

Biliary duct complications after liver transplant

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Currently, hepatic transplants are the treatment of choice for terminal liver disease. Optimal results require multidisciplinary treatment and a highly-qualified team. However, despite medical experience gained and standardization of surgical protocols which have occurred with the passage of time, there are still many immediate and delayed problems related to hepatic transplants which pose permanent challenges to the medical group involved with the procedure.

Complications originating in the bile ducts affect between 9% and 30% of all patients after liver transplantation and are the most frequent group of surgical complications (1, 2). This type of complication includes,

1. Stenosis affects 4% to 13% of transplant patients. Anastomotic stenosis at the site of *bile duct reconstruction accounts for 80% of the cases associated with technical or ischemic problems in early or late stages (up to 2 months after transplantation). Nonanastomotic cases account for the other 20%. They occur at a distance of 0.5 cm or more from site of anastomosis and have been associated with ischemic or immune events and with lower survival rates after liver transplantation.*
2. Biliary fistulas affect from 2% to 25% of transplant patients and are usually associated with bilomas. Their indications appear earlier than those of stenosis.
3. Choledocholithiasis affects 5% of transplant patients. It is related to alteration of biliary drainage caused by denervation secondary to the surgical procedure and by other factors such as cyclosporine usage (3).
4. Sphincter of Oddi dysfunction affects between 2% and 7% of transplant patients. It is diagnosed by exclusion when the previously described causes are discarded (3-7).

Multiple risk factors are associated with development of post-transplant biliary complications. Some have surgical origins such as hepatic artery thrombosis, over-dissection, and devascularization of the biliary tract during removal of the donor liver, prolonged cold and/or warm ischemia times, excessive use of electrocauterization and continuous tension at the site of an anastomosis. Other factors originate with the donor including donor livers extracted after the donor's heart has stopped, and whether or not donor's age is over 50 years. Still other factors are related to immune issues and infections. These include the serologic state and the possibility of previous cytomegalovirus infection (8). T-tube placement has been abandoned for prophylaxis to prevent post-transplant development of fistulas and stenosis because it resulted in greater incidence of biliary fistulas, cholangitis and peritonitis. Finally, recent studies have demonstrated that different types of surgical reconstruction (end to end bile duct anastomoses vs. hepaticojejunostomies)

have similar rates of complications. This conclusion favors the use of the end to end bile duct anastomoses because of the possibility of performing them endoscopically (9-11).

Clinical presentations of post-liver transplant biliary complications are very diverse ranging from totally asymptomatic patients with mild alterations in liver function tests to severe cases of cholangitis, itching and jaundice that require complementary studies and liver biopsy procedures to rule out associated clinical conditions such as the acute rejection, disease recurrence and vascular complications (8).

Diagnostic study begins with assessment using noninvasive methods such as ultrasound, Doppler ultrasound of the hepatic and portal vessels, and abdominal MRIs, after which invasive methods of assessment may be used. According to the result of the first methods and according to the specific case, endoscopic retrograde cholangiopancreatography (ERCP) and/or transparietohepatic cholangiography may be needed. New biliary interventions are being implemented such as the use of balloon-assisted enteroscopy and recoverable and self-expanding stents. This use of balloon-assisted enteroscopy in patients with hepaticojejunostomy reconstructions has lower morbidity rates than those associated with transparietohepatic cholangiography while the use of recoverable and self-expanding stents, placed by endoscopic procedures, provides greater durability and a lower frequency of replacement (8, 12).

The treatment of biliary complications entails an interaction of specialized medical staff including endoscopy specialists, radiologists and surgeons. Most of the time the first line treatment for anastomotic stenosis and biliary fistula require an ERCP plus stent placement and/or balloon dilatation. Success rates obtained have been over 90% with recovery without any additional therapy in the 3 first months. Stenoses which are late appearing and non-anastomotic stenosis may also require ERCP replacement of biliary stents replacement every 3 months for up to two years before new surgical intervention can be considered. Success rates between 70% and 100% have been obtained with up to 18% of cases suffering recurrences (13-18).

The article in this issue from the Transplant Group of the Hospital 'Pablo Tobón Uribe' in Medellín, Colombia, brings together valuable experience from a large retrospective series of cases. The low incidence of biliary complications (9.84%) reported should be highlighted, as it reflects the strength and experience of the group. It would have been interesting if the article had presented any associations between the reported cases and risk factors which have been clearly described in the literature. It would also have been interesting to read about patients who underwent

retransplantation who surely presented biliary complications. Our attention was drawn to the 28% frequency of biliary fistulas and the 50% rate of presentation of early anastomotic stenoses which surely reflect the complexity of the cases in question. It is also important to underline the high success rate of non-surgical treatment among this group of patients. This is a growing tendency that has been consolidated through acquisition of greater experience and new endoscopic and radiological techniques and equipment. Invasive surgical procedures are becoming the last resort when non-surgical treatment does not work. Finally, we think that these results should motivate the other transplant groups in Colombia to share their experiences to give us more of the positive feedback needed to help us continue improving.

It would be also interesting to ask ourselves, what can be done to further decrease the frequency of post-transplant biliary complications?

Without doubt, the experience of the transplant surgeon, not only the surgeon's perfect surgical technique, but also the obsessive treatment of the donor, allograft, and recipient, before, during and after the procedure, can explain the differences among groups.

