Liver

Nguyen, et al., J Liver 2015, 4:2
http://dx.doi.org/10.4172/2167-0889.1000179

Research Article Open Access

Biliary Reconstruction in Pediatric Liver Transplantation: A Case Report of Biliary Complications and Review of the Literature

Thao T. Nguyen N[1], Theresa R. Harring[1], John A. Goss[2,3] and Christine A. O'Mahony[4,5*]

[1]*Division of Abdominal Transplantation and Hepatobiliary Surgery, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas, USA*

[2]*Professor of Surgery, Division of Abdominal Transplantation, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas, USA*

[3]*Surgical Director, Liver Transplant Program at the Texas Children's Hospital, Houston, Texas, USA*

[4]*Associate Professor of Surgery, Section of Renal Transplant, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas, USA*

[5]*Surgical Director, Kidney Transplantation at Texas Children's Hospital, Baylor St. Luke's Medical Center, and the Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas, USA*

[*]**Corresponding author:** Christine A. O'Mahony, Baylor College of Medicine, Michael E. DeBakey, Department of Surgery, 6620 Main Street, Suite 1425, Houston, TX 77030, USA, Tel: 832-355-1400; E-mail: comahony@bcm.edu

Received date: July 17, 2014; **Accepted date:** April 03, 2015; **Published date: April** 07, 2015

Abstract

With the advent of segmental liver allografts from liver donors, reduced-size cadaveric allografts, and split cadaveric allografts, pediatric pre-transplantation patient mortality has reduced. However, this expansion of the donor pool for size-appropriate allografts for patients with end-stage liver disease has led to an increased incidence of biliary complications. We performed a retrospective review of our series of 242 pediatric patients who received a liver transplantation. Biliary complications at our institution are presented, with a review of the current literature identifying risk factors that predispose pediatric liver transplant patients to biliary complications. We present the protocol used at our institution to minimize risk of biliary complications in our pediatric post-operative patient population.

Keywords: Pediatric liver transplantation; Biliary reconstruction; Ischemic-type biliary lesion; Biliary leakage; Surgical technique

Introduction

The survival rate of pediatric liver transplant patients currently approaches 95%. This has been possible in part by an increased pool of donor allograft sources. Historically, the number of cadaveric organs available was insufficient to satisfy the needs of this patient group; therefore, in order to meet their needs, the donor pool of whole pediatric cadaveric allografts was expanded to include segmental liver allografts from living donors, reduced-size cadaveric allografts, and split cadaveric allografts. These technical variants have reduced the mortality rate of pediatric pre-transplantation patients to nearly zero by increasing the availability of size-appropriate grafts for patients with end-stage liver disease [1,2]. In addition, the overall survival has exceeded expectations because of the improvements in immunosuppressive therapy, organ preservation, donor allocation, and postoperative care. However, this expansion of the donor pool for size-appropriate organs has led to an increased risk in postoperative vascular and biliary complications [3-6]. Despite refinements of surgical techniques, the incidence of biliary complications is between 15% and 64%; they represent the most common problems after pediatric liver transplantation [3,4,7-10]. The complications include biliary stenosis and stricture with proximal dilatation, biliary leakage, intrahepatic biliary stones and sludge, hemobilia and bilomas. The most common of these complications are stricture of the biliary tree, both anastomotic and non-anastomotic, and biliary leakage.

Several risk factors affect the development of biliary complications after pediatric liver transplantation, including allografts of donors after cardiac death (DCD), blood type incompatibility, prolonged use of vasopressors in donors, cytomegalovirus (CMV) infection, x (PSC), and allograft rejection within the recipient [11-16]. Surgical techniques of biliary reconstruction play a major role in preventing complications postoperatively. Prolonged cold and warm ischemia times, reperfusion injury, previous biliary leak, need for reoperation immediately after transplantation, hepatic artery thrombosis, Roux-en-Y reconstruction, biliary reconstruction using a T-tube, and even the type of allograft infusate are risk factors for biliary complications [3,12,16-20]. A retrospective study at a high-volume academic center found that patients who had to be taken back to the operating room for nonbiliary issues (e g. bleeding), as well as patients who received an allograft from a DCD or a living donor, had a higher risk for biliary complications refractory to endoscopic therapy [21].

