Minimal Invasive (Endovascular and Percutaneous) Treatment of Post Liver Transplantation Complications in Pediatrics

Ghazwan Kroma, Jorge Lopera and Rajeev Suri
University of Texas Health Science Center at San Antonio
USA

1. Introduction

Liver transplantation is the only potentially curative treatment for patients with end-stage liver disease or unresectable primary hepatic tumors. Biliary atresia accounts for approximately 40% of liver transplant performed in children in the United State (Carter et al, 2006). Intra-hepatic cholestasis and inborn metabolic errors resulting in cirrhosis constitute the second most common group. Progressive liver failure and finally acute liver failure following hepatitis or drug toxicity represent a small referral group.

First human liver transplantation was performed by Starzl in 1963 at the University of Colorado Health Science Center on a three years old patient with biliary atresia and the patient died before the completion of the surgery (Starzl et al, 1963). First successful liver transplantation was performed in 1967 on an eighteen months old patient with malignant liver tumor and the patient survived for 400 days before she succumbed from disseminated malignancy (Carter et al, 2006). Survival after pediatric liver transplantation has improved significantly in recent decades because of the advances in surgical techniques, immunosuppressive therapy, and peri-operative care (Jain et al, 2002). Pediatric liver transplant recipients also have benefited from major technologic advances in diagnostic and interventional radiology. Radiology has acquired a key role in both pediatric and adult liver transplantation programs because it allows early detection and prompt treatment of post-transplantation vascular and nonvascular complications, helping to improve graft and patient survival and obviating surgical revision or repeat transplantation in most cases (Amesur & Zajko, 2006; Rose et al, 2001; Sze & Esquivel, 2002). Various interventional radiology procedures may be applied during the follow-up of pediatric liver transplant recipients to detect and diagnose graft disease and to treat vascular and biliary complications. The interventional radiology procedures most commonly used in this context include percutaneous and transjugular liver biopsies for the diagnosis of graft disease; angioplasty and stent placement for the treatment of vascular stenosis or occlusion; biliary drain placement for the treatment of biliary strictures; coil embolization and stent graft placement for the treatment of pseduaneurysm and arteriovenous fistulas. Brief description of the surgical technique for split liver transplantation, the technical considerations involved in interventional radiology procedures, the expected results, and the possible complications are described in details in this chapter.
2. Surgical technique for split liver transplantation

Reduced liver technique or split liver transplantation represents a major advance in liver transplantation that significantly reduced the waiting period for liver transplantation.

Most pediatric liver transplantations are performed today by using left lateral segmental (II&III) transplantation or so called split liver transplantation (Fig. 1), a technique that accommodates the needs of pediatric patients without depleting the pool of organs available for adult patients with excellent patient and graft survival rate (90 and 87% respectively) (Deshpande et al, 2002). Radiologist should be familiar with the surgical techniques used in the transplantation such as Piggy back technique for the anastomosis between the inferior vena cava of the recipient and the hepatic veins of the graft, end to end or interposition conduit for the hepatic arterial and the portal venous anastomosis, and Roux-en-y technique for the hepaticojejunostomy biliary anastomosis (Fig. 2).

Fig. 1. Schematic diagram of split liver to provide two grafts from single donor, left lateral segment for a child and the right lobe for an adult recipient

Fig. 2. Schematic diagram illustrating orthotopic segmental liver transplantation. Piggy back hepatic vein to IVC anastomosis. Hepatic arteries and portal veins end to end anastomosis. Roux-en-y hepaticojejunostomy biliary anastomosis
3. Imaging spectrum and image-guided procedures for the management of complications after split liver transplantation

3.1 Organ rejection

Organ rejection develops in about 50% of patients, but improved immunosuppressive medications permit successful management of this problem in most cases (Zalasin et al, 1998). The ultrasound appearances of acute rejection are nonspecific, and the only identifiable abnormality is heterogeneity of the liver parenchyma, which may, however, have other causes (Crossin et al, 2003; Marder et al, 1989; Zalasin et al, 1998). The role of imaging consists of excluding these other possible causes, which can manifest with clinical signs and symptoms similar to those of acute rejection (Crossin et al, 2003). The diagnosis of acute rejection, one of the most serious complications following liver transplantation, is established by graft biopsy and histologic study (Ngheim, 1998).

3.1.1 Percutaneous liver biopsy

Percutaneous ultrasonography (US)-guided random liver biopsy is frequently requested after pediatric liver transplantation. Any alteration in liver function test results that cannot be explained on the basis of findings at diagnostic imaging requires a liver biopsy to exclude organ rejection. US guidance of biopsy is necessitated by the small volume of the transplanted liver, especially in split-liver transplantation, and the need to avoid perforating the bowel, other adjacent organs, and important intrahepatic vascular structures. If a coagulation defect is present (eg, platelet count of less than 50 × 1000 per microliter, prothrombin activity less than 50% of the normal level), patients receive an infusion of platelets, fresh frozen plasma, or both. If the presence of massive perihepatic ascites make liver biopsy infeasible, a percutaneous drainage catheter might be placed first to eliminate the ascites. The use of a coaxial technique in pediatric patients also has been described. In this procedure, a coaxial sheath is used to inject slurry of microfibrillar collagen into the needle tract to reduce the risk of bleeding after biopsy (Hoffer, 2000). An antibiotic is administered prophylactically before the procedure. Core biopsies are performed by using an 18-gauge needle and monitored anesthesia care with additional local anesthesia administered at the site selected for puncture. An anterior approach is usually the only one possible in patients with a split-liver transplant. After the biopsy, manual compression is applied to the puncture site for ten minutes. Possible major complications of percutaneous liver biopsy are bleeding, hemobilia, arterioporal fistula, and infection; these have been reported in 4.6% of pediatric patients who have undergone the procedure (Amaral et al, 2006).

