The role of interventional radiology in complications after paediatric liver transplantation

J Cantrell, MB BCh, FCRad (SA)

Wits Donald Gordon Medical Centre, University of the Witwatersrand, Johannesburg, South Africa

Corresponding author: *J Cantrell (Cantrell_j@hotmail.com)*

Liver transplantation has become an established treatment in both adults and children for end-stage liver disease, acute hepatic failure and certain liver tumours. There is a significant risk of complications after all forms of liver transplantation. The interventional radiologist plays a critical role in the diagnosis and treatment of these complications. The use of image-guided, minimally invasive procedures reduces the need for surgical revision or retransplantation and improves graft and patient survival rate. This article reviews some of the most common vascular and non-vascular complications after paediatric liver transplantation, and the interventional radiology techniques used to diagnose and treat them.

S Afr Med J 2014;104(11):825-829. DOI:10.7196/SAMJ.8619

Originally, all liver transplants used deceased donors. There have been major advances over the last few decades, with the introduction of split liver grafts and living related donor transplants dramatically increasing the pool of potential donors. Ongoing technical advances have improved the rate of both graft and patient survival, but a liver transplant remains a procedure with significant morbidity and mortality.[1] A multidisciplinary approach to the post-transplant patient is vital, and image-guided, minimally invasive procedures improve graft and patient survival.[2]

Image-guided liver biopsy

Liver biopsy is a common procedure that is performed if there is unexplained derangement of liver functions, such as seen with rejection, ischaemia or cholestasis without biliary dilatation.[3] Most biopsies are performed percutaneously, unless the patient has a severe coagulopathy, in which case a transjugular biopsy is performed. Percutaneous biopsies are done with anaesthesia and under ultrasound (US) guidance, either using a right anterolateral or an epigastric approach, depending on the position of the graft. At our institution we use a Menghini-type suction needle to obtain core samples of the liver for histology. There is a risk of perihepatic haematoma, so compression is manually applied over the biopsy site for a few minutes post procedure. If there is ascites overlying the liver, this is first drained percutaneously.

Biliary complications

The rate of biliary complication is between 11% and 25%, and complications are more common in reduced, split and living related donor grafts, compared with whole grafts. Most biliary complications can be treated with interventional radiology (IR) techniques alone.[4] Biliary complications include bile duct stenosis, bile leaks and intraparenchymal or perihepatic biloma. The majority of complications occur within 3 months post transplant.

