Transplant International

INVITED COMMENTARY

Selective retransplantation after late hepatic artery thrombosis

Philippe Compagnon & Christian Toso

Department of Surgery, Divisions of Abdominal and Transplant surgery, Geneva University Hospitals, Geneva, Switzerland

Correspondence
Christian Toso, Department of Surgery, Division of Abdominal surgery, Geneva University Hospitals, rue Gabrielle-Perret-Gentil 4, 1205 Genève, Geneva, Switzerland.
Tel.: +41223727702;
fax: +41223727733;
e-mail: christian.toso@hcuge.ch

Transplant International 2019; 32: 470–472

Received: 10 February 2019; Accepted: 11 February 2019

Hepatic artery thrombosis (HAT) is a serious and life-threatening complication that can occur any time after liver transplantation. HAT is generally subdivided into two categories. Early HAT frequently presents with profound graft dysfunction and sepsis, and requires urgent revascularization or retransplantation. In contrast, late HAT (L-HAT) is usually milder, presumably thanks to the mitigating effect of established collaterals and the lower level of immunosuppression [1,2]. Its diagnosis can be incidental on imaging or after the development of ischemic complications [3]. L-HAT presents challenging management issues, with only few available data to guide therapeutic decision-making. Consequently, its treatment varies between centers. Retransplantation is considered the treatment of choice, but this option is restricted by both graft availability and the general condition of the potential recipient, and the identification of patients who will not need a retransplantation is paramount.

In this issue of *Transplant International,* Capelli *et al.* [4] from the Paul Brousse hospital in Paris evaluate the outcome of 56 patients with L-HAT, using their own center cohort. Patients were divided into three groups according to the clinical presentation. The authors advocate for a conservative management of patients with asymptomatic or mild presentations. Early retransplantation should be offered to patients with severe clinical presentations (usually biliary infections). The experience of the authors suggests that this approach is safe and does not increase mortality, provided that a short waiting time can be guaranteed after listing. Excellent patient survivals are reported after retransplantation in the present work, reaching 69% at 5 years [4]. Although this study is limited by its retrospective design, and the relative small number of patients, the findings are of great clinical value.

Waiting time until retransplantation is key in the management of patients with HAT, and those with L-HAT usually wait longer than those with early HAT [5]. This observation is linked to the absence of rescue strategies for L-HAT within most MELD-based systems. In addition, the timing for listing patients with L-HAT is difficult to determine as the burden of the ischemic biliary disease cannot be defined in a standardized and predictive fashion. In the present series, the good results after retransplantation may be linked to the short waiting time of 3.6 months, itself related to favorable French allocation rules. French patients with L-HAT have access to MELD exception points, the level of which is determined by experts from the French

doi:10.1111/tri.13411

national organ sharing organization based on the estimated waiting list mortality. Of note, the strategy still has limitations as three patients died of sepsis of liver origin before retransplantation.

MELD score and the presence of multidrug-resistant infection predict waiting list and post-retransplant deaths [5–8]. Keeping these data in mind, one can draw a window for relisting/retransplanting patients with L-HAT [9]. Some suggest that a median waiting time of 6 weeks leads to the best short- and long-term outcomes [5]. At the time of L-HAT diagnosis, a biliary infection is often present, leading to poor potential outcomes after a (too) early retransplantation. An appropriate treatment should first be applied, improving the recipient's condition or revealing those definitively unfit for retransplantation [3,10,11]. Conversely, a (too) long waiting time before retransplantation exposes the recipient to the risk of multidrug-resistant infection and death [5]. In the present series, patients with liver abscess were managed during the waiting period.

Following a conservative approach, retransplantation for HAT-related complications was necessary in 50% of the patients in this transplant program [4]. This rate is in line with other estimates [2,3,6,7,10]. The authors rightly advocate that every effort should be made to rescue as many liver grafts as possible following HAT, considering the chronic organ shortage and the high mortality after retransplantation. They found that 41% of patients without severe symptoms remain alive at 10 years without retransplantation [4]: a strong argument for a "wait and see policy" in such patients.

Although many risk factors, surgical (complex arterial reconstruction, a previous history of HAT, a previous history of upper abdominal surgery, aged donors, a low donor weight, a young recipient age, back table surgery for anatomic variations) [12,13] and nonsurgical (multiple and/or severe acute rejection, coagulation abnormalities, tobacco use, and CMV infection) [1] have been implicated in the development of HAT, the exact pathogenesis of this complication often remains unclear. The immediate initiation of aspirin therapy after transplantation may reduce the risk of HAT [14,15]. The use of microvascular surgical techniques and of Doppler ultrasound screening could prevent HAT, or allow its early detection [16]. In all cases, the risk for HAT should be estimated early, in order to tailor the screening protocol, and potentially allow urgent revascularization [17].