For example, in our group, an ex-situ biliary perfusion of 300 cc of Custodiol is routinely performed in addition to vascular perfusion. Furthermore, we recommended endoscopic, radiological and surgical procedures be performed by the same group which does the transplant and not by other specialists who are not familiar with the complexity of a liver transplant.

Finally, to put into perspective the additional possibilities that exist for preventing biliary complications, it is important to mention the study performed by C. Moench et al. in Germany in 2003 (19). They hypothesized that insufficient perfusion of the biliary arterial plexus explains the appearance of ischemic biliary stenosis. To test their hypothesis they conducted a controlled study of 131 transplants which had been perfused with standard in situ portal perfusion using Wisconsin solution and 59 transplants upon which arterial perfusion had been performed with the same solution. The results clearly favor arterial perfusion since only one out of 59 cases presented a biliary ischemic problem while 21 out of 131 cases presented problems related to ischemia with the standard technique. This difference was highly significant ($p = .009$ in Pearson's Chi-squared test).

Since Colombian groups still use the European preservation solution, Custodiol, rather than the Wisconsin solution, it would be interesting to conduct a multicenter (5 centers) study to evaluate the real importance of this hypothesis and the possibility of implementing it.

REFERENCES

1. Duailibi DF, Ribeiro MA Jr. Biliary Complications Following Deceased and Living Donor Liver Transplantation: A Review. *Transplantation Proceedings* 2010; 42(2): 517-20.
2. Thethy S, Thomson B, Pleass H, et al. Management of biliary tract complications after orthotopic liver transplantation. *Clin Transplant* 2004; 18(6): 647-53.
3. Park JS, Kim MH, Lee SK, et al. Efficacy of endoscopic and percutaneous treatments for biliary complications after cadaveric and living donor liver transplantation. *Gastrointest Endosc* 2003; 57(1): 78-85.
4. Koneru B, Sterling MJ, Bahramipour PF. Bile duct strictures after liver transplantation: a changing landscape of the Achilles' heel. *Liver Transpl* 2006; 12(5): 702-4.
5. Scanga AE, Kowdley KV. Management of biliary complications following orthotopic liver transplantation. *Curr Gastroenterol Rep* 2007; 9(1): 31-8.
6. Pascher A, Neuhaus P. Biliary complications after deceased-donor orthotopic liver transplantation. *J Hepatobiliary Pancreat Surg* 2006; 13(6):487-96.
7. Testa G, Malago M, Broelseh CE. Complications of biliary tract in liver transplantation. *World J Surg* 2001; 25(10): 1296-9.
8. Krok KL, Cardenas A, Thuluvath PJ. Endoscopic management of biliary complications after liver transplantation. *Clin Liver Dis* 2010; 14: 359-371.
9. Scatton O, Meunier B, Cherqui D, et al. Randomized trial of choledochocholedochostomy with or without a T tube in orthotopic liver transplantation. *Ann Surg* 2001; 233(3): 432-7.
10. Vougas V, Rela M, Gane E, et al. A prospective randomised trial of bile duct reconstruction at liver transplantation: T tube or no T tube? *Transpl Int* 1996; 9(4): 392-5.
11. Sotiropoulos GC, Sgourakis G, Radtke A, et al. Orthotopic liver transplantation: T-tube or no T-tube? Systematic review and meta-analysis of results. *Transplantation* 2009; 87(11): 1672-80.
12. Buis CI, Geuken E, Visser DS, Kuipers F, Haagsma EB, Verkade HJ, Porte RJ. Altered bile composition after liver transplantation is associated with the development of nonanastomotic biliary strictures. *Journal of Hepatology* 2009; 50: 69-79.
13. Rerknimitr R, Sherman S, Fogel EL, et al. Biliary tract complications after orthotopic liver transplantation with choledochocholedochostomy anastomosis: endoscopic findings and results of therapy. *Gastrointest Endosc* 2002; 55(2): 224-31.
14. Verdonk RC, Buis CI, Porte RJ, et al. Anastomotic biliary strictures after liver transplantation: causes and consequences. *Liver Transpl* 2006; 12(5): 726-35.
15. Graziadei IW, Schwaighofer H, Koch R, et al. Long-term outcome of endoscopic treatment of biliary strictures after liver transplantation. *Liver Transpl* 2006; 12(5): 718-25.
16. Pasha SF, Harrison ME, Das A, et al. Endoscopic treatment of anastomotic biliary strictures after deceased donor liver transplantation: outcomes after maximal stent therapy. *Gastrointest Endosc* 2007; 66(1): 44-51.
17. Zoepf T, Maldonado-Lopez EJ, Hilgard P, et al. Balloon dilatation vs. balloon dilatation plus bile duct endoprostheses for treatment of anastomotic biliary strictures after liver transplantation. *Liver Transpl* 2006; 12(1): 88-94.
18. Kulaksiz H, Weiss KH, Gotthardt D, et al. Is stenting necessary after balloon dilation of post-transplantation biliary strictures? Results of a prospective comparative study. *Endoscopy* 2008; 40(9): 746-51.
19. Moench C, Moench K, Lohse AW, Thies J, Otto G. Prevention of ischemic-type biliary lesions by arterial back-table pressure perfusion. *Liver Transpl* 2003; 9(3): 285-9.