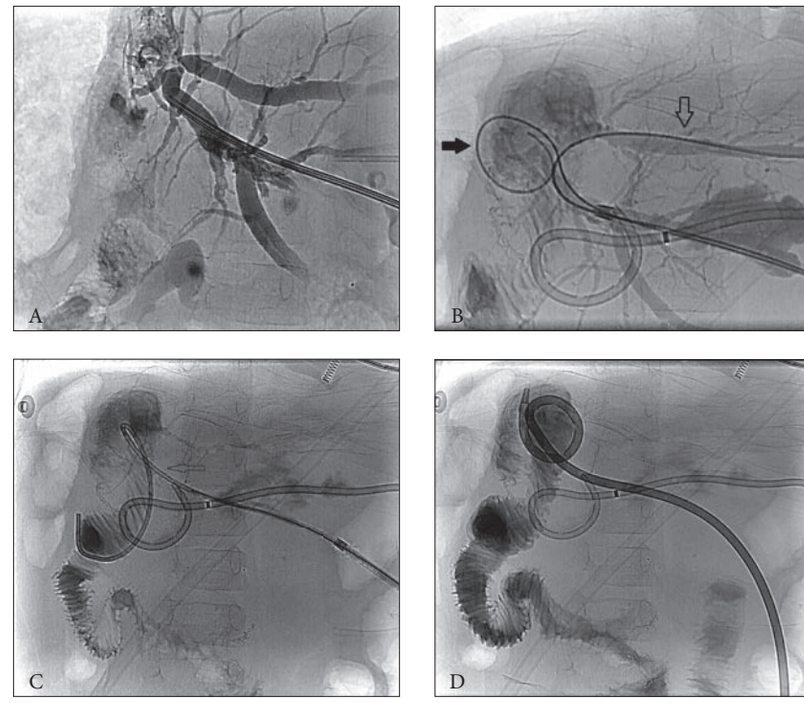

Fig. 1. Biliary stenosis in a 2-year-old patient with a living related donor transplant for biliary agenesis. She presented with sepsis and raised serum bilirubin. (A) PTC demonstrates moderately dilatated segment II and III ducts with a stenosis at the hepaticoenterostomy. (B) One guidewire is passed through the stenosis into the Roux loop (solid arrow) and another guidewire is passed from the segment III to segment II bile duct (open arrow). The visualised pigtail catheter lies in a perihepatic collection. (C) A 5 French catheter is passed over the guidewire into the Roux loop. (D) An internal-external biliary drain is positioned across the stenosis (proximal side holes were cut into this pigtail catheter in order to have side holes above and below the stenosis). (PTC = percuteneous transhepatic cholangiogram.)

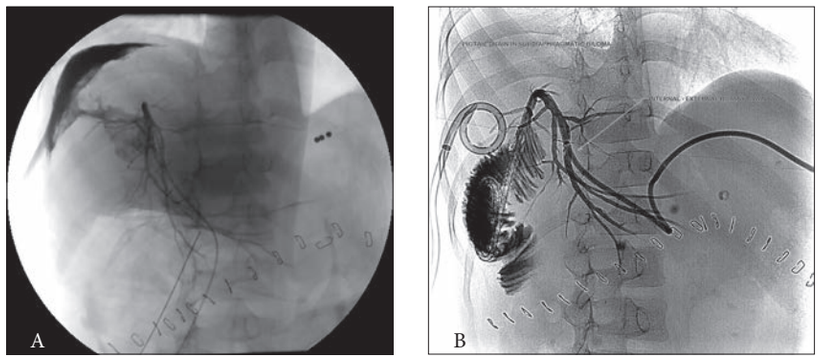

Fig. 2. Bile duct leak in a 7-year-old patient with a split liver transplant for Wilson's disease. He presented with raised liver enzymes and right subdiaphragmatic fluid seen on ultrasound. (A) PTC demonstrates non-distended bile ducts and an anastomotic leak at the hepaticoenterostomy, continuous with a right subdiaphragmatic biloma. There is no contrast in the Roux loop, which suggests a complete disruption of the hepaticoenterostomy anastomosis. (B) The patient had surgical revision of the hepaticoenterostomy and at the same time an intraoperative internal-external biliary drain was inserted. A percutaneous pigtail catheter was inserted into the subdiaphragmatic biloma under image guidance. (PTC = percuteneous transhepatic cholangiogram.)

Table 1. IR procedures performed on 19 paediatric patients post liver transplant from April 2011 to April 2014

IR procedures		Number performed
Biliary		
	PTC only	4
	PTC and external biliary drain	3
	PTC and internal-external biliary drain	3
	Conversion of external biliary drain to internal-external drain	3
Biopsy		
	US-guided, percutaneous liver biopsy	23
Other		
	Image-guided drainage of intra-abdominal collections or bilomas	15
	Image-guided drainage of pleural effusion	24
	Image-guided drainage of ascites	3
	Exchange of drains (all types)	4

IR = interventional radiology; PTC = percutaneous transhepatic cholangiogram; US = ultrasound.

Biliary stenosis

Biliary stenosis can occur at the anastomosis, usually caused by scarring, or less commonly at a non-anastomotic site, usually caused by ischaemia, infection or rejection. A stenosis is suspected if US, computerised tomography (CT) or magnetic resonance imaging demonstrates dilatated bile ducts upstream of the stenosis, but a significant number of obstructed bile ducts appear normal on US; percutaneous transhepatic cholangiography (PTC) is often required for a definitive diagnosis.[5] Most transplants use a Roux loop and hepaticoenterostomy, precluding the use of endoscopic retrograde cholangiopancreatography to image or treat the biliary tree.