Capelli *et al.* [4] argue that the observed favorable outcomes after L-HAT compared to early HAT, probably reflect the presence of collateral vessels from neighboring organs. The development of such vessels is promoted at the site of the arterial thrombosis (the closer to the hilum, the more likely collaterals develop), by the type of graft (split grafts may be more prone to collaterals), the presence of an hepatico-jejunostomy and/or multiple arteries, and the time since transplantation (patients with a late HAT are more likely to develop collaterals) [18]. Of note, the development of arterial collaterals does not always compensate for the HAT, and does not always prevent the occurrence of a biliary ischemia [19].

Overall, the work published by Capelli *et al.* [4] will further help managing patients with L-HAT. The message is addressed to clinicians, who should be more conservative in relisting/retransplanting patients with L-HAT, especially when they do not have significant symptoms. On their side, policy makers should also be more sensitive to the cause of patients with L-HAT, and design a more direct path to retransplantation when the need is validated. All strategies together should help saving more patients with L-HAT and minimizing the use of liver grafts.

Funding

The authors have declared no funding.

Conflicts of interest

The authors have declared no conflicts of interest.

REFERENCES

1. Oh CK, Pelletier SJ, Sawyer RG, *et al.* Uni-and multi-variate analysis of risk factors for early and late hepatic artery thrombosis after liver transplantation. *Transplantation* 2001; **71**: 767.
2. Panaro F, Gallix B, Bouyabrine H, *et al.* Liver transplantation and spontaneous neovascularization after arterial thrombosis: "the neovascularized liver". *Transpl Int* 2011; **24**: 949.
3. Bhattacharjya S, Gunson BK, Mirza DF, *et al.* Delayed hepatic artery thrombosis in adult orthotopic liver transplantation—a 12-year experience. *Transplantation* 2001; **71**: 1592.
4. Capelli R, Allard MA, Ciacio O, *et al.* Late hepaticartery thrombosis after liver transplantation: which strategy? A single-center retrospective study. *Transpl Int* 2019; **32**: 473.
5. Buchholz BM, Khan S, David MD, *et al.* Retransplantation in late hepatic artery thrombosis: graft access and transplant

outcome. *Transplant Direct* 2017; **3**: e186.
6. Leithead JA, Smith MR, Materacki LB, *et al.* Intercurrent infection predicts mortality in patients with late hepatic artery thrombosis listed for liver retransplantation. *Liver Transpl* 2012; **18**: 1353.
7. Gunsar F, Rolando N, Pastacaldi S, *et al.* Late hepatic artery thrombosis after orthotopic liver transplantation. *Liver Transpl* 2003; **9**: 605.
8. Petrowsky H, Rana A, Kaldas FM, *et al.* Liver transplantation in highest acuity recipients: identifying factors to avoid futility. *Ann Surg* 2014; **259**: 1186.
9. Lui SK, Garcia CR, Mei X, Gedaly R. Re-transplantation for hepatic artery thrombosis: a national perspective. *World J Surg* 2018; **42**: 3357.
10. Valente JF, Alonso MH, Weber FL, Hanto DW. Late hepatic artery thrombosis in liver allograft recipients is associated with intrahepatic biliary necrosis. *Transplantation* 1996; **61**: 61.
11. Margarit C, Hidalgo E, La zaro JL, Murio E, Charco R, Balsells J. Biliary com plications secondary to late hepatic artery thrombosis in adult liver transplant pati ents. *Transpl Int* 1998; **11**(suppl 1): S251.
12. Pastacaldi S, Teixeira R, Montalto P, Rolles K, Burroughs AK. Hepatic artery thrombosis after orthotopic liver transplantation: a review of nonsurgical causes. *Liver Transpl* 2001; **7**: 75.
13. Mourad MM, Liossis C, Gunson BK, *et al.* Etiology and management of hepatic artery thrombosis after adult liver transplantation. *Liver Transpl* 2014; **20**: 713.
14. Vivarelli M, La Barba G, Cucchetti A, *et al.* Can antiplatelet prophylaxis reduce the incidence of hepatic artery thrombosis after liver transplantation? *Liver Transpl* 2007; **13**: 651.
15. Shay R, Taber D, Pilch N, *et al.* Early aspirin therapy may reduce hepatic artery thrombosis in liver transplantation. *Transplant Proc* 2013; **45**: 330.
16. Heaton ND. Hepatic artery thrombosis: conservative management or retransplantation? *Liver Transpl* 2013; **19** (s2): S14.
17. Yilmaz S, Kirimlioglu V, Isik B, *et al.* Urgent revascularization of a liver allograft with a saphenous vein interposition graft between the hepatic artery and the recipient splenic artery after late hepatic artery thrombosis. *Dig Dis Sci* 2005; **50**: 1177.
18. Heaton ND. Hepatic artery thrombosis: conservative management or retransplantation? *Liver Transpl* 2013; **19** (Suppl 2): S14.
19. Fujiki M, Hashimoto K, Palaios E, *et al.* Probability, management, and long-term outcomes of biliary complications after hepatic artery thrombosis in liver transplant recipients. *Surgery* 2017; **162**: 1101.