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HEPATIC ARTERY THROMBOSIS: RELATED RISK FACTORS AFTER LIVER TRANSPLANTATION

Summary. *The purpose of this retrospective study is to evaluate the risk factors hepatic artery thrombosis (HAT) after orthotopic liver transplantation (OLT) in a consecutive series from a single center.*
Methods. *Between 2011 and 2013, we performed 278 living donor liver transplantations, including 189 males and 89 females. We compared the risk factors between HAT and non-HAT groups according to the following variables: age, gender, body mass index, graft weight, use of graft, Child-Pugh classification and model for end stage liver disease score, level of hemoglobin, blood pressure, operation time, blood transfusion, presence of ascites, international normalized ratio (INR), and etiology.*
Results. *Eighteen patients, including 15 males and 3 females (mean age — 45.1 years; age range — 22–60 years), had HAT after the operation. There were no pediatric patients in the HAT group. HAT rate was 6.5 % in our series. Graft failure and retransplantation due to HAT was 38.7 % in a 2-year period. Biliary leakage was observed in 72 (25.8 %) living donor liver transplantations; this rate was higher in patients with HAT (44.4 %). The infection rate was 50 % (n = 9) in the HAT group and 32.7 % (n = 91) in the non-HAT group. Mean INR value was 2.15 in the HAT group and 1.72 in the non-HAT group. When we compared the groups according to use of graft for anastomosis, biliary leakage, infection, and INR value, the differences were statistically significant (P < 0.05).*
Conclusion. *Although the results of OLT have improved over the past years, HAT is still associated with substantial morbidity, high incidence of graft failure, and high mortality rates. The most important findings associated with HAT in our series were found as INR levels, biliary leakage, and resistant infections. Use of vascular graft for hepatic artery anastomosis was found to increase HAT risk.*

Introduction

Vascular complications after orthotopic liver transplantation (OLT) are one of the most frightening problems that frequently result in graft and patient loss. Arterial complications in liver transplantation are the most frequent cause of vascular complications and are present in 3 to 12 % of all transplantation [1, 2]. Hepatic artery thrombosis (HAT) is a serious complication in patients undergoing OLT. In general, HAT is divided into 2 categories: early HAT and late HAT [2–4]. Early HAT is a major complication following liver transplantation and it is an important cause of graft loss and mortality [5–8]. The cornerstone of this therapy has been urgent retransplantation that is limited by organ availability [3]. In this study, we retrospectively analyzed the risk factors for the development of HAT after living donor liver transplantation.

Materials and Methods

This is a single-center study and data was derived from a prospectively collected data base at the Organ Transplantation Unit of Inonu University Turgut Ozal Medical Center of the Turkish Republic from 2011 to 2013. In terms of risk factors that may be associated with early (< 30 day) and late (> 30 day) HAT, 278 living donor liver transplantation patients were evaluated. There were 189 males and 89 females (mean age — 41.6 years; age range — 4 months — 72 years). The mean model for end-stage liver disease score before transplantation was 16.3. Routine Doppler screening was performed peroperatively and on the first day after surgery. Diagnoses of arterial complications were performed based on clinical and biological findings. Multislice computed tomography (CT) and arteriography were performed when the Doppler showed pathological findings or when the clinical and laboratory profile suggested thrombosis. Anticoagulant therapy was not routinely administered. Hepatic artery anastomosis was performed using interrupted 8–0, 9–0 (in some pediatric cases) polypropylene sutures under the vision of surgical loupes (8x) by the same surgeon.

Statistical analyses were performed using SPSS Advanced Statistics 16.0 software package (SSPS Inc, Chicago, IL, United States).

Results

In this series with 278 OLT, HAT rate was 6.5 % (n = 18). According to the time of diagnosis, the rate of early HAT was 17/18 and late HAT was 1/18. Eighteen patients, including 15 males and 3 females, had HAT after the operation (mean age — 451 years; age range — 22–60 years). Graft loss and retransplantation due to HAT was 38.7 % in the 2-year period. There were 10 pediatric patients (age range — 4–60 months). There were no pediatric patients in the HAT group.