When a PTC confirms a stricture, balloon dilatation is performed and an internal-external biliary drain is placed across the stricture to prevent restenosis (Fig. 1). The biliary drain is left *in situ* for 4 - 6 weeks and dilatation is usually repeated on a few occasions until the cholangiogram demonstrates resolution of the stricture with adequate bile drainage, at which point the biliary drain is removed. Self-expanding metal stents are reserved for the few cases resistant to repeat balloon dilatation.

Bile leak

Bile leaks are well demonstrated with PTC and most often occur at the anastomosis. They are usually treatable with an internal-external biliary drain that crosses the anastomosis and is left *in situ* for a few weeks. The drain can be removed once cholangiography, through the drain access, shows no further leakage. If there is complete disruption of the anastomosis, surgical revision is necessary (Fig. 2). Non-anastomotic bile leaks can occur on the cut surface of the liver in the case of split and living related donor transplants.

Biloma

Perihepatic bilomas are common and occur if there is a bile duct leak; small bilomas can be treated conservatively. It is also common to have a bile collection adjacent to the cut edge of the liver in the case of a split liver transplant, which may on occasion be associated with stenosis at the hepaticojejunal anastomosis. Bilomas increase the risk of sepsis and can be treated by means of a percutaneous pigtail catheter, usually inserted under US and fluoroscopic guidance.

Vascular complications

Hepatic artery stenosis

The rate of hepatic artery stenosis (HAS) is between 11% and 19%[6] and stenosis usually occurs within 3 months post transplant. HAS increases the risk of ischaemia and hepatic artery thrombosis (HAT). In adults, 65% of untreated HAS progresses to thrombosis within the first 6 months.[7] Stenoses usually occur at the site of anastomosis but can occur elsewhere as a result of rejection and ischaemia. There is often a nonspecific clinical picture, which usually includes abnormal liver function tests, and diagnosis is usually made on Doppler US. Stenosis is suspected if there is spectral broadening and an increase in the peak velocity above 2 m/s at the site of the anastomosis. Sometimes the stenosis itself is obscured on US, but if there is an abnormal waveform in the distal artery, with an acceleration time of >0.08 seconds and a resistive index <0.5, it indicates the presence of a stenosis.

If HAS is suspected, a formal angiogram can confirm the stricture, and the trans-stenotic pressure is measured to confirm a pressure gradient (Fig. 3). A gradient above 10 mmHg is considered significant. A microcatheter is necessary owing to the small calibre of the hepatic artery.[7]

Long-term patency rates after percutaneous transluminal angioplasty (PTA) in adults are 60 - 80% at 1 year, but there are poor data on long-term studies in children. PTA is typically performed with a 2 - 5 mm balloon; stents are reserved for when repeat PTAs are unsuccessful. Complications such as rupture or dissection can also be treated with stents.[3]