3.1.2 Transjugular liver biopsy

The transjugular approach is widely used for random liver biopsies in adult patients with massive perihepatic ascites, severe coagulopathy, or both because it is associated with a lower rate of bleeding complications than is percutaneous biopsy (Furuya, 1992). The transjugular technique incurs a lower risk of hemorrhage because a biopsy specimen is acquired through the hepatic vein and any bleeding from the puncture site remains within the vascular space. In addition, if there are clinical signs of portal hypertension, the hepatic vein pressure gradient can be measured during the transjugular biopsy procedure. The use
of combined US and Fluoroscopic guidance during transjugular hepatic biopsies in pediatric patients has been reported to help reduce the risk of capsule perforation (Habdank, 2003). Complications of this biopsy procedure, which have been reported in 3%–11% of cases, include subcapsular hematoma, intraperitoneal bleeding, Subclavian artery puncture, pneumothorax, and hemothorax (Furuya, 1992; Kaye et al, 2000; Habdank, 2003). Transjugular random liver biopsy with catheterization of the right hepatic vein also has been reported in pediatric whole-liver transplant recipients (Habdank, 2003). Prophylactic antibiotics are routinely administered before the biopsy procedure, and an infusion of platelets or fresh frozen plasma is administered if coagulation defects are present. The small size of the liver in pediatric patients with a left lateral transplant and patient weight of less than 15 kg are considered relative contraindications to the procedure.

3.2 Vascular complications and treatment

Vascular complications that occur after pediatric liver transplantation are associated with high rates of morbidity, graft loss, and mortality (Sieders et al, 2000). These complications may involve the hepatic artery, hepatic vein, portal vein, or inferior vena cava. Most vascular complications appear within 3 months after transplantation. Clinical manifestations vary from mildly elevated values on hepatic function tests to fulminant hepatic failure (Bergey et al, 1998; Furuya, 1992; Hasegawa et al, 2002; Hoffer, 2000). Because their clinical manifestations often are indistinguishable from those of biliary complications, graft rejection, graft dysfunction, and infection, imaging is necessary for diagnosis. Color Doppler US, Multidetector computed tomography (CT), and magnetic resonance (MR) imaging all are useful for the diagnosis and follow-up. US is the primary screening modality used for the detection of vascular complications and imaging by Doppler US starts intra-operatively, in the ICU and twice daily for the first three days. The normal Doppler US parameters should include hepatopetal (toward the liver), pulsatile, low resistant flow in the hepatic artery with systolic velocity of more than 30 cm/s (fig. 3a), hepatopetal flow in the portal vein with velocity of at least 10 cm/s (fig. 3b) and phasic hepatofugal (outward the liver).

Fig. 3. Normal Doppler US study of the hepatic artery and portal vein after liver transplantation. (A) Pulsatile, low resistant hepatopetal flow in hepatic artery with velocity of 58.6 cm/s. (B) Phasic hepatopetal flow in portal vein with velocity of 18.5 cm/s.
flow in the hepatic veins. MR angiography is performed to confirm abnormalities demonstrated at US or in patients in whom the US study is suboptimal. CT scan is less frequently used today in this patient population due to the concern about the high radiation dose associated with it. Conventional vascular studies are currently reserved for endovascular treatment of these complications.

### 3.2.1 Hepatic artery stenosis

Hepatic artery stenosis occurs in 11%–20% of patients who have undergone pediatric liver transplantation (Moray, 2005). Most hepatic artery stenosis arise at the anastomosis site within 3 months after transplantation and are due to the small caliber of the arteries or to arterial injury by a vascular clamp during transplantation. However, nonanastomotic stenosis may occur in cases of graft rejection or necrosis. Early diagnosis and intervention may help to reduce ischemic damage to the graft, consequent bile duct damage, and progression to hepatic artery thrombosis. Doppler US is the imaging modality of choice for diagnosis and follow-up. The reported sensitivity of Doppler US for the detection of hepatic artery stenosis is 80%–90% (Abbasoglu et al, 1997; Crossin et al, 2003; Kok et al, 1998). Spectral broadening and focal accelerated velocity greater than 2 m/sec (Crossin et al, 2003; Nghiem et al, 1996; Platt et al, 1997) at the site of arterial anastomosis indicate stenosis. However, the site of narrowing is often difficult to identify by US due to overlying bowel gas especially in conduit graft, and the diagnosis is usually made on the basis of the Doppler US findings obtained distal to the stenosis. Intrahepatic arterial waveforms distal to the stenosis display a tardus parvus pattern with a decreased resistive index (<0.5) and prolonged acceleration time (80 msec) (Fig. 4a) (Dodd et al, 1994; Platt et al, 1997; Vignali et al, 2004). Associated turbulences distal to the stenosis are commonly observed at color Doppler US (Crossin et al, 2003; Platt et al, 1997). A tardus parvus pattern may be a normal finding during the first 72 hours after transplantation due to edema at the anastomotic site (Kok et al, 1998). In these cases, serial US will reveal a normal waveform 3–4 days after transplantation. MR angiography offers an alternative noninvasive technique for confirming the stenosis and for better evaluation of the anastomosis and the entire hepatic artery (Ito et al, 2000; Vignali et al, 2004). Conventional arteriography is currently reserved for endovascular treatment of the stenosis (Boraschi & Donati, 2004; Vignali et al, 2004). Early hepatic artery stenosis (less than two weeks post transplantation) should be treated surgically because endovascular treatment has the risk of suture line rupture. The use of percutaneous transluminal angioplasty with or without stent placement to treat hepatic artery stenosis in adult and pediatric liver transplant recipients have been reported (Hashikura et al, 2001; Kok et al, 1998; Nghiem et al, 1996). Possible complications that have been described include dissection, pseudoaneurysm, and rupture of the hepatic artery. When Doppler US or MRA findings are suggestive of hepatic artery stenosis, hepatic arteriography is performed by using a transfemoral approach and a standard 4-F angiographic catheter with monitored anesthesia care or general anesthesia. A coaxial microcatheter is then advanced through the stenosis, and the trans-stenotic pressure gradient is measured. If a significant pressure gradient is present (>10 mm Hg), angioplasty is performed. Before angioplasty, 0.2 mg nitroglycerin and 100 IU heparin per kilogram of body weight are infused into the hepatic artery to reduce the risks of spasm and thrombosis. A 6-F guiding catheter is inserted, and a balloon catheter is advanced over a 0.018- or 0.014-inch stiff wire. The balloon diameter varies in accordance with the diameter of the hepatic...
artery (Figs. 5&6). Procedural success is defined as the reduction or absence of stenosis at arteriography, accompanied by a significant reduction of the trans-stenotic pressure gradient. Angioplasty is technically successful in about 80% of the cases with restenosis rate of 30-60%. The long-term patency of stents is unknown; for this reason, stent placement in pediatric patients is recommended only if angioplasty fails or if complications such as hepatic artery dissection or rupture ensue. Doppler US is performed the day after the procedure to obtain baseline measurements of the intra and extrahepatic arterial resistive index (RI) and systolic acceleration time for comparison with follow up measurements (Fig. 4c).

