ORIGINAL ARTICLE

Re-vascularization may not increase graft survival after hepatic artery thrombosis in liver transplant recipients

Vrochides D, Hassanain M, Metrakos P, Barkun J, Paraskevas S, Chaudhury P, Cantarovich M, Tchervenkov J

Department of Surgery, Multi-Organ Transplant Program, McGill University, Montreal, Quebec, Canada

Abstract

Background and aim: Hepatic artery thrombosis (HAT) occurs in 3% to 11% of all liver transplantations. Some authors have reported good outcomes with early thrombectomy. To investgate the impact of re-vascularization on graft survival.

Methods: A total of 566 primary, cadaveric, single organ, adult liver transplants were performed. Hepatic arterial Doppler was performed routinely and patients with abnormal findings during the first two post-operative weeks were re-explored. Abnormal findings after this time-point were verified by non-invasive angiogram. The 47 patients that were diagnosed with arterial thrombosis, either intra-operatively or by angiogram, were divided into three groups. No further action was taken for group A, thrombectomy alone was performed for group B1, thrombectomy and anastomotic revision was employed for group B2.

Results: Arterial thrombosis was diagnosed in 47 (8.3%) patients. Mean patient survival was 42, 62 and 98 months for groups A, B1 and B2 respectively (p: 0.0629). Mean graft survival was 24, 29 and 60 months for groups A, B1 and B2 respectively (p: 0.3386). Re-transplant incidence was 8.7%, 40% and 28.6% for groups A, B1, and B2 respectively (p: 0.035).

Conclusions: Early diagnosis of HAT by surveillance Doppler may lead to improved recipient survival secondary to earlier re-transplantation and not because of successful graft re-vascularization. Hippokratia 2010; 14 (2): 115-118

Key words: doppler, surveillance, re-transplantation, thrombectomy, anastomosis, revision

Corresponding author: Vrochides Dionisios, Royal Victoria Hospital, 687, Pine Avenue West, S10.26, Montreal, Quebec, H3A 1A1, Canada, tel: +1 +514 +8431600, fax: +1 + 514 +8431434, e-mail: vrochides@yahoo.com

Hepatic artery thrombosis (HAT) occurs in 3% to 11% of all liver transplantations. In the early post-transplant period (4 weeks), it presents with acute graft failure, biliary leak or sepsis. Later, it presents as biliary tree abnormalities (pruning, arborization, stenosis, dilatation, that lead to cholangitis or sepsis[1,2]. The most frequent cause of HAT is technical problems related to differences in size and quality of donor and recipient arterial vessels or to the presence of arterial abnormalities that require reconstructions[3]. HAT signifies poorer prognosis secondary to severe graft dysfunction; it needs early intervention to prevent death[1].

HAT is diagnosed (most of the times) by the use of hepatic artery Doppler echo when there is clinical suspicion[4]. If in doubt, non-invasive angiography is performed, usually by computer tomography (CT) scan[5].

The "gold-standard" treatment of choice in HAT is re-transplantation [2]. However, some authors have reported good outcomes with early thrombectomy[1,6], especially if there was a high level of suspicion and an early diagnosis was obtained[4]. Furthermore, endovascular thrombectomy and intraluminal stenting techniques for the treatment of HAT are rapidly evolving and most of them have yielded satisfactory results[7,8]. The purpose of this study was to investigate the role of aggressive surgical intervention in adult liver transplant recipients that were diagnosed having HAT.

Patients and methods

This is a single center, retrospective study of prospectively collected data. Between 1990 and 2006, 566 primary, cadaveric, single organ, adult liver transplants were performed. Induction immunosupression included antithymocyte globulin (6 mg/kgr, divided in 4 doses), tacrolimus (target levels of 8 – 12 ng/ml) or cyclosporine (C_0 target levels of 120 – 180 ng/ml), mofetil mycophenolate or azathioprine and steroids. Maintainance immunosupression included tacrolimus (target levels of 4 – 8 ng/ml) or cyclosporine (C_0 target levels of 50 – 100 ng/ml), mofetil mycophenolate or azathioprine and prednisone.

Hepatic arterial Doppler was performed on the first postoperative day (baseline) and each time that an elevation of SGOT or SGPT was observed (checked daily). Patients with abnormal Doppler findings during the first two post-operative weeks were explored operatively. Patients with abnormal Doppler findings after this time point underwent a CT angiogram. Patients diagnosed to have arterial inflow complications (n=79, 13.9%) were divided in two cohorts.

