Original Articles

Hepatic artery thrombosis after orthotopic liver transplantation

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ABSTRACT

Objective: Hepatic artery thrombosis after liver transplantation is uncommon, but represents an important cause of morbidity and mortality. The aim of this study is to identify the possible risk factors for the development of hepatic artery thrombosis, and the impact of hepatic artery thrombosis on the patients and graft survival.

Methods: Between January 1994 and June 1998, we reviewed retrospectively a series of 86 liver transplant procedures performed on 81 adult patients. Arterial anomalies of the donor graft, rejection episodes, cold ischemia time, ABO matching, the use of blood/fresh frozen plasma during and after surgery, and the use of heparin as prophylactic anticoagulation therapy were examined as a possible contributing risk factors for the development of hepatic artery thrombosis.

Results: Hepatic artery thrombosis occurred in 7 procedures out of 86 (9%). Early cases of Hepatic artery thrombosis within 15 days after transplant occurred in 4 patients. Late thrombosis occurred in 3 patients. Analysis of potential risk factors for the development of hepatic artery thrombosis was carried out. Five out of 40 patients who did not received prophylactic heparin had hepatic artery thrombosis (12.5%), while only 2 out of 46 patients who received prophylactic heparin had hepatic artery thrombosis 4%. On the other hand, 6 out of the 7 patients developed hepatic artery thrombosis received more than 5 units of blood transfusion during the transplant procedure (11%) while only one patient developed hepatic artery thrombosis who received less than 5 units intra-operatively (3%). Management of hepatic artery thrombosis cases were carried out in the form of: thrombectomy (n=1), thrombectomy followed by retransplantation (n=2), and non-surgical or conservative treatment (n=4). The overall survival rate was (43%) (3 out of 7). Out of four deaths, 3 were directly related to hepatic artery thrombosis while the cause of death iin the remaining patients was attributed to pulmonary sepsis.

Conclusion: Early hepatic artery thrombosis leads to death unless quick retransplantation follows. Conservative treatment for the late onset hepatic artery thrombosis on occasion has been useful. The use of postoperative prophylactic anticoagulation therapy might be of benefit in the prevention of hepatic artery thrombosis after liver transplantation. Increased transfusion requirement for red blood cells during transplant procedure was independently associated with increase incidence of hepatic artery thrombosis.

Keywords: Liver, hepatic artery, thrombosis, transplantation.

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Hepatic artery thrombosis (HAT) after liver transplantation is uncommon, but represents an important cause of morbidity and mortality. Many studies attempted to identify its possible risk factors. Identification and minimization of these responsible factors is necessary to reduce the incidence of hepatic artery thrombosis.[1] The aim of this study is to identify the possible risk factors for the development of HAT, and the impact of HAT on the patients and graft survival.

Methods.   Between January 1994 and June 1998, we reviewed retrospectively a series of 86 liver transplant procedures performed on 81 adult patients at King Fahad National Guard Hospital, Riyadh, Saudi Arabia. The standard methods for patient selection, techniques of donor hepatectomy, and recipient transplantation were used.[1]   Veno-venous bypass was utilized in most patients. Immunosuppressive protocol was based on Cyclosporin/Steroid combination.   Several months into the program, it was changed to new formulation of Cyclosporin (Neoral, Sandoz Pharmaceutical). Two years later, immunosuppression was based on Tacrolimus (Prograf, Fujisawa Pharmaceutical). Hepatic artery reconstruction was performed in an end-to-end fashion using 6/0 polypropylene continuous suture in all patients.   Arterial anomalies of the donor graft, rejection episodes, cold ischemia time, ABO matching, the use of blood/fresh frozen plasma during and after surgery, and the use of heparin as prophylactic anticoagulation therapy were examined as a possible contributing risk factors for the development of HAT. Routine postoperative duplex ultra-sonography was performed in all patients in the first day after transplant to confirm the patency of the hepatic artery and portal vein. The diagnosis of HAT was clinically suspected in the presence of allograft dysfunction, biliary leak/sepsis or recurrent bacteria. Further evaluation was made with biochemistry, liver biopsy and is confirmed with Duplex ultrasonography. In all cases, arteriography was carried out to confirm the diagnosis. Early hepatic artery thrombosis was defined as that occurring within 15 days of transplant procedure and was always considered as a technical complication.