Fig. 4. Early hepatic arterial stenosis (Surgically treated). (A) Doppler US performed day 5 post liver transplant shows tardus parvus waveform and low acceleration times in the right, left and main hepatic arteries. (B) Catheter angiogram, subtracted and un-subtracted images, confirms the stenosis at the proper hepatic artery. (C) post surgical revision follow up Doppler US reveals normal hepatic arteries wave forms

Fig. 5. (A) Celiac angiogram demonstrates sever stenosis at the anastomosis (arrow). (B) Hepatic artery stenosis (arrow) confirmed with selective proper hepatic angiogram with a small outpouching due to a ligated gastroduodenal artery (arrowhead). (C) Post angioplasty with no significant residual stenosis
Fig. 6. Hepatic artery stenosis treated with stent. (A,B,C) angiogram of the aorta-hepatic artery conduit with persistent severe stenosis (arrow in A) in the proper HA. As stenosis persists after angioplasty (arrowhead in B), it was treated with a 4 x 20 mm balloon expandable stent (arrow in C). Stenosis is resolved in post stenting angiogram (C). (D) Follow up MRA demonstrates stent artifact in the proper hepatic artery with adequate flow proximal and distal to the stent.

### 3.2.2 Hepatic artery thrombosis

In the past, hepatic artery thrombosis was the most common and dreads vascular complication of orthotopic liver transplantation, with a prevalence of 4%–12% in adult recipients, a prevalence of up to 40% in children, and a mortality rate of 50%–58% (Mazzaferro et al, 1989). Microsurgical techniques have improved these results, and the prevalence of hepatic artery thrombosis during the first thirty days after transplantation has been reduced to approximately 5% in whole liver transplantation (Settmacher et al, 2000). However, hepatic artery thrombosis is more common in split or living donor liver transplantation (Ghobrial et al, 2000; Hashikura et al, 2001; Katyal et al, 2000). Associated risk factors include prolonged cold ischemia time of the donor liver, previous orthotopic liver transplantation, significant differences in caliber between the donor and recipient hepatic arteries, an interposition conduit for the anastomosis, small donor or recipient vessels, acute rejection, ABO blood type incompatibility, and cytomegalovirus infection (Crossin et al, 2003; Dodd, 1995; Vivarelli et al, 2004). As in hepatic artery stenosis, clinical manifestations vary considerably, ranging from mild elevation of liver enzyme levels to delayed bile leak, bile duct stricture or ischemic changes, or fulminant hepatic necrosis (Ametani et al, 2001; Dodd et al, 1994; Ito et al, 2000). Patency of the hepatic artery is vital for long-term survival of the graft because this artery is the sole blood supply to the biliary epithelium of the transplanted liver, unlike in a native liver (Crossin et al, 2003; Kaneko et al 2004). As a result, complete occlusion of the hepatic artery results in infarction or necrosis of the liver parenchyma and may lead to fulminant hepatic failure in the early post-transplantation period. Doppler US allows correct identification of hepatic artery thrombosis in up to 90% of cases (Crossin et al, 2003; Garca-
Criado et al, 2003; Glockner & Forauer 1999; Nghiem et al, 1996). At doppler US examination, there is usually complete absence of both proper hepatic and intrahepatic arterial flow (Chong, 2004; Kok T et al, 1998; Nghiem et al, 1996). The initial doppler waveform of the hepatic artery may be normal, with follow-up doppler US images showing a progressive decrease in systolic and diastolic flow, followed by absent diastolic flow, dampening of the systolic peak, and, finally, total loss of the hepatic waveform (Nolten & Sproat, 1996). After thrombosis, arterial collateral vessels can develop, especially in children, and intrahepatic flow may be identified. Nevertheless, the intra-hepatic arterial waveform will display a tardus parvus pattern with an acceleration time greater than 80 msec and a resistive index less than 0.5 (Chong, 2004; Crossin et al, 2003; Dodd, 1995). Therefore, a complete absence of flow in the main hepatic artery and a tardus parvus pattern in the intrahepatic branches of the hepatic artery are highly suggestive of hepatic artery thrombosis and should be confirmed with other imaging techniques (Hall et al, 1990). MR angiography is a useful and noninvasive method for evaluating the patency of the hepatic artery and may play an important role in identifying patients who require hepatic angiography (Glockner et al, 2000; Ito et al, 2000). When thrombosis is present, MR angiography accurately demonstrates the location of the thrombus by showing arterial opacification up to the thrombus, abrupt cutoff of the hepatic artery at the thrombus, and lack of opacification of distal branches (Fig. 7a) (Glockner et al, 2000; Ito et al, 2000).

Fig. 7. Hepatic artery thrombosis (A) MRA demonstrating common hepatic artery (arrow) visualized to the level of the anastomosis, and complete occlusion of the hepatic artery beyond the anastomosis. (B) Selective celiac angiogram confirms hepatic artery thrombosis

Angiography is useful when fibrinolytic endovascular therapy is indicated (Fig. 7b). With early diagnosis, thrombectomy and revision of the transplant can be used to salvage the graft. Thrombolysis has high risk of hemorrhage in early hepatic artery thrombosis, especially if associated with liver infarction. If occlusion occurs at a late stage, the graft may survive with the support of portal venous flow, but there may be necrosis of the bile duct epithelium and consequent biliary strictures or leaks (Chong, 2004; Lorenz et al, 2001). Late hepatic artery thrombosis can be treated safely with thrombectomy, fibrinolysis, angioplasty and stenting Fig. 8.