Etiologic factors associated with chronic liver disease are shown in Table 1 The indications for OLT in those recipients subsequently developing HAT were as follows: 9 (50 %) had a history of hepatitis B virus (HBV)-related liver cirrhosis, 3 (16.6 %) had HBV + hepatitis D virus (HDV), 2 (11.1 %) had HBV + hepatocellular carcinoma (HCC). Two patients (2/18) had HCV, another one (1/18) Wilson's disease, and one patient (1/18) had cryptogenic liver disease.

We performed 2 retransplantations as a result of recurrence of liver disease during this study period. The HAT rate was 27.3 % (3/11) in the vascular graft group and 5.6 % (15/267) in the without vascular graft group (P < 0.05). Double-hepatic artery anastomosis was the preferred technique for 12 patients of the 278 patients. There was no HAT in the double-hepatic artery anastomosis group. Three saphenous vein grafts, 3 cadaveric arterial grafts were used and 4 splenic artery interpositions, 1 gastric artery interposition were performed due to intimal dissection in the artery or peroperative thrombosis during the initial surgery. Among these patients, there was 1 HAT in a saphenous vein graft, 1 in a splenic artery interposition group, and 1 in a left gastric artery group.

As a treatment, we performed end-to-end anastomosis of the graft artery and recipient splenic artery with interposition in 2 HAT patients, end-to-side anastomosis between the graft hepatic artery and the recipient aorta with synthetic graft in 1 HAT patient's end-to-end anastomosis of the graft artery, and recipient hepatic artery with cadaveric arterial and saphenous vein grafts in 2 HAT patients. We gained hepatic inflow with embolectomy in 3 patients and with end-to-end hepatic artery re-anastomosis in the remaining patients.

Table 1. Etiologic Factors Associated with Chronic Liver Disease

Etiologic Factors	Number of Patients, n (%)
HBV	137 (49.2)
HBV+ HCC	17 (6.1)
HCC	5 (1.7)
HCV	15 (5.3)
Ethanol	4 (1.4)
Autoimmune	3 (1.07)
Biliary atresia	1 (0.3)
Echinococcus alveolaris	2 (0.7)
Budd-Chiari syndrome	7 (2.5)
Fulminant hepatitis	25 (8.9)
Cryptogenic	46 (16.5)
Primary biliary cirrhosis	3 (1.07)
Other	13 (4.6)

Mean international normalized rate (INR) value was 2.15 in the HAT group and 1.72 in the non-HAT group. Biliary leakage was seen in 72 (25.8 %) living donor liver transplantations; this rate was higher in patients with HAT (n = 8; 44.4 %). The infection rate was 50 % (n = 9) in the HAT group and was 32.7 % (n = 91) in the non-HAT group. When we compared the groups according to biliary leakage, infection, and INR, the differences were statistically significant (P < 0.05). The mortality due to sepsis, multiple-organ failure, and graft dysfunction was 38.9 % (n = 7) of the patients with HAT and 20.1 % (n = 52) of the non-HAT patient group (P < 0.05).

Discussion

HAT after liver transplantation is a severe complication that may lead to graft infarction and subsequent graft loss HAT when it occurs early post OLT may present with acute graft failure, sepsis, or liver abscess, and bile duct complications such as biliary leak or structuring [5]. The incidence of HAT was reported as 3–12 % of adult liver transplantations and subsequently resulted in retransplantation in 50–75 % of these patients in the literature [2]. The HAT rate was 6.5 % in our series and the graft loss due to HAT was 38.7 % in a 2-year period. Several series reported HAT in 10 % of recipients, with higher rates for children [6]. The number of pediatric patients was 10 (age range — 4–60 months) in our series. There were no pediatric patients in the HAT group.

The symptoms, signs, and abnormal laboratory values are mostly absent in early HAT because its presentation is mostly acute; screening by routine Doppler ultrasound is very important. In addition to Doppler ultrasound, multislice CT and digital angiography technologies have provided an accurate and rapid method for detecting HAT before ischemic damage of the allograft [7, 8]. We systematically use routine Doppler screening at our institution first intraoperatively after the anastomosis and daily during the first week.