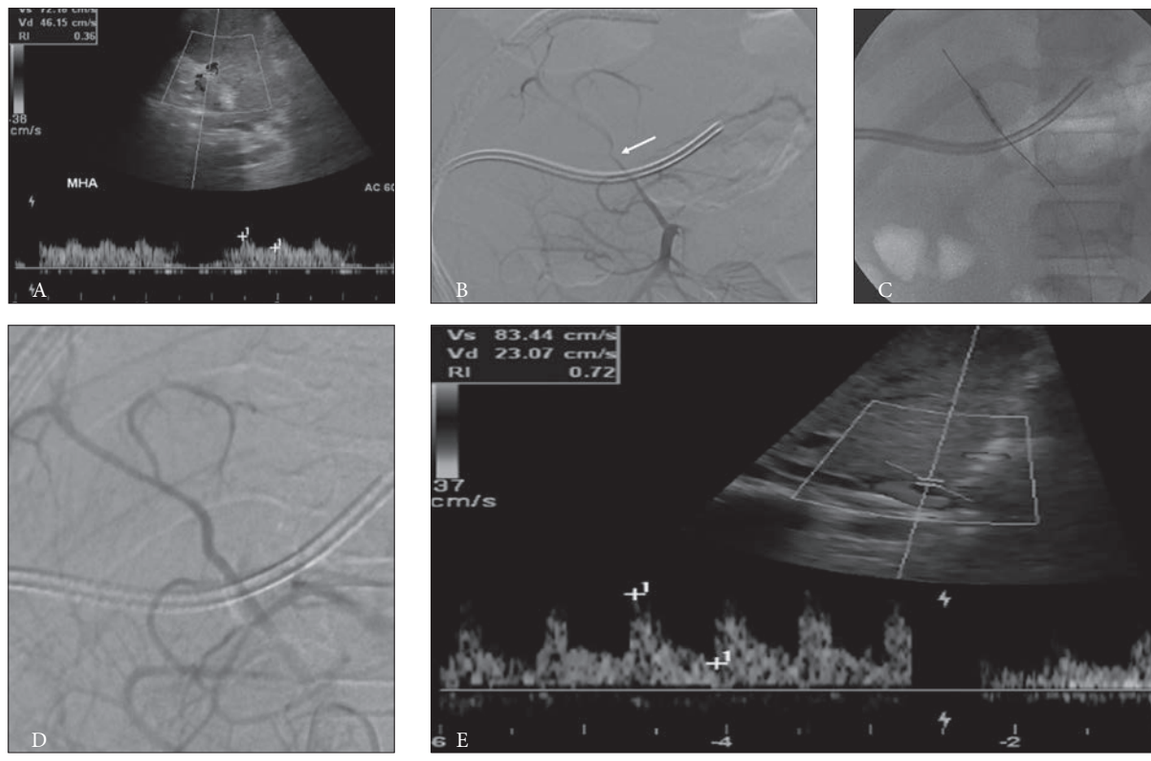

Fig. 3. HAS in a 13-year-old girl with a split liver transplant for treatment of hepatocellular carcinoma. (A) Doppler US shows a low resistive index (0.30 - 0.45) in the hepatic artery. (B) DSA confirms an HAS at the anastomosis. The trans-stenotic pressure gradient was 25 mmHg, measured with a 3 French microcatheter. (C) Angioplasty with 4 mm diameter balloon catheter. (D) Post-angioplasty DSA shows resolution of the stenosis. The pressure gradient decreased to 5 mmHg. (E) Follow-up Doppler US shows a normal hepatic arterial waveform with a normal resistive index of 0.72. (HAS = hepatic artery stenosis; US = ultrasound; DSA = digital subtraction angiography.)

Hepatic artery thrombosis

HAT is an infrequent but devastating post-transplant complication with high morbidity and mortality, often leading to graft loss if untreated. The reported incidence of HAT is highly variable, but is ~5% in high-performing transplant centres.[8] Doppler US is sensitive in detecting HAT (92%), with non-visualisation of the artery and loss of arterial Doppler signal along the anticipated course of the hepatic artery.[9] Surgical treatment options include thrombectomy with revascularisation (if diagnosed early) and repeat transplantation. Endovascular thrombolytic treatment (selective percutaneous thrombolysis followed by angioplasty) has been described in paediatric transplant HAT, but there are few data on long-term studies in children.[10]

Portal vein stenosis

The rate of portal vein complications, including portal vein stenosis (PVS), is between 4% and 8%.[11] Patients typically present with signs of portal hypertension such as splenomegaly, variceal bleeding and ascites. Diagnosis is usually made with Doppler US. The stenosis is best confirmed with direct portal venography via transhepatic puncture, where the pressure gradient across the stricture can also be measured. An indirect portogram (on the delayed phase of a superior mesenteric angiogram) also allows visualisation of the portal vein, but no direct access for interventions.

Balloon angioplasty (Fig. 4) results in good long-term patency rates, with 10-year primary patency rates of 70% and 10-year primary assisted patency rates (patency of the stenosis after repeat intervention following symptomatic restenosis at the same site) of 96%. Metal stents are reserved for recurrent or elastic lesions.[12]

Hepatic vein stenosis

Hepatic venous outflow obstruction is an uncommon complication, with an overall incidence of 6%. Patients typically present with ascites, abnormal liver function tests and new-onset splenomegaly.