In this report we present our patient experiences in a single, high-volume liver transplant center and offer our surgical technique to be considered as a part of standard of surgical care in pediatric liver transplantation. We reviewed the current literature on biliary complications after pediatric liver transplantation for a thorough examination of risk factors.

Methods and Materials

We reviewed the liver transplantation data of 1080 patients treated at our institution from September 1998 to October 2011 and identified 242 pediatric patients who had received a liver transplant. Of these 242 patients, two (0.8%) presented with postoperative anastomotic biliary strictures that was successfully treated with image guided interventional therapy. One of the patients had received a whole organ allograft and the other a partial deceased donor allograft. We reviewed the charts of these patients and present their clinical course below.

Case Reports

Case 1

A 7 week-old female patient with extrahepatic biliary atresia and situs inversus was treated with a Kasai procedure, which subsequently failed. At 17 months of age she received an ex-vivo left lobe cutdown allograft with an end-to-side hepaticojejunostomy and an internal pediatric feeding tube. Her course was complicated by an intrahepatic abscess which was percutaneously drained on POD 14. Two months postoperatively, the patient had moderate-to-severe acute cellular rejection that required pulse steroidal therapy. She also tested positive for CMV antigenemia that required IV ganciclovir. At 7 months postoperatively, she suffered posttransplant lymphoproliferative disease (PTLD). In addition, an abdominal ultrasound performed for obstructive symptoms revealed dilatation of the extrahepatic biliary tree with mild intrahepatic biliary ductal dilatation when compared with the ultrasound result from the previous month. Results of a percutaneous transhepatic cholangiography (PTC) showed a choledocho-jejunal stricture at the anastomotic site, which was treated with an external biliary catheter. Eight months after the transhepatic catheter was placed (15 months after the liver transplantation) a cholangiography showed that the stricture had resolved and the biliary drain was removed. The patient has since not had further biliary issues and is currently in remission after chemotherapy for her PTLD.

Case 2

The second patient received a diagnosis of ornithine transcarbamylase deficiency (OTCD) when he was 2 days old. He underwent transplantation with a whole organ allograft at 4 months of age. The allograft required an iliac interposition arterial graft because the initial recipient hepatic artery to donor celiac trunk anastomosis did not offer acceptable flow, opening the possibility of tension on the original anastomosis. We performed a Roux-en-Y hepaticojejunostomy for biliary reconstruction with a pediatric feeding tube placed to serve as an internal stent. The patient presented with obstructive symptoms months after transplantation. PTC results confirmed a biliary stricture at the site of the choledochojejunostomy anastomosis, which was treated with an externalized catheter. This resulted in resolution of the stricture 16 months after transplantation.

Techniques of Biliary Reconstruction

The Roux-en-Y choledochojejunostomy was the original technique of biliary reconstruction used by Starzl, the pioneer of a successful pilot liver transplantation program more than 50 years ago [22]. Today, as half a century ago, Roux-en-Y choledochojejunostomy reconstructions are used in pediatric patients with size discrepancies between donor and recipient biliary systems, minute biliary ducts difficult to anastomose, and pre-existing biliary disease. Duct-to-duct anastomosis of the biliary system is also a viable option for workable duct sizes, preferred when feasible because of its advantages, which include preservation of the sphincter of Oddi, preservation of the bilioenteric physiology (and thus prevention of biliary colonization with enteric bacteria) and a shorter operative time. Not the least of these advantages is the convenience of allowing for endoscopic access to the biliary system, which is especially critical for treating biliary complications that may arise postoperatively [23].

Baylor college of medicine biliary reconstruction technique

Our constant review of the literature has suggested that our procedure has evolved to a standard operative technique. Basic tenets guide our liver transplantation procedures, both in the donor allograft preparatory stage and the recipient implantation stage which has allowed for better than average outcomes and is as follows.

Basic principles of biliary reconstruction

- Avoid ductal trauma
- Use HTK solution as preservative and flush
- Minimize cold and warm ischemia times
- Use interrupted biliary and arterial anastomoses
- Use continuous suture on posterior wall and interrupted suture of anterior venous vascular walls
- Use absorbable sutures
- Use knots outside the vascular and biliary lumen
- Do not use T-tube
- Use stents in place for Roux-en-Y choledochojejunostomy

Donor surgical technique

Bile duct trauma is avoided at all cost by refraining from electrocautery anywhere near the biliary system, and using only sharp dissection when working in that anatomical territory. Gentle handling of the donor allograft is essential because biliary tension may lead to ischemic injury, a significant risk factor for biliary stricture. Another principle is to flush donor organs strictly with HTK solution. It's been suggested that the lower viscosity of the HTK solution, compared to UW solution, allows for greater perfusion of biliary vasculature, again preventing ischemic injury of the biliary system [24,25].