3.2.3 Hepatic artery pseudoaneurysms (HAP)

Hepatic artery pseudoaneurysm is a rare complication after liver transplantation seen mostly at the donor-recipient anastomosis and less often at the ligation site of the gastroduodenal artery and those are likely related to infection, technical failure or biliary leakage. Intrahepatic
pseudoaneurysm can also be seen and may be related to percutaneous biliary procedures or liver biopsies. Mycotic hepatic artery pseudoaneurysm can fistulize to the portal vein or biliary tree and presents with hemobilia, gastrointestinal bleeding or hemoperitoneum. Endovascular treatment may be performed by transcatheter or percutaneous coil embolization or exclusion of the pseudoaneurysm with covered stent (Figs. 9&10). Surgical excision and revascularization using bypass graft can also be performed.

Fig. 8. Management of late hepatic artery thrombosis (A) Pre- and (B) Post-thrombolysis hepatic angiograms demonstrating recanalization of the hepatic artery (arrow). Sever stenosis (arrowhead) is seen at the hepatic artery bifurcation. (C) The stenosis was angioplastied with a 5 x 20 mm balloon (arrow) with no residual stenosis seen in the final angiogram (D)

3.2.4 Hepatic vein stenosis/thrombosis

Hepatic vein stenosis with resultant outflow insufficiency is a major postoperative complication that leads to graft failure in 5% of pediatric liver transplant recipients; most often in those with a partial liver graft (Buell et al, 2002) and Piggy back hepatic venous anastomosis. Hepatic veins stenosis usually produce hepatic congestion, refractory ascites and alteration of liver function test results. Transjugular or transfemoral angioplasty or metallic stent placement usually is selected as the first-line treatment for this complication (Cheng et al, 2005; Lorenz et al, 2006). In pediatric patients, balloon dilation is the preferred treatment choice because the long-term patency of metallic stents is unknown and repeat transplantation is always possible. Metallic stent placement should be reserved for the treatment of persistent hepatic vein stenosis that is unresponsive to multiple angioplasties. The persistence of a pressure gradient of more than 5 mm Hg between the hepatic vein and the right atrium after several angioplasties is an indication for metallic stent placement (Lorenz et al, 2006). Good technical and clinical success rates are reported after hepatic veins angioplasty and stenting with patency rates ranging from 70% at 3 months to 50% at 36 months (Lorenz et al, 2006). Long term patency may require repeated interventions. In adult
and pediatric patients in whom transjugular or transfemoral recanalization of the stenotic or occluded hepatic vein stenosis has failed, the use of a percutaneous transhepatic approach or a combined transhepatic-transjugular approach has been reported (Kubo et al, 2006; Miraglia et al, 2007). For the transhepatic approach, preprocedural drainage of ascites and postprocedural embolization of the transhepatic tracts are, in our opinion, mandatory to reduce the risk of bleeding. Hepatic vein stenosis usually occurs at the anastomosis site; less frequently, an intrahepatic stenosis is found that is likely due to injury of the hepatic vein during a previous surgical or percutaneous procedure (eg, biopsy or biliary catheter placement). Treatment is performed with angioplasty or metallic stent placement (Fig. 11). Doppler US should be performed the day after the procedure for a baseline evaluation of the hepatic vein velocity and flow spectrum, which are compared with the findings at follow up Doppler US evaluations. Imaging follow-up is performed every 3 months in the first post-procedural year or at any occurrence of ascites or any alteration in liver function test results.

Fig. 9. Management of hepatic artery pseudoaneurysms (HAP). (A,B,C) Extrahepatic aneurysm: (A) MRA and (B) graft hepatic angiogram revealing an outpouching (HAP) at the lateral aspect of the graft (arrowhead). (C) After stent graft deployment, angiogram reveals no further filling of the Pseudoaneurysm. (D,E,F) Intrahepatic HAP s/p ERCP (D&E) catheter angiography shows a bilobed collection of contrast from the right hepatic artery (arrow) in this patient with hemobilia. (F) Post-coil embolization (arrowhead), no filling of the HAP is seen.
Fig. 10. Management of hepatic arteriovenous fistula. (A) Right hepatic angiogram reveals filling of the portal vein (arrowhead) and the hepatic artery (arrow) at the same time. (B) Post coil embolization reveals minimal filling of the fistulous communication (arrow).

Fig. 11. Management of hepatic vein stenosis/thrombosis. (A) Doppler US reveals thrombus in the left hepatic vein (arrow) with abnormal monophasic flow. (B) Hepatic venogram reveals patent hepatic veins-IVC anastomosis and non-occlusive thrombus (arrow) in the hepatic vein confluent. (C) After local thrombolysis, thrombectomy and venoplasty, improved flow with residual thrombus (arrow) both being suggestive of stenosis recurrence. If clinical or imaging signs of recurrent stenosis are present, hepatic vein phlebography with trans-stenotic pressure gradient measurement is recommended.
3.2.5 Inferior vena cava stenosis/thrombosis