Percutaneous balloon angioplasty is a very effective method of treating hepatic venous outflow obstruction, with 10-year primary patency rates of 52% and 10-year primary assisted patency rates of 95%.[13]

A venogram is performed and the pressure gradient is measured to confirm the diagnosis, usually via a transjugular or transfemoral route (Fig. 5). After balloon dilatation, the stenosis may recur, requiring reintervention. Insertion of a metal stent is reserved for cases that do not respond to repeat balloon dilatation. Doppler US is used for short- and long-term follow-up.

Inferior vena cava stenosis

Stenosis of the inferior vena cava is uncommon, with an incidence of <2%. The stenosis is usually at the superior anastomosis and can occur in conjunction with a hepatic vein stenosis. Patients present with hepatomegaly, ascites, lower limb oedema, pleural effusions or abnormal liver function tests. The diagnosis is usually made with Doppler US, which can demonstrate the stenosis, sometimes with adjacent thrombus and associated increased flow velocities.

A cavogram confirms the stenosis, and the trans-stenotic pressure gradient is measured before and after angioplasty. As with most venous stenoses, balloon angioplasty is the treatment of choice, with stent placement reserved for post-dilatation pressure gradients of >5 mmHg or persistent stenosis on post-angioplasty cavogram.[14]

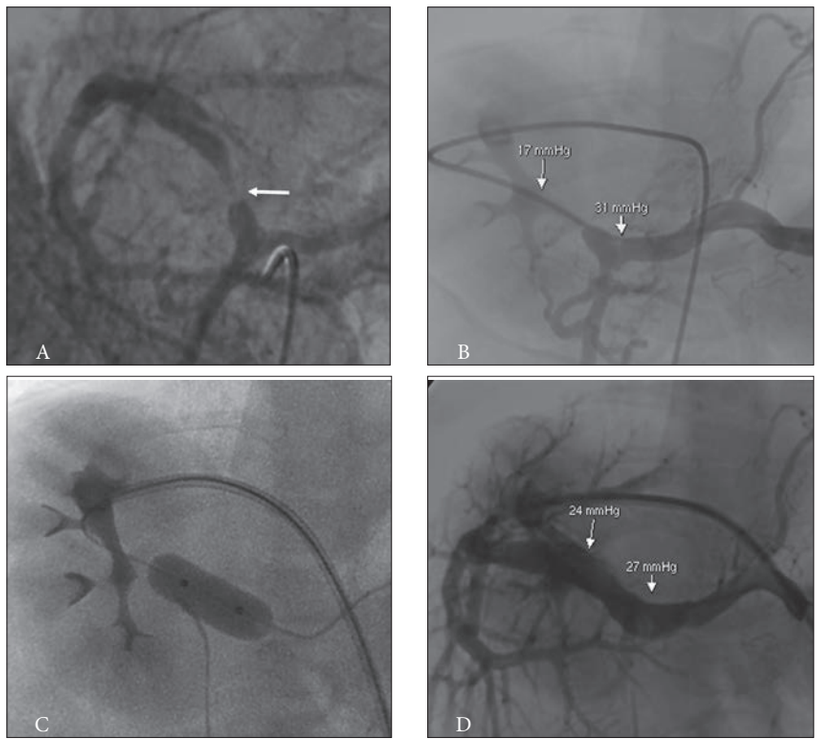

Fig. 4. PVS in a 9-month-old with a split liver transplant for treatment of biliary atresia. Stenosis suspected on US. (A) Indirect portogram shows the stenosis at the portal vein anastomosis (arrow). (B) Direct transhepatic portogram shows the stenosis and filling of collateral veins, and allows measurement of the trans-stenotic pressure gradient of 14 mmHg. (C) Angioplasty with a 10 mm balloon catheter. (D) Post-angioplasty portogram shows resolution of the stenosis and a reduction in the pressure gradient to 3 mmHg. (PVS = portal vein stenosis; US = ultrasound.)