Silva et al reported that bile leak was associated with 12 of the 61 patients who developed HAT, as compared to 39 of the 1196 recipients who did not develop HAT (P = 0.001) in their 10-year period [8].When we compared the biliary leakage rates between the HAT and non-HAT groups, we also found statistically significant difference (P < 0.05) between the 2 groups. Treatment modalities for HAT include thrombectomy alone, intrahepatic arterial thrombolysis with thrombolytic agents, creation of a new anastomosis between a more proximal part of the recipient artery and a more distal part of the donor hepatic artery, and introduction of an interposition graft or retransplantation. Early diagnosis is a prerequisite for these revascularization strategies. Early HAT presents mostly with acute fulminant hepatic failure and these conditions require retrans-

plantation. Retransplantation is limited by both organ availability and the patient's clinical condition. Urgent revascularization with thrombectomy and a combination of thrombectomy with revision of anastomosis has been successful in some patients with an early diagnosis.

Treatment modality depends on the time of diagnosis [2, 9]. The rate of early HAT was 17/18 and late HAT was 1/18 in patients with HAT in our series. Because of the rate of early HAT, an early aggressive treatment procedure was selected and embolectomy and reanastomosis with/without graft was performed in 11 patients. The retransplantation rate was 38.9 %. According to the current literature almost 50 % of HAT patients died without retransplantation [9, 10]. Those who did survive inpatients with HAT suffered significant morbidity, related to problems of hepatic sepsis and biliary tree complications [9]. Although retransplantation has been credited with reducing the mortality of HAT, the inadequate supply of donor organs has limited this option in our country. Therefore, we are supposed to diagnose this condition early and apply embolectomy and reanastomosis techniques to preserve the transplanted liver. The feasibility of using immediate revascularization to avoid the need for retransplantation has been reported in the literature. The use of the splenic artery for the arterial inflow in HAT has been previously described and there have been several reports of transplant arterial reconstruction using some interposition grafts [11–15]. We preferred following procedures for hepatic inflow in patients with HAT: end-to-end anastomosis of the graft artery and recipient splenic artery with interpositions, end-to-side anastomosis between the graft hepatic artery and recipient aorta with synthetic graft, end-to-end anastomosis of the graft artery and recipient hepatic artery with cadaveric arterial and saphenous graft, embolectomy, and end-to-end hepatic artery reanastomosis.

Urgent revascularization with the reuse of recipient hepatic artery may carry the risk for inadequate flow or other problems in this vessel, which may contribute to re-HAT [8, 9]. But we suggest a revascularization procedure if the presence of back-bleeding from the graft hepatic artery is present with normal-appearing liver.

Surgical technique is probably not a major risk factor at our high-volume transplantation center. Some studies demonstrated that the HAT rate was higher in case of multiple hepatic artery anastomoses. When we compared the number of arterial anastomoses for reconstruction, we observed that there was no HAT when double hepatic artery anastomoses were performed in our series.

Bile leak and infection (cholangitis and so on) were also found to be common in patients with HAT. It is unclear whether these biliary complications were the cause of or a consequence of HAT. INR values in our study were also found to be significantly different in the HAT group, although other series found it was not significantly associated with increased risk for HAT [9, 16].

In conclusion, the HAT rate was 6.5 % in our series and HAT has a significant impact on survival, with a 38.9 % mortality rate in those with the complication in the 2-year period. Revascularization procedures are the most important approaches regarding the patient's life because of the inadequate supply of donor organs. Early diagnosis is a prerequisite for revascularization strategies. The most important findings associated with HAT are bile leakage and presence of resistant infections. Use of vascular grafts increases risk for HAT.

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ТРОМБОЗ ПЕЧЕНОЧНОЙ АРТЕРИИ: ОЦЕНКА ФАКТОРОВ РИСКА ПОСЛЕ ТРАНСПЛАНТАЦИИ ПЕЧЕНИ

Резюме. Целью данного ретроспективного исследования является оценка факторов риска тромбоза печеночной артерии (ТПА) после ортотопической трансплантации печени (ОТП) в последовательной серии в одном центре.