Recipient surgical technique

Minimizing both cold and warm ischemia times helps to minimize leaks and the risk of biliary stricture. We do not use venoveno bypass. We suture arterial anastomoses with interrupted suture technique. We anastomose the celiac trunk of the donor allograft to the common hepatic artery of the recipient in an end-to-end, interrupted fashion with 8-0 Prolene-sutures.

In a review of the techniques used in 321 transplant patients, one study noted a tendency toward a lower incidence of strictures with interrupted sutures and a lower incidence of leakage with continuous sutures [26]. We apply this principle by running a continuous suture on the posterior wall and completing it with interrupted stitches on the anterior wall in all venous systems [27]. For biliary reconstruction using choledochocholedochostomy or duct-to-duct anastomosis, we use interrupted Prolene sutures. The knots are tied outside of the lumen and no T-tube is ever used.

For biliary reconstructions with the Roux-en-Y, we also use interrupted absorbable sutures, as well as a feeding tube as a stent for the bilioenteric anastomosis.

In a sample group of 49 patients with a biliary complication rate of 2%, Tsuchie et al. have shown that biliary reconstruction with wide-interval interrupted suture can prevent anastomotic strictures and biliary leakage in pediatric living donor liver transplants [28]. We create a Roux-en-Y hepaticojejunostomy for biliary reconstruction with a pediatric feeding tube placed to serve as an internal stent. After a defunctionalized jejunum limb is created, a jejunojejunostomy is

sewn in a side-to-side, functional end-to-side manner in two layers. The outermost layer is sewn with 4-0 silk in an interrupted Lembert fashion and the innermost layer with of 4-0 Vicryl in a running Connell fashion. The mesenteric defect is closed with 4-0 running silk stitches. The common hepatic duct is anastomosed to the Roux limb in an end-to-side fashion with 7-0 PDS interruptedly. The pediatric feeding tube is placed as an internal stent in an anticolic manner.

Surgical risk factors to biliary complications

Biliary complications delay post-OLT recovery, reduce quality of life, and may also reduce function and long-term survival of the allograft, which necessitates re-transplantation. Biliary complications are a major source of morbidity, graft loss and potential mortality that cannot be dismissed [5,9,29-31]. A 15-year study of 389 pediatric liver transplant patients in a single institution in Spain showed that 105 patients had biliary complications (27%), usually in the first three months after transplantation [3]. This illustrates the pervasiveness of the problem, which plagues even high volume centers with greater experience. Early postoperative biliary complications are described as technical in nature, and can encompass insufficiency of the biliary anastomosis to the dislocation of T-tubes [32]. Biliary complications that develop months or years after liver transplantation can be categorized by localization into anastomotic, i.e., those affecting the anastomotic site or the ampulla of Vater, or nonanastomotic, ie those affecting the intra- or extrahepatic biliary tree [20]. The former can be treated successfully with endoscopic dilatation and stenting [21,33,34]. In contrast, nonanastomotic strictures are a major therapeutic difficulty, often leading to re-transplantation.

A. Ischemia

Biliary strictures and leaks are one of the most common and troublesome complications of a pediatric liver transplantation. Although the exact pathophysiology is not yet determined, ischemia is often correlated with progression toward these complications.

Ischemic arterial events include hepatic arterial stenosis or thrombosis and can result in bile duct strictures, leaks, cholangitis, sepsis, and abscess formation. Ischemia is responsible for infarction of the biliary epithelium, which creates multiple foci of intrahepatic biliary ductal strictures anywhere in the biliary tree [3]. Anatomically, the common bile duct of the recipient has rich collateral blood flow uninterrupted by surgery, but the donor's duct and the proximal intrahepatic ducts receive blood from the reconstructed hepatic artery. Because the blood supply to the biliary tract depends solely on arterial inflow, blood flow disruptions through the peribiliary plexus may result in insufficient preservation and subsequent damage of the biliary epithelium [35].