Statistical analysis.   Univariant analysis was performed, with the usage of Chi-Square test for categorical variables.

Results.   Hepatic artery thrombosis (HAT) occurred in 7 procedures out of 86 (9%).   All 7 patients were adults (children were excluded from this study group).   There were 5 males and 2 females. The age of the recipients ranged between 37-59 years with an average 50 years. Early cases of (HAT), within 15 days after transplant, occurred in 4 patients.   These were attributed to technical complications. While HAT in the remaining 3 patients occurred later after transplant. Analysis of potential risk factors for the development of HAT is shown in Table 1.   At the beginning of the transplant program, anticoagulants were not used routinely in the first 40 procedures. The subsequent forty-six procedures were managed with low dose heparin (10 units/kg/hour) given intravenously for one-week post transplant. Five patients had HAT in the first group (12.5%) compared to only two in the second group who received prophylactic heparin (4%). This shows that increased risk for HAT in the first group as compared to the second group, although the difference was not found to be statistically significant. On the other hand, 6 of the 7 patients developed (HAT) (11%) received more than 5 units blood transfusion/plasma during the transplant procedure while only one patient developed (HAT) (3%) who received less than 5 units intra-operatively. This shows that increased transfusion requirement for RBCS during transplant procedure increased risk for

Table 1 - Analysis of potential risk factors for the development of hepatic artery thrombosis.

Variable			Hepatic artery thrombosis (%)
Liver rejection	Yes	16	2/16 (12.5)
	No	70	5/70 (7)
Heparin	Yes	46	2/46 (4)
	No	40	5/40 (12.5)
ABO Matching	Identical	76	6/76 (8)
	Compatible	10	1/10 (10)
Intraoperative blood	<5U	30	1/30 (3)
Transfusion	>5U	56	6/56 (11)
Cold ischemia time	<7h	11	1/11 10)
	>7h	75	6/75 (8)

Table 2 - Management and outcome of HAT patients

Procedure	No	Outcome	Cause of death
Thrombectomy	1	Died	HAT
Thrombectomy & retransplantation	2	Died	HAT
Conservative	4	3 Survived	-
Treatment		1 Died	Pulmonary sepsis
HAT-Hepatic Artery Thrombosis			

development HAT, although it was found to be statistically insignificant. Histological evidence of rejection was present in two patients. All the seven patients had organs from donors with identical blood group. Vascular anomalies of the donor graft were not present in any of the cases of HAT. Hepatic artery reconstruction was performed in an end-to-end fashion by using of 6/0 polypropylene running suture. Vascular anomalies were dealt with at the back table except one who had right hepatic reconstruction done intraoperatively. One patient had HAT with cold ischemia time less than 7 hours, while the other 6 patients developed HAT with cold ischemia time more than 7 hours. Clinical presentation of HAT was either a sudden deterioration in he liver function tests, or unexplained fever with or without biliary sepsis/leak. Routine postoperative Duplex ultra-sonography was detected only one case of HAT before symptoms started. On other hand, Duplex ultra-sonography was diagnostic in all remaining cases of HAT after occurrence of symptoms. Angiography was used to confirm the diagnosis and/ or delineate the surgical anatomy. Management of HAT cases was carried out in the form of: thrombectomy (n=1), thrombectomy followed by retransplantation (n=2) and non-surgical or conservative treatment (n=4). The overall survival rate was (43%) (3 out of 7). Out of four deaths, 3 were directly related to HAT, while the cause of death in the remaining patients was attributed to pulmonary sepsis Table 2.

