhosis and hepatocellular carcinoma are procoagulant conditions [26], we considered these separately as well as a prothrombotic group together. However, no significant associations with early HAT were noted in our analysis. Several other groups have analysed this association and found the same result [18,23]. However, other aetiologies such as familial amyloidotic polyneuropathy may exhibit an increased risk of early HAT [27].

The results of this study indicate that surgical factors are highly significant in the development of early HAT and are likely to be causally related. In high-risk patients who have had a long reperfusion time, bench arterial reconstruction with the use of aortic conduits, anticoagulant prophylaxis should be considered.

Although patients with liver disease are considered to have a bleeding tendency, haemostasis tends to normalize rapidly after OLT [28]. Moreover, delayed recovery of plasma levels of antithrombin III and protein C post-OLT induce a hypercoagulable state for about 14 days after the operation [29]. This may be further exacerbated by other factors such as inherited hypercoagulability, haemostatic agents administered such as FFP and platelets, and CMV viraemia [28]. These factors have been highlighted in a recent review [19]. Hence, a controlled use of anticoagulants should be considered in patients at high risk of early HAT. Either all high-risk patients could be anticoagulated or regular TEGs could be performed to monitor these patients' clotting status and only those that become hypercoagulable could then be anticoagulated.

The use of antiplatelet drugs is an attractive option. Vivarelli *et al.* showed a reduction in late HAT with long term aspirin, with an added benefit of reducing cardiovascular disease [30]. However, aspirin is not a drug which can be prescribed in the immediate postoperative period. Intravenous heparin, on the other hand, has a short half-life and is reversible should a bleeding complication occur. Therefore, it would be a safer choice in the immediate postoperative period. This could then be followed by long-term aspirin. There is one small study that demonstrated the benefit of heparin use (10 U/kg/h) in the immediate postoperative period. In this analysis with only 86 patients, an increased incidence of early HAT was found in the group that did not receive heparin prophylaxis [2]. Another study has shown its benefits in the paediatric population [31].

While a number of centres use prophylactic heparin and aspirin post-OLT [1,2,23,32] a randomized controlled trial needs to be performed to analyse the risks versus benefits of such a regime. Other prophylactic regimes that warrant analysis include the maintenance of a haemoglobin level between 8–10 g/dl and the administration of warfarin for 3 months.

There are limitations in our study. Although, it is the largest of its kind, the relatively small proportion of individuals who developed early HAT may still have limited the number of significant associations we were able to detect.

In conclusion, in our cohort of patients, bench arterial reconstruction and an increased reperfusion time are strongly associated with an increased risk of early HAT. This allows identification of a high-risk group that should have daily surveillance with Doppler and/or microbubble contrast-enhanced ultrasound [9] and should benefit from prophylactic anticoagulation. Multicentre studies would be useful in to assess this high-risk group.

Authorship

PW, GF, GKG, AKB: participated in writing the paper. PW, GF, NR, DP, DS, BRD, KR, AKB: participated in research design. PW, GF, NR: participated in data collection. CAS: participated in data analysis.

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