The previous experiences highlight the importance of minimizing both warm and cold ischemia times intraoperatively. Prolonged ischemia time has been shown to increase the risk of biliary complications. Cold ischemia time (CIT) has repeatedly shown to increase the risk of these complications, which are usually associated with intrahepatic strictures [12,17,18,36]. Warm ischemia time (WIT) has been described as an independent risk factor for biliary complications, associated with both anastomotic and intrahepatic strictures as well as biliary leaks [19,37,38]. The procurement time affects the first warm ischemia time (WIT) in addition to the subsequent cold ischemia time (CIT) and reperfusion injury [35].

Sánchez-Urdazpal showed a correlation between CIT and ischemic type biliary lesions (ITBL); the incidence of biliary complications increased with increasing CIT [36]. About 2% of patients presented biliary complications when CIT was < 11.5 hours, but this percentage increased to 35% and 52% when CIT was 11.5 to <13 hours, and ≥13 hours, respectively. This study has influenced the use of this liver transplant technique; many centers now try to keep CIT less than 10 hrs. It's been suggested that CIT may promote ITBL by direct ischemic injury of the biliary epithelium which then increases susceptibility of the biliary epithelium to a second factor, such as reoxygenation injury or secondary ischemia of the biliary epithelium due to damage of the peribiliary arterial plexus [35,36].

Noack et al. have shown that reperfusion injury is contributory to ITBL; biliary epithelial cells are more vulnerable to reperfusion/reoxygenation injury than hepatocytes [39]. Although anoxia did decrease ATP levels, cell death rate after reoxygenation was higher in bile duct epithelial cells. The authors have suggested that the difference in cell susceptibility might be explained in part by the differences in reactive oxygen species between both cell types.

In an attempt to understand the biliary changes that occur after hepatic artery ischemia, Lu et al. used a canine model to replicate the ischemic event during liver transplant (in situ hepatic infusion via the gastroduodenal artery and gastroduodenal vein) [40]. The authors then compared the outcomes of dogs with constant hepatic perfusion with those of dogs with 60 minutes of hepatic artery clamping (after portal perfusion was reestablished). The dogs with 60 minutes of hepatic artery clamping had significantly more collagen deposits and leukocytic infiltration in the biliary ductal walls at 6 hours, 3 days, and 14 days post-operatively than the control group. Lu et al. suggested that the collagen deposits might have induced myofibroblast transdifferentiation in the intrahepatic bile duct that resulted in biliary fibrosis [40].

After reviewing transplant data of 1843 patients (3.9% developed ITBL), Heindenhain et al. reported donor age and cold ischemia time to be significant variables in the development of ischemic-type biliary lesions [20]. Furthermore, those allografts perfused with University of Wisconsin solution developed ITBL more often that Histidine-Tryptophan-Ketoglutarate (HTK)-perfused organs (p=0.036), and were imported organs, i.e. organs that did not undergo hepatic arterial perfusion pressure. These findings changed their clinical protocol to enforce strict limitation of CIT to <10 hrs and the exclusive use of HTK solution.

Hepatic artery thrombosis and stenosis (HAT/HAS) has been reported a risk factor for biliary complications. A retrospective study by Dacha et al. found a statistically significant increased risk for biliary strictures, both anastomotic and nonanastomotic, in patients who had experienced HAS [18]. The condition worsened when accompanied by prolonged CIT.

B. Choledochocholedochostomy with T-tube

Choledochocholedochostomy with T-tube placement was a surgical standard of care in the 1970s and 1980's. The technique was intuitive enough, and had the advantages of allowing for monitoring the quantity and quality of bile postoperatively and providing easy access for cholangiography of the biliary system. The rational was that by reducing the intraluminal pressure, the bile ducts would be less likely to leak, and the T-tube could potentially serve as a stent to reduce the incidence of stricture. Unfortunately, the procedure also caused biliary peritonitis and cholangitis. Furthermore, Wang et al. have suggested that 10-60% of biliary complications were directly related to T-tube use in biliary reconstruction [37]. Although there is great debate in

regards to the use of T-tube and its after-effects in the postoperative stage, no clear evidence exists for the standard use of T-tubes during liver transplantation. Riediger et al. [41] performed a meta-analysis on 6 randomized controlled trials, and found no clear evidence in favor of using T-tube during orthotopic liver transplantation; the odds ratio for biliary complications between use and no use of T-tubes was 1.15 and not significant. Sundaram et al. found not only that the incidence of biliary strictures has increased between the pre-and post-MELD eras, but those biliary leaks were strongly linked to the use of T-tubes during liver transplantation [42].