Discussion. Hepatic artery thrombosis after liver transplantation is considered as a devastating event associated with significant morbidity and mortality. Its overall incidence is about 7-8% of the whole liver transplant population.[3] Children have been reported to be at greater risk of developing hepatic artery thrombosis than adults due to the small size of their hepatic arteries and the postoperative hyper-coagulable state.[4] HAT usually occurs early in the post-operative period. Late thrombosis may also occur several months after transplantation and is usually associated with bile duct strictures or with recurrent sepsis. Changes in liver function studies are minimal in cases of late thrombosis because of partial compensation of the hepatic arterial blood supply via collaterals around the liver.[5] Complications due to HAT are usually less severe if occurred in the late post-operative period, this explains the lower mortality of the late HAT in our patients. In our series, the incidence of HAT was 9% (n=7 out of 86 adult liver transplant procedures), which are comparable to those of other series.[3] Early cases of HAT within 15 days after transplant occurred in 4 patients. Late thrombosis occurred in 3 patients at a mean of 140 day ranging between 90-225. There are many studies attempting to identify a number of potential risk factors for the development of HAT. Tzakis and associates,[3] originally, reported an increased rate of HAT in the presence of donors" arterial anomalies. Merion et al,[6] found that neither donor nor recipient arterial anatomy contributed significantly to the incidence of HAT. In this study, the presence of arterial anomalies did not increase the risk of hepatic artery thrombosis. Other proposed risk factors for the development of HAT include: rejection episodes, cold ischemia time, and ABO match. In a study done by Samuel and associates,[7] rejection was found to be the most prevalent factor in the development of HAT after transplantation. Mor E et al, reported a significant effect of cold ischemia time on the rate of HAT.[8] We could not confirm a role of these other factors in the development of hepatic artery thrombosis in this study. At the beginning of the transplant program, anticoagulants were not used routinely in the first forty procedures. The subsequent forty-eight procedures were managed with low dose heparin (10 unit/kg/h) intravenously for one week post-operatively. Five patients had HAT in the first group (12.5%) compared to only 2 in the second group who received prophylactic heparin (4%). This finding suggest that the use of post-operative prophylactic anticoagulation therapy might have a protective effect against the development of HAT, although this improvement in the results might be also attributed to improved learning curve. Mazzafero et al, Hashikura et al[1,9] reported a decreased incidence of thrombosis with the use of anticoagulant following pediatric liver transplantation. In regard to the effect of intraoperative blood transfusion during liver transplantation, 30 patients in our series received less than 5 units of packed RBCs intra-operatively only one of them developed HAT (3%). On the other hand 56 patients received more than 5 units of packed RBCs, six of them developed HAT (11%). From the above result, we found that increased transfusion requirement for packed RBCs during surgery was independently a risk factor associated with increased incidence of HAT. Our result is

comparable with other study carried out by Cacciarelli TV et al.[10] Management of HAT in our series include: one patient who underwent thrombectomy with revision of the anastomoses, thrombectomy followed by retransplantation in two, and conservative therapy in four patients. The survival rate among those patients was (43%), 3 out of 7. Our result is comparable with other studies done by Lerut and associates[11] who reported a patient survival rate of 36% (9 out of 25) in the setting of HAT. Tisone and co-workers[12] reported eight cases of HAT with a 25% survival rate. In our series, deaths were directly attributed to technical complications in 3 patients who developed early HAT, and pulmonary sepsis in the remaining one. Sheiner PA et al[13] reported that HAT was detected on routine duplex ultrasound at day (1-5) among a- symptomatic group and urgent revascularization was successful, while retransplantation in the symptomatic patients lead to improve graft and patient survival. In our study, only one patient discovered to have HAT by routine Duplex ultrasound on post-operative day-1, and urgent revascularization was not successful among early symptomatic HAT. Generally, the only treatment for patients with hepatic artery thrombosis is retransplantation. The outcome is usually favorable if the retransplantation is performed in a timely manner.[14] Out of the five retransplants in our series only two were for HAT. In our patients, because of severe organ shortage it was invariably the case that either no organ was available for a retransplant, or if an organ became available, it was too late. By then the patient was already in a septic condition, which produces inferior transplant results if the retransplant did occur. Because of the delay in obtaining organs, neither of the two patients was saved with a retransplant. It can be hypothized that if organ became available in a timely fashion for the retransplant, then it is likely that at least 25% of our deaths could have been prevented.

In conclusion, HAT is the most serious complication following liver transplantation. Early HAT leads to death unless quick retransplantation follows. Late cases can have a protracted course of septic period, or even symptomless due to formation of arterial collaterals. Conservative treatment for late onset HAT on occasion has been useful. The use of postoperative prophylactic anticoagulation therapy might be benefit in preventing HAT after liver transplantation, which can be validated only by prospective randomized studies. Increased transfusion requirement for RBCs during transplant procedure was independently associated with increase incidence of HAT.

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