Inferior Vena Cava (IVC) stenosis is more common in the pediatric population, especially among recipients of partial liver transplants, including living donor liver transplants, reduced-size liver transplants, and split liver transplants (Carnevale et al, 2004; Egawa et al, 1997). IVC stenosis may occur acutely secondary to an anastomotic size discrepancy or suprahepatic caval kinking from organ rotation. Delayed caval stenosis may occur secondary to fibrosis, a chronic thrombus, or neointimal hyperplasia (Carnevale et al, 2004; Katyal et al, 2000). Clinical manifestations include pleural effusions, hepatomegaly, ascites, and lower extremity edema. A significant suprahepatic caval stenosis may result in reversed flow or absence of phasicity in the hepatic veins (Crossin et al, 2003). Nevertheless, monophasic waveforms are not specific for hepatic vein stenosis (Chong, 2004). A monophasic flat waveform with a relatively low average peak velocity in the hepatic vein (mean, 11 cm/sec) is a common finding. Sometimes, graft growth and twisting are causes of IVC pseudostenosis (Ametani et al, 2001), which may increase or disappear depending on the patient’s posture. Hemodynamically significant IVC stenosis can be differentiated from pseudostenosis on the basis of the presence of features of Budd-Chiari syndrome and Doppler velocity measurements. IVC stenosis and hepatic vein stenosis may manifest as Budd-Chiari syndrome, with hepatomegaly, ascites, reversed flow or absence of phasicity in the hepatic veins, and reversed flow in the portal vein (Buell et al, 2002; Crossin et al, 2003; Katyal et al, 2000). Contrast-enhanced CT is useful in demonstrating congestive changes in the liver parenchyma as a manifestation of blocked outflow but is of little help in depicting the stenosis itself (Ametani et al, 2001; White et al, 2004). Coronal MR imaging is useful in determining the extent of IVC stenosis and associated anomalies (Ito et al, 2000). Frequently, cavogram is required to confirm the stenosis. Pressure gradient measurements can help distinguish physiologically significant lesions from pseudostenoses (Carnevale et al, 2004). Treatment includes IVC recanalization, balloon angioplasty and stent placement (Fig. 12). Color Doppler US performed after the interventional procedure is also useful in confirming the restoration of normal hepatic venous flow by demonstrating a multiphasic waveform and an objective increase in flow velocity (Huang et al, 2004; Totsuka et al, 2004). Ascites usually disappears rapidly after the procedure. IVC thrombosis is a rare occurrence. It tends to occur at the superior and inferior caval anastomoses. Risk factors include technical problems during transplantation, use of intravascular catheters, and compression of vessels by a fluid collection. Color Doppler US may reveal obvious vessel narrowing or an echogenic intraluminal thrombus with absence of flow. At MR angiography, IVC thrombosis is seen as an intraluminal defect. Coronal imaging is useful for determining the extent of IVC thrombosis (Chong, 2004; Glockner et al, 2000).

3.2.6 Portal vein stenosis

Portal vein stenosis has been reported to occur as a postoperative complication in 4%–8% of pediatric liver transplant recipients (Ueda et al, 2005). It occurs more frequently in reduced-size liver transplantation than in whole liver transplantation owing to the limited length of the portal vein that can be obtained from the donor (Unsinn et al, 2003). A difference in caliber between donor and recipient portal veins is normal and can be helpful in locating the portal venous anastomosis. An echogenic shelf like ring can often be seen at the anastomotic site. These findings should not be misinterpreted as a stenosis. At gray-scale US, portal vein
Minimal Invasive (Endovascular and Percutaneous) Treatment of Post Liver Transplantation Complications in Pediatrics

Fig. 12. Management of IVC occlusion. (A&B) CT scan of the upper abdomen demonstrating absence of the suprahepatic IVC in (A) and congested azygus vein (arrow) in B. (C) Initial cavogram confirms the occlusion of the IVC with opacification of the azygus system. (D&E) Successful recanalization and stenting of the IVC. The arrow in E points to the piggyback stump. (F) Follow up cavogram after six months confirms the patency of the stented IVC.

Stenosis is diagnosed when a reduction of the vessel lumen of 50% or more is observed (Fig. 13) at the site of narrowing relative to the prestenotic area, or when the caliber of the vessel is 2.5 mm or less at the site of narrowing (Boraschi & Donati, 2004; Crossin et al, 2003; Glockner & Forauer, 1999). Color Doppler US shows focal color aliasing at the vascular anastomosis. At pulsed doppler US, the waveform shows a systolic velocity greater than 20 m/sec or a velocity in the stenotic segment that is three to four times greater than that in the prestenotic segment. A poststenotic jet with a velocity between 1 and 3 m/sec is a characteristic finding (Crossin et al, 2003; Nghiem et al, 1996; Stell et al, 2004). MR angiography can provide excellent visualization of portal vein stenosis (Fig. 13). Portography helps confirm the presence of the stenosis, and a pressure gradient may be obtained to determine the hemodynamic significance of the stenosis (Nghiem, 1996). Clinical symptoms of hemodynamically significant portal vein stenosis are related to portal hypertension and include bleeding from varices, splenomegaly, and ascites. Percutaneous transhepatic angioplasty is considered the standard treatment for portal vein stenosis. The placement of metallic stents also has been reported for treatment of recurrent or nonresponsive elastic stenosis (Funaki et al, 2000; Zajko et al, 1994). In the largest patient series for which data are available, a very good patency rate of 100% was found at 46 months after treatment with angioplasty and metallic stent placement (Funaki et al, 2000). A transhepatic puncture of the portal vein is performed with a 21-gauge needle while using US for guidance. An introducer system is advanced over an 0.018-inch nitinol wire to the portal branch and then exchanged for a 6-F vascular sheath over a 0.035-inch wire. The trans-stenotic pressure gradient is measured by using a 5-F hydrophilic catheter. Before balloon dilation, a bolus of heparin...
(100 IU/kg) is administered intravenously to reduce the risk of thrombosis during balloon induced occlusion. Technical success is represented by resolution of the stenosis on a follow-up portogram and by a significant reduction in the trans-stenotic pressure gradient (Fig. 14). The persistence of a pressure gradient of more than 5 mm Hg has been considered an indication for metallic stent placement (Funaki et al, 2000). Coils or gelfoam embolization of transhepatic needle tracts can be done to reduce the risk of bleeding. Doppler US should be performed on the day after the procedure for baseline evaluation of the portal vein velocity and flow spectrum. If findings at doppler US or clinical signs are suggestive of stenosis recurrence, MRI can be performed to confirm the findings before percutaneous intervention is repeated.