C. Biliary Stent

Stent placement is associated with minimal risk of complications. However, this is supported only by small amount of data that shows a decrease in biliary leak rate. Welling et al. used multivariate analysis to retrospectively study liver transplant data of 256 patients and found that use of an internal stent was an independently protective factor against biliary strictures, and that use of a transcystic/internal stent trended toward protecting against leaks as well, though it was not statistically significantly [19].

D. Allograft Infusate: HTK vs UW

Histidine typtophan ketoglutarate (HTK) and University of Wisconsin (UW) solutions are used in the preservation of liver allografts for transplantation. Biliary complication rates of patients infused with UW solution are higher than the rates of patients infused with HTK solution. Conversely, HTK solution has a protective effect against biliary stricture [19,25,29].

Studies have suggested that the viscosity of the solution used to infuse donor allografts may play a role in the development of biliary lesions. The UW preservation solution is highly viscous; concern exists that it might not completely flush out the small peribiliary arterial plexus and therefore lead to obstruction that may result in poor bile duct preservation with subsequent ischemia [35]. Moench et al. have provided more evidence that insufficient perfusion of the peribiliary plexus might contribute to the development of ITBL, though acknowledges they could not differentiate these outcomes between preservation solutions [43]. These investigators have shown that additional flushing of the peribiliary plexus with controlled arterial backtable pressure perfusion is associated with considerable reduction in ITBL after preservation. In addition, proper use of liver and the extrahepatic bile duct harvesting techniques is essential to preserve the viability and vasculature of the bile duct. Although it has never been studied in a clinical trial, the benefit of covering the extrahepatic bile duct with as much tissue as possible is accepted by every surgeon. Stripping of the bile duct should be avoided to prevent injury to the microcirculatory blood supply [35].
Finally, Heidenhain et al. reviewed the data of over 1800 patients and found that allografts perfused with UW solution developed ITBL more often than allografts perfused with HTK solution (p=0.036) [20].

Discussion

In an effort to reduce the incidence of biliary complications, we do not use extended ischemic times, both warm and cold. Because biliary epithelia cells are more sensitive than hepatocytes, ductal trauma is avoided at all cost; we do not use electrocautery near the biliary tree. We have abandoned use of UW solution, replaced by HTK solution to preserve and flush the allografts. We perform wide interrupted biliary and arterial anastomoses with a continuous portion on the venous posterior wall. Our sutures are absorbable and the knots are placed outside of the lumen.

In our institution, the size of the donor allograft and the recipient's biliary systems determine whether to use duct-to-duct anastomosis or a Roux-en-Y hepaticojejunostomy. Heffron et al. presented data on 89 pediatric patients treated with either duct-to-duct anastomosis or Roux-en-Y hepaticojejunostomy [5]. Patient outcomes in both groups were similar, but partial liver grafts did have higher incidence of biliary complications. Haberal et al.'s retrospective study of 31 pediatric patients who had received living donor liver transplantation found duct to duct biliary reconstruction without a stent to be a safer technique for biliary reconstruction (15% biliary complication rate) [23]. Another study by Kakamoto et al. suggested that the use of a trans-anastomotic biliary tube may help to avoid biliary complications when using left-lobe grafts in selected cases of duct-to-duct anastomoses [44]. Our institution has not found that to be a necessary addition to our operative technique.

Another study by Shirouzu et al. reported no differences in the outcomes of 10 infant patients who underwent a duct-to-duct choledochocholedochostomy or a Roux-en-Y hepaticojejunostomy for biliary reconstruction [45]. We employ both techniques as the anatomy allows, preferring choledochocholedochostomy anastomosis where it is feasible and safe; the advantages range from decreased ischemia time to accessibility for endoscopic imaging and therapy, should the need arise.