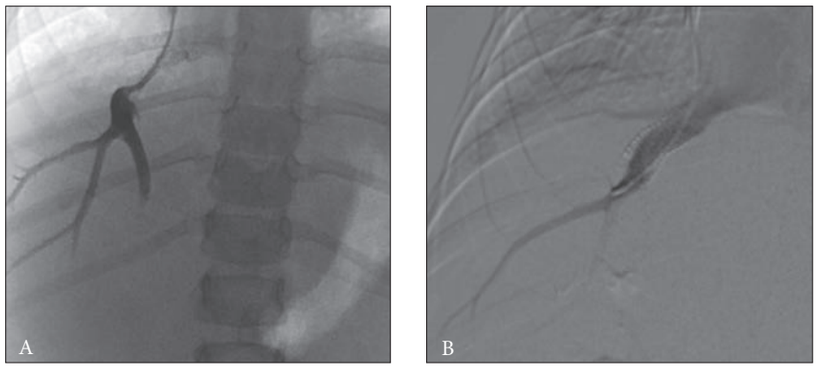

Fig. 5. Hepatic vein stenosis in a 6-year-old patient with a split liver transplant for treatment of biliary atresia. The patient had refractory ascites and abnormal Doppler US findings 1 year post transplant. (A) Hepatic venogram shows a severe anastomotic stenosis with a pressure gradient of 30 mmHg. There was poor response to multiple angioplasties with balloons up to 10 mm in diameter. (B) Because of the poor response to angioplasty, a 10 mm diameter metal stent was deployed across the anastomosis with good imaging and clinical results. (US = ultrasound.)

Aspiration of pleural effusions

Pleural effusions are common post transplant, occurring in 76% of patients, and most occur on the right. Approximately 40% of these effusions will persist for >7 days, and this is associated with an increased incidence of graft rejection.[15] When there are signs of sepsis or the effusion is large, the effusion is aspirated under US guidance and the fluid is sent for a microscopy, culture and sensitivity test. When there is rapid reaccumulation of pleural fluid or the fluid is clearly infected, a percutaneous pigtail catheter may be inserted and allowed to drain into a catheter bag.

Percutaneous drainage of collections

Post-transplant collections are common and can include postoperative perihepatic haematomas, bilomas and ascites. These collections are at risk of becoming septic, and often have a nonspecific presentation; a high index of suspicion for infection must be maintained.

Collections, haematomas and ascites are identified on US or CT, and vary from simple to gelatinous in consistency. If there is suspicion of infection or a significant mass effect, collections can be aspirated or a percutaneous pigtail catheter can be inserted. Both are usually done using a combination of US and fluoroscopic guidance, or with CT guidance alone.

Experience at the Wits Donald Gordon Medical Centre (WDGMC)

Since 2005, 60 paediatric liver transplants have been performed in 58 patients at the WDGMC. Only one patient received radiological vascular intervention, this being a PVS treated with angioplasty, later requiring re-angioplasty and placement of a metal stent.

In the 3-year period between April 2011 and April 2014, 25 transplants were performed on 24 patients, and 82 IR procedures were performed on these patients (an average of 3.3 IR procedures per transplant).

Five of the 24 patients (21%) had no IR procedures, and 19 of the 24 patients (79%) had one or more IR procedures (Table 1).

Conclusion

Liver transplantation is established as a very successful treatment of end-stage liver disease and several other metabolic diseases in children, but vascular and non-vascular complications may occur. An array of image-guided, minimally invasive techniques allow an interventional radiologist to treat many of these complications, improving graft and patient survival and reducing the rate of surgical revision and retransplantation.

Acknowledgements. Case courtesy of Dr C Sanyika: Fig. 2. Cases courtesy of Miraglia R, Maruzzelli L, Caruso S, *et al.* Interventional radiology procedures in pediatric patients with complications after liver transplantation. Radiographics 2009;29(2):567-584: Figs 3, 4 and 5.

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