Editorial

Identification and treatment of biliary complications after liver transplantation: more relevant than ever

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Liver transplantation remains the treatment of choice for patients with end-stage liver diseases. Given the increasing demand for liver transplantation, the spectrum of potential grafts has been widened and includes now not only regular grafts from donation after brain death (DBD) but also organs from donation after cardiac death (DCD), split liver and living donor grafts, as well as so-called "*marginal grafts*" from donors with extended criteria such as significant steatosis hepatis or older age (1). These grafts are associated with higher rates of early allograft dysfunction and primary non-function—which stresses the healthcare system with increased length of hospital stay for patients and higher costs (2,3). Moreover, marginal grafts are at risk for biliary complications such as anastomotic and non-anastomotic strictures as well as biliary leakages, which is caused by more severe ischemia reperfusion injury and in consequence reduced micro perfusion of the biliary tract (4). One currently emerging technology to improve the preservation, evaluate graft quality, and potentially avoid early allograft dysfunction or biliary complications is *ex vivo* liver machine perfusion, either Hypothermic Oxygenated Perfusion (HOPE) or normothermic ex vivo liver machine perfusion (NEVLP) (5). The recent review by Magro *et al.* (6) from the University of Palermo is more relevant than ever in this context, providing a structured approach describing the risk factors, etiology and treatment of biliary complications after liver transplantation.

Magro *et al.* (6) address the ongoing discussion of the type of biliary anastomosis (duct to duct with end-to-end or side-to-side anastomosis, or hepaticojejunostomy) and whether a T-tube should be used. They conclude that the overall inconclusive data for the insertion a T-tube possibly might reflect a trend for more duct-to-duct anastomosis, if technically feasible. Especially, if a tension free anastomosis is possible, reduced surgery time might be an additional argument for omitting the T-tube. The removal of the T-tube might require another clinic visit (depending on local standards) and can be associated with further complications. Moreover, shortage of T-tube supply, which is currently the case in Germany, limits the everyday availability.

The authors also discuss donor and recipient characteristics as well as risk scores to predetermine graft failure. Instead of the donor risk index, which is based on donor data only, recent publications focus on more comprehensive postoperative recipient characteristics such as the Early Allograft Failure Simplified Estimation (EASE) and L-Graft Score that might predict graft loss more precisely (3,7,8). However, none of these scores has been shown to predict biliary complications. Marginal grafts are especially susceptible to ischemia reperfusion injury (IRI), especially if exposed to prolonged cold ischemia. This combination can increase the risk of non-anastomotic biliary strictures, especially in DCD organs (9). For example, three out of ten initially declined DCD liver grafts that were transplanted after passing quality assessment by NEVLP as part of the Viability Testing and Transplantation of Marginal Livers

(VITTAL) trial developed biliary complications and required retransplantation (9).

Ischemic type biliary lesions often require prolonged endoscopic treatment with balloon dilatation and stenting. Magro *et al.* (6) provide a diagnostic flow-chart in case of suspicion of biliary complications with a focus on diagnostics and then intervention. Especially in centers without high expertise, the authors propose that retrograde cholangiopancreatography should be the last modality of choice, given the relatively high rates of complications such as pancreatitis and cholangitis.

Prevention of IRI through the means of *ex vivo* liver machine perfusion seems like the logical next step to prevent biliary complications. However, research regarding perfusion duration and modality, as well as regarding robust parameter for hepatocellular and cholangiocellular viability is still ongoing (10). Multicenter trials are necessary to analyze the effects of machine perfusion, either hypothermic or normothermic concepts, on the prevention and identification of biliary complications. Animal models with clinically available liver machine perfusions can be used with porcine livers, however, costs and logistics are both quite high. Small animal models for liver machine perfusion can therefore be a solution, as previously proposed (11,12). In small animal models of NEVLP, dual vessel perfusion and modification of vasodilation improved the viability of the bile duct. Analysis of bile pH, bicarbonate and glucose have additionally been proposed as markers of viability in NEVLP (13,14). Furthermore, defatting strategies have been proposed to reduce the impact of IRI in grafts with macrovesicular steatosis (15,16).

Since the liver transplantation community continues to pioneer machine perfusion and the limits of donor marginality, identification and treatment of biliary complications is more relevant than ever. Magro *et al.* (6) provide a thoughtful insight with their review of literature of biliary complications. We expect more research detailing the prevention or reduction of biliary complications through HOPE or NEVLP to be of outmost relevance for clinical practice in the near future.

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Footnote

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