Материалы и методы. В период с 2011 по 2013 год мы провели 278 трансплантаций печени от живых доноров, 189 мужчин и 89 женщин. Мы сравнили факторы риска между группами с ТПА и без ТПА с соответствии со следующими переменными: возраст, пол, индекс массы тела, вес трансплантата, использование трансплантата, классификация Child-Pugh и модель последней стадии оценки заболевания печени, уровень гемоглобина, артериального давления, время выполнения операции, переливание крови, наличие асцита, международный нормализованный индекс (МНИ) и этиология.

Результаты. У восемнадцати пациентов, 15 мужчин и 3 женщин (средний возраст — 45,1 года, возрастной диапазон — 22–60 лет), после операции наблюдался ТПА. В группе не было детей с ТПА. В нашей серии частота ТПА составил 6,5 %. Частота отторжения трансплантата и ретрансплантации из-за ТПА составляла 38,7 % в течение 2-летнего периода. Желчеистечение наблюдалось у 72 (25,8 %) живых доноров для трансплантации печени; этот показатель был выше у пациентов с ТПА (44,4 %). Уровень инфицирования составил 50 % (n = 9) в группе с ТПА и 32,7 % (n = 91) в группе без ТПА. Среднее значение МНИ — 2,15 в группе с ТПА и 1,72 в группе без ТПА. При сравнении групп в соответствии с использованием трансплантата для анастомоза, желчеистечения, инфекции и значения МНИ различия были статистически значимыми ($P < 0,05$).

Заключение. Хотя результаты ОТП за последние годы улучшились, ТПА все еще ассоциируется с существенным уровнем заболеваемости, высоким уровнем отторжения трансплантата и высокими показателями смертности. Наиболее важные выводы в отношении ТПА в нашей серии были связаны с уровнями МНИ, желчеистечением и устойчивыми инфекциями. Было обнаружено, что использование сосудистого трансплантата для анастомоза печеночной артерии увеличивает риск ТПА.

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ТРОМБОЗ ПЕЧІНКОВОЇ АРТЕРІЇ: ОЦІНКА ФАКТОРІВ РИЗИКУ ПІСЛЯ ТРАНСПЛАНТАЦІЇ ПЕЧІНКИ

Резюме. Метою цього ретроспективного дослідження є оцінка факторів ризику тромбозу печінкової артерії (ТПА) після ортотопічної трансплантації печінки (ОТП) у послідовній серії в одному центрі.

Матеріали і методи. У період із 2011 по 2013 рік ми провели 278 трансплантацій печінки від живих донорів, 189 чоловіків і 89 жінок. Ми порівняли фактори ризику між групами із ТПА й без ТПА відповідно до таких змінних: вік, стать, індекс маси тіла, маса трансплантата, використання трансплантата, класифікація Child-Pugh і модель останньої стадії оцінки захворювання печінки, рівень гемоглобіну, артеріального тиску, час виконання операції, переливання крові, наявність асциту, міжнародний нормалізований індекс (МНІ) та етіологія.

Результати. У вісімнадцяти пацієнтів, 15 чоловіків і 3 жінок (середній вік — 45,1 року, віковий діапазон — 22–60 років), після операції спостерігалася ТПА. У групі не було дітей із ТПА. У нашій серії частота ТПА становила 6,5 %. Частота відторгнення трансплантата й ретрансплантації через ТПА становила 38,7 % упродовж 2-річного періоду. Жовчовитікання спостерігалося в 72 (25,8 %) живих донорів для трансплантації печінки; цей показник був вищим у пацієнтів із ТПА (44,4 %). Рівень інфікування становив 50 % (n = 9) у групі з ТПА і 32,7 % (n = 91) у групі без ТПА. Середнє значення МНІ — 2,15 у групі із ТПА і 1,72 у групі без ТПА. При порівнянні груп відповідно до використання трансплантата для анастомозу, жовчовитікання, інфекції і значення МНІ розбіжності були статистично значимими ($P < 0,05$).

Висновок. Хоча результати ОТП за останні роки покращилися, ТПА усе ще асоціюється з суттєвим рівнем захворюваності, високим рівнем відторгнення трансплантата і високими показниками смертності. Найбільш важливі висновки щодо ТПА в нашій серії були пов'язані з рівнями МНІ, жовчовитіканням і стійкими інфекціями. Було виявлено, що використання судинного трансплантата для анастомозу печінкової артерії збільшує ризик ТПА.