We decided not to use T-tubes in the management of our transplant patients. Meta-analysis of a randomized controlled trial showed that, although reconstruction with a T-tube may have the potential to reduce long term morbidity with respect to late strictures, there is no equivocal evidence in favor of using a T-Tube during OLT. The odds ratio for biliary complications was 1.15 and not significant, ultimately revealing no differences in biliary complication rates between usages of T-tubes [41]. Chang et al.'s study included 253 liver transplant recipients with 17% biliary complication rate [46]. Multivariate analysis found that use of T-tube and older age were significant variables that predisposed to leakage and that organ rejection and male sex predisposed to stricture. Before 2002, T-tube usage was the strongest risk factor for biliary leakage in transplants performed in a Sri Lankan institution [42]. Other institutions have reported a decrease in biliary complication rate over 2 decades, most likely because they abandoned the routine use of T-tubes [47]. Because biliary leaks are risk factors for biliary stricture, we have found little benefit in using T-tubes, and in fact, have not observed significant patient complications after we abandoned this procedure.

In the two cases of biliary stricture presented here, we diagnosed and treated the patients with percutaneous transhepatic cholangiography (PTC). Although PTC offers options, including balloon dilatation, drainage, and stent placement, surgical reconstruction or re-transplantation may be required in refractory cases. Biliary leaks are another threat to the pediatric liver transplant patient. Clinical manifestations vary, ranging from mild abdominal symptoms to septicemia shock [3]. Effective use of appropriate techniques is required to prevent morbidity and potential mortality associated with pediatric liver transplantation, understanding the risk factors involved. Because our institution has experienced favorable outcomes with our current protocol, we offer our technique for consideration.

Summary

Biliary stricture and leakage are common complications after liver transplantation, but represent just some of the biliary complications that can occur. These include ischemic type biliary lesions, sphincter of Oddi dysfunction, hemobilia, and biliary obstruction by stones or sludge. A variety of contributing factors are implicated, including the type of reconstruction technique, use of biliary splintage, type of liver transplant procedure, organ preservation, acute/chronic rejection, hepatic artery thrombosis, and other recipient and donor characteristics. Among these, strictures related to anastomotic procedures in association with reconstruction technique are the most common and also the most controversial in the recent literature [48].

Often called the 'Achilles heel' of liver transplantation, biliary complications have long troubled the outcomes of transplant patients. In the pediatric population, these complications have a high frequency, and often need long-term, repeated treatment which can introduce potentially detrimental effects on graft and patient survival.

Recent improvements throughout liver transplant care, including donor allograft selection, organ preservation, immunosuppressive therapy, and standardization of biliary reconstruction, have dramatically reduced the incidence of biliary complications. We believe further improvement is possible. Biliary reconstruction is the most common site of postoperative complications in liver transplantation and thus serves as the first target for preventive measures [48]. In an effort to contribute to this advancement, we offer our patient experiences and outcomes as well as our surgical technique to be considered as a part of the surgical standard of care in liver transplantation.