Fig. 13. Portal vein stenosis. (A&B) MRA reveals moderate stenosis (arrow) of the main portal vein. (C&D) US and color US shows portal vein stenosis and turbulent flow

Fig. 14. Angioplasty of portal vein (PV) stenosis. (A&B) Percutaneous portogram reveals saccular dilatation of the portal vein (arrowhead) and moderate stenosis at the PV anastomosis (arrow) with an 8 mm pressure gradient noted. (C&D) Post venoplasty with 6 x 40 mm balloon, mild residual stenosis is noted with gradient drop to 3 mm Hg indicating successful treatment. (E) follow up US demonstrates improved velocities and decrease in the spatial gradient across the stenosis
3.2.7 Portal vein thrombosis

Portal vein thrombosis occurs more frequently in reduced size liver transplantation, mostly involving the main extrahepatic portal segment. Risk factors include surgical difficulties, decreased portal venous inflow; the presence of portosystemic shunts before transplantation; prior splenectomy; excessive vessel redundancy; and use of the venous conduits, most commonly cryopreserved iliac veins (Buell et al, 2002; Hashikura et al, 2003; Nghiem, 1998). Clinical manifestations include new-onset massive ascites, variceal bleeding, elevated values on hepatic function tests, splenomegaly, hepatic failure, and lower extremity edema (Buell et al, 2002; Millis et al, 1996). An acute thrombus is frequently anechoic and may be imperceptible on gray-scale US images and the portal vein appears normal. In these cases, color flow and spectral doppler analysis will show no detectable flow within the portal vein (Langnas et al, 1991; Nghiem, 1998). Vessel narrowing or an echogenic luminal thrombus with no Doppler flow may also be seen (Nghiem et al, 1996). Partial portal vein thrombosis may appear as a nonocclusive filling defect at US. Resultant luminal narrowing can be mistaken for portal vein stenosis at gray-scale, spectral, and color doppler US (Funaki et al, 2000; Langnas et al, 1991). Occasionally, reversed flow in the intrahepatic branches may be observed in patients with portal vein thrombosis with complete absence of flow in the main portal vein. This finding is due to arterioportal shunts that develop soon after the thrombosis. Care should be taken to avoid making a false-negative diagnosis (Nghiem, 1996, 1998; Stell et al, 2004). MR venography can provide an excellent visualization of portal vein thrombosis and can facilitate the differentiation of thrombosis from slow flow (Stafford-Johnson et al, 1998; Unsinn et al, 2003). At contrast material-enhanced CT, portal vein thrombosis is seen as a low-attenuation filling defect (Ametani et al, 2001; García-Criado et al, 2003; Unsinn et al, 2003). Portal vein stenosis with thrombus formation in the immediate postoperative period is quickly diagnosed with Doppler US and is managed surgically. Treatment of portal vein thrombosis may include mechanical thrombectomy, segmental portal vein resection, percutaneous thrombolysis and stent placement, or balloon angioplasty (Fig. 15) (Holbert et al, 1995; Rossi et al, 2004). However, when the thrombus extends to the periphery of the intrahepatic portal venous branches, it can no longer be treated with balloon dilation or thrombolysis, and the patient must undergo repeat transplantation (Ametani et al, 2001). Thus, early diagnosis of portal vein thrombosis before formation of a complete thrombus is important. Occasionally, portal vein thrombosis is

Fig. 15. Portal vein thrombosis. (A) Percutaneous portogram reveals occlusion of the main portal vein. (B) The portal vein was recanalized and thrombectomy was performed. (C) Post recanalization portogram reveals patent mesenteric veins (arrow) with filling of collateral varices
detected in patients with normal allograft function and no portal hypertension. In these patients, sufficient hepatopetal collateralization has developed to maintain adequate venous flow (Holbert et al, 1995; Unsinn et al, 2003). A cavernomatous transformation is the usual finding at Doppler US in these cases.

3.3 Biliary complications imaging and treatment

Biliary complications are the most common complications following pediatric liver transplantation estimated to involve 20%–40% of pediatric liver transplant recipients, more frequently seen in children who have undergone reduced-size transplantation. Most biliary complications develop during the first 3 months after pediatric liver transplantation, but strictures and stones may develop months or years later. Complications include anastomotic leakage and stenosis with bile duct dilatation; intrahepatic bile duct stones, sludge, or debris; and biloma. These complications are related to the surgical method of biliary reconstruction and to prolonged cold ischemia time, immunologic reactions, hepatic artery thrombosis, ABO blood group system incompatibility between donor and recipient, and cytomegalovirus infection (Ametani et al, 2001). Non-anastomotic strictures are probably caused by hepatic arterial insufficiency from either stenosis or thrombosis. These ischemic arterial events may result in bile duct strictures or leaks, increasing the risk of cholangitis, sepsis, and abscess (Boraschi & Donati, 2004; Glockner & Forauer, 1999). The blood supply to the recipient CBD is rich because of collateral flow, whereas the vascularity of the donor duct and the proximal intrahepatic ducts is derived solely from the reconstructed hepatic artery. Biliary disease should be suspected in a post-transplantation patient who presents with elevated values on hepatic function tests, jaundice, fever, or abdominal pain (Lorenz et al, 2001; Vitellas & Guttikonda, 2002). The clinical manifestations of biliary complications often are indistinguishable from those of vascular complications, graft rejection, graft dysfunction, and infections. Although US is commonly performed to screen for biliary complications, the false-negative rate is high; therefore, negative findings at US do not suffice to exclude biliary complications. MRCP can be used as a non-invasive imaging tool to confirm US findings. Percutaneous trans-hepatic cholangiography can depict the type, location, and severity of biliary complications, allowing treatment in many cases.