The first one (n=47) included all patients with graft arterial thrombosis, with or without concomitant stenosis. The second (n=32) included patients with graft arterial stenosis alone.

The arterial thrombosis cohort had a median follow-up of 18 months. Of these 47 recipients, 12 (25.5%) were followed-up for more than 72 months, whereas none was lost to follow-up. This cohort was divided into three groups. No further action was taken in group A (n=23), thrombectomy and arterial re-anastomosis at the same site was performed in group B1 (n=10) and thrombectomy and arterial re-anastomosis at a different site was performed in group B2 (n=14). Group A included all patients diagnosed with HAT after the first two post-operative weeks, whereas groups B1 and B2 included all the patients that were diagnosed with HAT within the first two post-operative weeks. The baseline characteristics of the three groups are depicted in Table 1.

Graft actuarial survival, patient actuarial survival and re-transplantation rate (re-graft per initial graft) were calculated, stratified by the type of rescue intervention. Data entry and statistical analysis was performed using the SPSS statistical software, version 16.0.1 for Mac (SPSS Inc., Chicago, IL, USA). For continuous data description, mean values (± standard deviation) were utilized. Statistical significance was tested by Mann Whitney U test. For categorical data description, absolute numbers were always provided with percentages only in brackets. Statistical significance was tested by the χ^2 test (Fisher's Exact Test). Kaplan-Meier analysis was employed to calculate and compare actuarial survivals, which were presented by mean values and confidence intervals.

Results

There were no statistical significances among the baseline characteristics of the study groups (Table 1).

Mean graft survival was 24.12 (95% CI: 0.72, 47.64) months for group A and 48.84 (95% CI: 16.44, 81.82) months for groups B1 and B2 combined (p: 0.3386). Mean patient survival was 42.24 (95% CI: 15.12, 69.48) months for group A and 101.16 (95% CI: 64.2, 138) months for groups B1 and B2 combined (p: 0.0629).

Table 1: Baseline characteristics of liver transplant recipients diagnosed with hepatic artery thrombosis. Comparison is performed between patients that were treated expectantly (group A, n = 23) and those that were treated with re-vascularization (groups B1 & B2, n=24).

CATEGORICAL PARAMETERS			
PARAMETER	**GROUP A n (%)**	**GROUPS B1 & B2 n (%)**	**p**
Female recipient's gender	5 (21.7%)	8 (33.3%)	0.288
Female donor's gender	16 (69.6%)	18 (75%)	0.464
Cause of liver failure Ethanol HBV HCV PBC / PSC Other	 5 (21.7%) 3 (13%) 3 (13%) 4 (17.4%) 8 (34.8%)	 2 (8,3%) 4 (16.7%) 6 (25%) 1 (4.2%) 11 (45.8%)	0.321
Hypertension	7 (30.4%)	8 (33.3%)	0.540
Diabetes mellitus	2 (8.7%)	3 (12.5%)	0.521

CONTINUOUS PARAMETERS					
PARAMETER	**GROUP A n (%)**		**GROUPS B1 & B2 n (%)**		**p**
	Mean	**Standard Deviation**	**Mean**	**Standard Deviation**	
Recipient's age (years)	58.27	7.55	58.29	6.62	0.995
Donor's age (years)	49.19	8.96	50.37	6.39	0.590
MELD score	19.48	3.52	20.08	5.05	0.638
CTP score	10.57	1.37	10.71	1.82	0.764
Cold ischemia time (h)	9.56	2.51	9.91	2.22	0.614
Warm ischemia time (h)	0.86	0.32	0.95	0.35	0.371

Mean graft survival stratified by rescue intervention is depicted in Figure 1. Two patients of group A (8.7%) and eight patients of groups B1 and B2 combined (34.8%) were re-transplanted respectively (p: 0.035).

Further stratification between groups B1 and B2 revealed that mean graft survival was 29.28 (95% CI: 3.72, 54.96) months for group B1 and 59.64 (95% CI: 16.92, 102.36) months for group B2 (p: 0.4872). Mean patient survival was 62.16 (95% CI: 37.8, 86.64) months for group B1 and 98.16 (95% CI: 51.12, 145.32) months for group B2 (p: 0.1205). Four patients of group B1 (40%) and four patients of group B2 (28.6%) were re-transplanted respectively (p: 0.095).