References

1. Yersiz H, Renz JF, Farmer DG, Hisatake GM, McDiarmid SV, et al. (2003) One hundred in situ split-liver transplantations: a single-center experience. Ann Surg 238: 496-505.
2. Vagefi PA, Parekh J, Ascher NL, Roberts JP, Freise CE (2011) Outcomes with split liver transplantation in 106 recipients: the University of California, San Francisco, experience from 1993 to 2010. Arch Surg 146: 1052-1059.
3. Berrocal T, Parrón M, Alvarez-Luque A, Prieto C, Santamaría ML (2006) Pediatric liver transplantation: a pictorial essay of early and late complications. Radiographics 26: 1187-1209.
4. Anderson CD, Turmelle YP, Darcy M, Shepherd RW, Weymann A, et al. (2010) Biliary strictures in pediatric liver transplant recipients - early diagnosis and treatment results in excellent graft outcomes. Pediatr Transplant 14: 358-363.
5. Heffron TG, Pillen T, Welch D, Smallwood GA, Redd D, et al. (2003) Biliary complications after pediatric liver transplantation revisited. Transplant Proc 35: 1461-1462.
6. Gunawansa N, McCall JL, Holden A, Plank L, Munn SR (2011) Biliary complications following orthotopic liver transplantation: a 10-year audit. HPB (Oxford) 13: 391-399.
7. Brown RS Jr1 (2008) Live donors in liver transplantation. Gastroenterology 134: 1802-1813.
8. Soejima Y, Taketomi A, Yoshizumi T, Uchiyama H, Harada N, et al. (2006) Biliary strictures in living donor liver transplantation: incidence, management, and technical evolution. Liver Transpl 12: 979-986.
9. Ryu CH, Lee SK (2011) Biliary strictures after liver transplantation. Gut Liver 5: 133-142.
10. Koneru B, Sterling MJ, Bahramipour PF (2006) Bile duct strictures after liver transplantation: a changing landscape of the Achilles' heel. Liver Transpl 12: 702-704.
11. Jay CL, Lyuksemburg V, Ladner DP, Wang E, Caicedo JC, et al. (2011) Ischemic cholangiopathy after controlled donation after cardiac death liver transplantation: a meta-analysis. Ann Surg 253: 259-264.
12. Li F, Ye B, Hong L, Xu H, Fishbein MC (2011) Epigenetic modifications of histone h4 in lung neuroendocrine tumors. Appl Immunohistochem Mol Morphol 19: 389-394.
13. Sanchez-Urdazpal L, Batts KP, Gores GJ, Moore SB, Sterioff S, et al. (1993) Increased bile duct complications in liver transplantation across the ABO barrier. Ann Surg 218: 152-158.
14. Busquets J, Castellote J, Torras J, Fabregat J, Ramos E, et al. (2007) Liver transplantation across Rh blood group barriers increases the risk of biliary complications. J Gastrointest Surg 11: 458-463.
15. Cholongitas E, Shusang V, Papatheodoridis GV, Marelli L, Manousou P, et al. (2008) Risk factors for recurrence of primary sclerosing cholangitis after liver transplantation. Liver Transpl 14: 138-143.
16. Chok KS, Chan SC, Cheung TT, Sharr WW, Chan AC, et al. (2011) Bile duct anastomotic stricture after adult-to-adult right lobe living donor liver transplantation. Liver Transpl 17: 47-52.
17. Cag M, Audet M, Saouli AC, Panaro F, Piardi T, et al. (2010) Does arterialisation time influence biliary tract complications after orthotopic liver transplantation? Transplantation Proceedings 42: 3630-3633.
18. Dacha S, Barad A, Martin J, Levitsky J (2011) Association of hepatic artery stenosis and biliary strictures in liver transplant recipients. Liver Transpl 17: 849-854.
19. Welling TH, Heidt DG, Englesbe MJ, Magee JC, Sung RS, et al. (2008) Biliary complications following liver transplantation in the model for end-stage liver disease era: Effect of donor, recipient, and technical factors. Liver Transplantation 14: 73-80.
20. Heidenhain C, Pratschke J, Puhl G, Neumann U, Pascher A, et al. (2010) Incidence of and risk factors for ischemic-type biliary lesions following orthotopic liver transplantation. Transpl Int 23: 14-22.
21. Buxbaum JL, Biggins SW, Bagatelos KC, Ostroff JW (2011) Predictors of endoscopic treatment outcomes in the management of biliary problems after liver transplantation at a high-volume academic center. Gastrointestinal Endoscopy 73: 37-44.
22. Otte JB1 (2002) History of pediatric liver transplantation. Where are we coming from? Where do we stand? Pediatr Transplant 6: 378-387.
23. Haberal M, Karakayali H, Atiq A (2011) Duct-to-duct biliary reconstruction without a stent in pediatric living-donor liver transplantation. Transplantation Proceedings 43: 595-597.
24. Amenomori M, Ayabe S, Bi XJ, Chen D, Cui SW, et al. (2006) Anisotropy and corotation of galactic cosmic rays. Science 314: 439-443.
25. Canelo R, Hakim NS, Ringe B (2003) Experience with hystidine tryptophan ketoglutarate versus University Wisconsin preservation solutions in transplantation. Int Surg 88: 145-151.
26. Ando H, Kaneko K, Ono Y (2011) Biliary reconstruction with wide-interval interrupted suture to prevent biliary complications in pediatric living-donor liver transplantation. J Hepatobiliary Pancreat Sci 18: 26-31.
27. Kasahara M, Egawa H, Takada Y, Oike F, Sakamoto S, et al. (2006) Biliary reconstruction in right lobe living-donor liver transplantation: Comparison of different techniques in 321 recipients. Ann Surg 243: 559-566.
28. Tsuchie H, Miyakoshi N, Hongo M, Kasukawa Y, Ando S, et al. (2010) Insufficiency fractures of bilateral distal tibias associated with chronic liver disease. J Orthop Sci 15: 678-681.
29. Cui DX, Yin JQ, Xu WX, Chai F, Liu BL, et al. (2010) Effect of different bile duct flush solutions on biliary tract preservation injury of donated livers for transplantation. Transplant Proc 42: 1576-1581.
30. Pascher A, Neuhaus P (2005) Bile duct complications after liver transplantation. Transpl Int 18: 627-642.
31. Hampe T, Dogan A, Encke J, Mehrabi A, Schemmer P, et al. (2006) Biliary complications after liver transplantation. Clin Transplant 20 Suppl 17: 93-96.
32. Moser MA, Wall WJ (2001) Management of biliary problems after liver transplantation. Liver Transpl 7: S46-52.