3.3.1 Anastomotic biliary strictures

Anastomotic biliary strictures are a common problem after pediatric liver transplantation, with a reported incidence of 10%–35% (Lallier et al, 1993; Heffron et al, 1992). Such strictures are usually related to scar tissue and retraction at the suture site. Untreated biliary strictures are associated with high morbidity and mortality. Because hepatico-jejunostomy with Roux-en-Y reconstruction is the most common type of biliary anastomosis in pediatric liver transplant recipients, endoscopy is rarely feasible and percutaneous intervention is usually the only treatment approach possible. Percutaneous treatment of biliary strictures in pediatric liver transplant recipients is considered safe and effective, and in most cases obviates surgical revision of the affected anastomoses (Lorenz et al, 2005; Schwarzenberg et al, 2002). Possible complications of percutaneous transhepatic cholangiography include hemobilia, intra- or extrahepatic hematoma, and fever with bacteremia; a cumulative incidence of 10.8% is reported for these complications in the pediatric population (Lorenz et al, 2005). Among 35 pediatric liver transplant recipients who underwent percutaneous
treatment of biliary strictures, the reported success rate was 34% after a single course of therapy and 60% after repeat percutaneous therapy, with a median follow-up period of 4.5 years (Sunku et al, 2006). Suspicion about the presence of a biliary stricture may be aroused by one or more of the following findings, clinical manifestations such as fever or cholangitis; biochemical indicators such as increased levels of alkaline phosphatase, direct bilirubin, and transaminases; biliary duct dilatation observed at US, CT, or MR imaging; and liver biopsy with histologic findings indicative of cholestasis due to biliary obstruction. Biliary strictures may be present also in the absence of ductal dilatation (Berrocal et al, 2006). Some investigators have reported better sensitivities (80%–100%) when using MR cholangiography for the detection of biliary obstruction (Kitazono et al, 2007; Norton et al, 2001). However, in pediatric patients, deep sedation or general anesthesia is necessary during MR cholangiography and adds considerably to the cost of management; for this reason, MR cholangiography is not generally used as a screening modality in children. It does afford a global evaluation of the ductal anatomy, a capability that might be especially helpful when planning the placement of a biliary drainage catheter in a patient with two separate hepaticojejunostomies and a nondilated bile duct, because it allows avoidance of puncture of a hepatic segment with a normal bile duct. As an alternative, hepatobiliary scintigraphy with technetium 99m Mebrofenin iminodiacetate could be performed, with a segmental delay in clearance of the radiotracer being suggestive of a biliary stricture. Percutaneous transcatheter cholangiography is performed to confirm clinical, histologic, or imaging evidence of biliary strictures. Percutaneous transcatheter cholangiography is performed with monitored anesthesia care, spontaneous respiration, and additional local anesthesia. Intravenous antibiotic prophylaxis is administered before the procedure. If coagulation defects (platelet count < 50 × 1000/μL, prothrombin activity < 50%) are present, the patient receives an infusion of platelets, fresh frozen plasma, or both. Percutaneous transcatheter cholangiography is usually performed with a subxiphoid approach by using a 20-gauge needle positioned in a peripheral bile duct with US and fluoroscopic guidance. If the cholangiogram shows an anastomotic stricture, the biliary tree is catheterized by using an introducer system over a nitinol wire; the stricture is crossed, when possible, with a 0.035- or 0.038-inch hydrophilic wire, and a transanastomotic biliary catheter (diameter range, 5–6.6 F) is placed with side holes above and below the stricture (Fig. 16).

The catheter is left in place to allow external gravity drainage for at least 1 day. If the patient has no fever or cholangitis the day after the procedure, the catheter is clamped to allow internal drainage. Diagnostic cholangiography and the first session of balloon dilation of the anastomosis are performed on different days to reduce the risk of sepsis. The first session of balloon dilation is usually performed 1 week after cholangiography, with a 5-F or 6-F sheath and with a balloon size ranging from 5 mm to 7 mm at a pressure of 6–11 atm. The balloon size selected is usually 1 mm larger than the diameter of the intrahepatic bile duct above the stricture. In every session, trans-anastomotic balloon dilation should be performed three times, 10 minutes each. A transanastomotic biliary catheter is placed after every session of dilation, with the catheter size ranging from 6 to 12 F, according to the diameter of the anastomosis. The antibiotic infusion is repeated 6 hours after the procedure. A minimum of three separate sessions of biliary anastomotic dilations are performed, followed by a cholangiographic evaluation, and if necessary, further sessions of dilation every 4–6 weeks. At each session of dilation, the size of the balloon catheter is increased by 1 mm, until a maximum diameter of 10 mm is reached. The drainage catheter is finally removed when
Fig. 16. Anastomotic biliary stricture. (A) Percutaneous cholangiogram demonstrating dilated biliary ducts with total occlusion of the hepatico-jejunostomy (arrow). (B) Successful recanalization and a balloon cholangioplasty of the biliary anastomosis. (C) Final cholangiogram demonstrated patent anastomosis with contrast drained into the jejunum. (D) Internal\external biliary drain placed across the anastomosis.

cholangiography performed through a sheath depicts resolution of the stricture and a good transanastomotic bile flow, which is defined as a complete passage of contrast material from the bile duct to the bowel loop within three minutes after injection. Biliary manometry or clinical trial using a capped “end-hole” catheter proximal to the treated duct or anastomosis can also be performed to determine the treatment success and the resolution of the anastomotic biliary stricture (Scott et al, 1998). In up to 41% of left lateral split-liver transplant recipients, the ducts for segments II and III are separately anastomosed to the jejunum (Broelsch et al, 1991). In these patients, biliary strictures may develop in one or both anastomoses (Fig. 17 a&b). For this reason, it is mandatory to know the number of hepatojejunostomies present in a patient before performing percutaneous transhepatic cholangiography. In partial liver transplant recipients with an occlusive anastomotic biliary stricture that is not traversable with standard interventional radiology techniques, sharp percutaneous recanalization of the hepatojejunostomy may be performed using a long needle, thus obviating surgery (Miraglia et al, 2007) (Fig. 17 C&D).

3.3.2 Intrahepatic biliary strictures and bilomas

Intrahepatic biliary strictures are usually related to chronic transplant rejection or arterial insufficiency caused by hepatic artery stenosis or thrombosis. A single focal stricture or
multiple or combined intrahepatic and anastomotic strictures may be present (Fig. 18). Percutaneous treatment of intrahepatic biliary strictures is usually performed with the same techniques used for anastomotic biliary strictures; however, a recurrence rate of 90% was reported in a long-term follow-up study of intrahepatic strictures (Sunku et al, 2006).

Intrahepatic bilomas develop in the presence of arterial insufficiency due to hepatic artery stenosis or thrombosis or because of ABO incompatibility. Bilomas frequently are infected by gram-negative organisms that enter via the biliary anastomosis from the gastrointestinal tract. Percutaneous drainage of intrahepatic bilomas usually is performed with US guidance and is mandatory to reduce the risk of sepsis and graft loss (Hoffer et al, 1988).

### 3.3.3 Bile leakage

Postoperative bile leakage is a complication that usually occurs within few weeks after pediatric liver transplantation. Bile may leak from the bile duct anastomosis or from the resection margin in a split-liver transplant. Nonanastomotic leaks are usually associated with hepatic artery thrombosis.