Survival of Liver Recipients with Hepatic Arterial Thrombosis

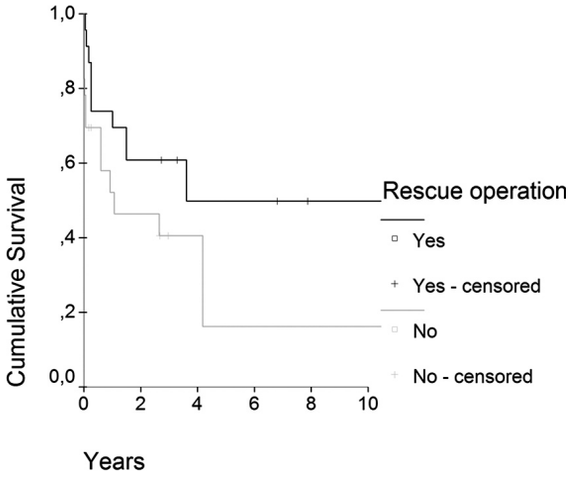

Figure 1: Survival curves (in years) of liver transplant grafts in patients that were diagnosed with hepatic artery thrombosis. Recipients either underwent no rescue operative procedure (group A, grey line) or underwent thrombectomy with anastomotic revision (groups B1 and B2 combined, black line).

Discussion

Arterial inflow complications range from the clinically indolent arterial stenosis alone (usually discovered long after the engraftment) to the clinically "loud" hepatic artery thrombosis (usually close to the engraftment)[2]. Very early hepatic artery thrombosis leads to primary dysfunction and death[1]. A recent systematic review of 71 out of 999 screened studies revealed an adult recipient mortality of 34.3% (range: 0 – 80%) after early HAT[9].

Most studies report the early and hence the most catastrophic hepatic artery thrombosis, up to the fourth postoperative week, especially since it usually occurs by the seventh postoperative day[9]. In our series, we report a follow-up of up to 16 years. This is why the rate of arterial thrombosis is 8.3%, among the highest in the literature[2]. Of these 47 patients, 24 were diagnosed by the 14th post-operative day, whereas the rest 23 were diagnosed thereafter.

Routine Doppler echo played an important role to the early diagnosis of HAT. All 24 patients of that were explored (within the first two postoperative weeks) had an abnormal Doppler, some of them (n = 3, 12.5%) with normal liver enzymes. Doppler ultrasound is an invaluable aid to the prompt detection of early HAT[10]. There are very few limitations to its use and it is rarely (<15%) inconclusive. In addition, the clinical utility of microbubble contrast-enhanced ultrasound in the diagnosis of HAT after liver transplantation, with an accuracy of 100%, has practically eliminated inconclusive results[11]. In any case, at the present study, the diagnosis of HAT by Doppler was verified for all the 24 recipients of groups B1 and B2 who underwent surgical exploration.

We chose not to proceed with surgical exploration in all recipients diagnosed with HAT after the second postoperative week (group A, n=23), since all of these patients were clinically stable and already out of the intensive care unit. On the other hand, of the 24 recipients that were explored for HAT (groups B1 and B2), 18 were clinically unstable and still remained in the intensive care unit. The observation that the earlier the HAT the graver the prognosis is already known and well described by many authors[2,4].

Despite aggressive intervention, re-vascularized grafts failed in an almost similar manner as the non re-vascularized ones. This is because of HAT recurrence in almost all of those (n = 22, 91.7%) within seven to 28 days.

However, patient survival was higher in patients that underwent re-vascularization. The absence of statistical significance is due to the small size of the population. In fact, if the two group's size was greater than 30 instead of 23 and 24 respectively, this trend in patient survival would yield statistical significance. Recipient survival in groups B1 and B2 was higher not because graft survival was improved by its re-vascularization but because the patients that were explored because of the early (within 14 days) detection of HAT were "sicker" and therefore were led promptly to re-transplantation. It was the re-transplantation and not the re-vascularization that led to the superior patient survival in the recipients who underwent surgical exploration for HAT. The fact that thrombolysis and revision rarely salvage grafts after HAT and that re-transplantation provides superior patient survival has been recently described in a large (more than 4200 patients), single center, retrospective study[12].

In conclusion, early diagnosis of HAT by the use of daily surveillance Doppler leads to improved recipient survival secondary to earlier re-transplant and not because of successful surgical re-vascularization. Since no vascular interventional radiology rescue procedures were utilized in this study, no conclusions can be drawn about endovascular thrombectomy or stenting. However, the present study verified the necessity of re-transplantation whenever the diagnosis of HAT is placed, since surgical (the most optimal) thrombectomy and anastomotic revision failed to improve graft survival.

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