33. Sunku B, Salvalaggio PR, Donaldson JS, Rigsby CK, Neighbors K, et al. (2006) Outcomes and risk factors for failure of radiologic treatment of biliary strictures in pediatric liver transplantation recipients. Liver Transpl 12: 821-826.
34. Sanna C, Giordanino C, Giono I, Barletti C, Ferrari A, et al. (2011) Safety and efficacy of endoscopic retrograde cholangiopancreatography in patients with post-liver transplant biliary complications: Results of a cohort study with long-term follow-up. Gut and Liver 5: 328-334.
35. Buis CI, Hoekstra H, Verdonk RC, Porte RJ (2006) Causes and consequences of ischemic-type biliary lesions after liver transplantation. J Hepatobiliary Pancreat Surg 13: 517-524.
36. Sanchez-Urdazpal L, Gores GJ, Ward EM, Maus TP, Wahlstrom HE, et al. (1992) Ischemic-type biliary complications after orthotopic liver transplantation. Hepatology 16: 49-53.
37. Wang MF, Jin ZK, Chen DZ, Li XL, Zhao X, et al. (2011) Risk factors of severe ischemic biliary complications after liver transplantation. Hepatobiliary Pancreat Dis Int 10: 374-379.
38. Sibulesky L, Nguyen JH (2011) Update on biliary strictures in liver transplants. Transplant Proc 43: 1760-1764.
39. Noack K, Bronk SF, Kato A, Gores GJ (1993) The greater vulnerability of bile duct cells to reoxygenation injury than to anoxia. Implications for the pathogenesis of biliary strictures after liver transplantation. Transplantation 56: 495-500.
40. Lu HW, Chen YB, Li YM, Dong JH, Yang HN (2010) Role of hepatic arterial ischaemia in biliary fibrosis following liver transplantation. Chin Med J (Engl) 123: 907-911.
41. Riediger C, Müller MW, Michalski CW, Huser N, Schuster T, et al. (2010) T-tube or no T-tube in reconstruction of the biliary tract during orthotopic liver transplantation - systematic review and meta-analysis. Liver Transplantation 16:105-117.
42. Sundaram V, Jones DT, Shah NH, de Vera ME, Fontes P, et al. (2011) Posttransplant biliary complications in the pre- and post-model for end-stage liver disease era. Liver Transpl 17: 428-435.
43. Moench C, Otto G (2006) Ischemic type biliary lesions in histidine-tryptophan-ketoglutarate (HTK) preserved liver grafts. Int J Artif Organs 29: 329-334.
44. Sakamoto S, Egawa H, Ogawa K, Ogura Y, Oike F, et al. (2008) The technical pitfalls of duct-to-duct biliary reconstruction in pediatric living-donor left-lobe liver transplantation: The impact of stent placement. Pediatr Transplant 12: 661-665.
45. Shirouzu Y, Okajima H, Ogata S, Ohya Y, Tsukamoto Y, et al. (2008) Biliary reconstruction for infantile living donor liver transplantation: Roux-en-Y hepaticojejunostomy or duct-to-duct choledochocholedochostomy? Liver Transpl 14: 1761-1765.
46. Chang JH, Lee IS, Choi JY, Yoon SK, Kim DG, et al. (2010) Biliary stricture after adult right-lobe living-donor liver transplantation with duct-to-duct dnastomosis: Long-term outcome and its related factors after endoscopic treatment. Gut Liver 4: 226-233.
47. Gantxegi A, Caralt M, Bilbao I, Castells L, Lázaro JL, et al. (2011) Evolution of biliary complications after liver transplantation: a single European series. Transplant Proc 43: 745-748.
48. Akamatsu N, Sugawara Y, Hashimoto D (2011) Biliary reconstruction, its complications and management of biliary complications after adult liver transplantation: a systematic review of the incidence, risk factors and outcome. Transplant International 24: 379-392.