![Fig. 17. Sharp recanalization of occlusive hepatico-jejunostomy. (A&B) MRI coronal images and MRCP demonstrating two separate heptico-jejunostomy with multiple filling defects in the superior bile duct. (C) Cholangiogram demonstrated external drain in the lower segmental bile duct with total occlusion of the inferior anastomosis, a plastic stent is noted across the superior anastomosis. (D) S/p sharp recanalization of the inferior anastomosis with the contrast drained through the anastomosis into the jejunum](www.intechopen.com)
Fig. 18. Ischemic biliary duct injuries. (A) Intra-hepatic biliary ducts stenosis seen by ERCP cholangiogram. (B) Combined intra-hepatic and anastomotic biliary stricture.

Fig. 19. (A) CT showing multiple bilomas (arrows). (B) Percutaneous cholangiogram reveals irregular and dilated bile ducts (arrow) consistent with ischemic injury due to hepatic artery thrombosis. (C) Percutaneous cholangiogram in different duct reveals a small biloma (arrowhead). (D) Follow up CT of the abdomen reveals resolving bilomas with draining catheter in site (arrow). Retroperitoneal lymphadenopathy (curved arrow) consistent with post transplant lymphoproliferative disorder (PTLD).
Fig. 20. (A&B) ERCP demonstrating bile leakage from CHD (arrow in A) and stricture at the distal CBD (arrowhead). Plastic stent is placed through the scop (arrow in B). (C) Percutaneous cholangiogram after the removal of the internal stent revealing a kink and narrowing at the CBD anastomosis (arrow). (D) 6.5 Fr internal/external drainage catheter was placed.

Another possible site of leakage is the T-tube insertion in patients with a choledocho-choledochal anastomosis. Small leaks usually resolve spontaneously; whereas large ones are associated with significant morbidity and occasional mortality, thus require treatment. Clinical manifestation of bile leak vary, and can be presented as fever, abdominal pain, fluid and electrolyte depletion, fat malabsorption, and the possibility of sepsis or bleeding due to hilar vascular erosion. The bile extravasates into the peritoneal cavity or forms a perihilar fluid collection. These fluid collections are usually well depicted at US. Percutaneous drainage catheters are placed with US guidance to drain these large bile collections. Bile leak can be confirmed by hepatobiliary scintigraphy with Technitum 99m Mebrofenin iminodiacetate. Recently, MR cholangiography performed with specific contrast agents has proved useful in the diagnosis of small bile leaks (Akin et al, 2004; Vitellas & Guttiikonda, 2002). Adult patients who have undergone endoscopic or percutaneous transhepatic treatment for large bile leaks have experienced good outcomes obviating surgical repair in most cases (Akin et al, 2004; Kok et al, 1996). In pediatric liver transplant recipients, percutaneous transhepatic cholangiography and biliary catheter placement may be attempted for the treatment of large bile leaks from anastomoses only if the bile duct and the jejunal loop have not completely separated. A modified multipurpose drainage catheters,
can be placed in the intrahepatic biliary ducts crossing the leaking anastomosis into the
distal bowel loop by adding holes proximally to reduce the contact between the bile and the
anastomotic lesion and thereby facilitate the repair process Fig. (20). Surgical revision often
is necessary or strongly recommended if cholangiography shows complete separation of the
bile duct from the jejunal loop.

Fig. 21. Percutaneous retrieval of biliary stones. (A) a basket inserted co-axially with the
cholangioscope through a large percutaneous access sheath to the left hepatic duct. (B) On
table mage shows the retrieved stones. (C and D) pre and post stone retrieval
cholangiogram demonstrated successful treatment with no residual stone and resolution of
the biliary duct dilatation

3.3.4 Bile duct stones

Although stones and sludge occur only infrequently after transplantation, they are
associated with high morbidity. Several factors can lead to the formation of biliary stones
and sludge. Cyclosporine can alter the bile composition, inducing crystal formation, which
results in biliary sludge and stone formation (Fulcher & Turner, 1999). Other causes include retained stones within the graft or stones formed secondary to bile stasis from biliary strictures. Biliary stones are well depicted with US and MR imaging (Kok et al, 1996; Laghi et al, 1999; Linhares et al, 2004). Interventional procedures may be useful for obviating surgery in these patients (Lorenz et al, 2005). Biliary stone removal can be performed through the percutaneous access to the involved bile duct and the stone can be retrieved using a basket or can be fragmented into small pieces using small forceps to drain with the bile into the intestine Fig. (21).

4. Conclusion

Liver transplantation is the ultimate treatment for children with end-stage liver disease. The application of reduced-size transplantation and the development of living related donor partial liver transplantation have expanded the donor pool, which, however, has in turn increased the risk for vascular and biliary complications. Imaging studies are extremely important for early diagnosis of post-transplantation complications because the clinical manifestations of these complications are frequently nonspecific and vary widely. Doppler US plays the leading role in the postoperative evaluation of pediatric patients. It is the imaging tool of choice for initial screening for biliary, arterial, and venous complications and is helpful in determining the next logical imaging test to confirm these complications. Current MR imaging techniques, including MR angiography and MR cholangiography, may provide a comprehensive evaluation of the transplanted liver; reveal abnormalities of vascular structures, bile ducts, and liver parenchyma; and depict extrahepatic tissues. If available, MR imaging should be used when US is inconclusive. CT is a valuable complement to US in the evaluation of complications involving the hepatic parenchyma as well as extrahepatic sites, especially the thorax. A number of complications can be corrected by using interventional radiologic techniques. Advances in minimally invasive, image-guided percutaneous and endovascular techniques of various vascular and nonvascular complications of liver transplantation, have led to improved Graft and patient survival and have obviated surgical revision or repeat transplantation in most cases.

5. References


Liver Transplantation – Technical Issues and Complications


This book covers a wide spectrum of topics including, but not limited to, the technical issues in living and deceased donor liver transplant procedures, cell and experimental liver transplantation, and the complications of liver transplantation. Some of the very important topics, such as the arterial reconstruction in living donor liver transplantation, biliary complications, and the post-transplant-lymphoproliferative disorders (PTLD), have been covered in more than one chapter.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:
