A REVIEW OF THE IMAGING AND INTERVENTION OF LIVER TRANSPLANT COMPLICATIONS

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Liver transplantation has become a successful surgical solution to a variety of medical and oncological parenchymal liver diseases. As a result, these patients are being encountered more frequently within diagnostic imaging departments which may be remote from the transplant centre. Radiologists must therefore be proficient in identifying normal post-transplant anatomy which involves the anastomosis of four structures between the donor and recipient, namely the hepatic artery, the main portal vein, the retro-hepatic inferior vena cava and the extra-hepatic bile ducts. A number of potential complications can arise involving any or all of these structures, which can be potentially devastating and lead to graft failure. Radiologists must familiarise themselves with the normal post-operative appearances of liver transplantation and become competent in diagnosing post-transplant complications. Where possible, complications should be treated using interventional radiological techniques, thus avoiding the need for repeat surgical intervention or retransplantation.

Key-word: Liver, transplantation.

Since the first liver transplant was performed in Colorado in 1963, advances in surgical techniques, perioperative and postoperative care, and immunosuppression have made this procedure a successful surgical solution to a wide range of medical and oncological parenchymal liver diseases. As transplantation has become widely available, organ supply has become the major limiting factor, although transplant research continues to extend boundaries to combat this through initiatives such as split-liver transplanting and living lobe donation. Such progress has resulted in transplant patients being frequently encountered in the hospital system, and in particular, within diagnostic imaging departments which may be remote from the transplant centre. Therefore radiologists must become proficient in identifying both the normal post-transplant anatomy and potential associated complications.

Complications of liver transplant may be classified into mechanical and nonmechanical. Nonmechanical complications include graft rejection, disease recurrence and complications of immunosuppression, with imaging playing a limited role in the investigation of these complications. Mechanical complications refer to technical problems involving anastomotic structures. Liver transplantation surgery involves the anastomosis of four anatomical structures between the donor and recipient, namely arterial (hepatic artery) anastomosis, venous inflow (portal vein) anastomosis, venous outflow (hepatic vein and inferior vena cava) anastomosis, and biliary anastomosis. A number of complications can arise involving any of these structures leading to graft failure, and radiology thus plays a crucial role in the diagnosis and potential treatment of these complications.

Non-invasive imaging of liver transplant

Non-invasive imaging of the post-transplant liver is performed using ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI). Ultrasound utilising both grey-scale assessment of the liver parenchyma and biliary tree and Doppler evaluation of hepatic and portal vasculature, is an ideal initial screening tool. Its widespread availability and ease of use, in addition to its lack of ionizing radiation make it an ideal imaging modality for use in these patients. Furthermore, it offers real-time imaging and can be performed peroperatively or at the bedside post-operatively. The quality of the images depends on patient size, available windows, and operator experience. For optimal views a curved transducer is used and transabdominal, subcostal and intercostal windows are scanned (1). The normal hepatic artery waveform on Doppler US shows a rapid systolic upstroke with continuous diastolic flow (Fig. 1). The normal portal vein Doppler waveform is a continuous flow pattern towards the liver with mild respiratory induced velocity variations (2).

In cases where ultrasound images are suboptimal or inconclusive, further imaging using CT or MRI may be warranted. Multidetector CT (MDCT) has diffused rapidly into clinical imaging practice in recent years and compared with single-detector scanners, it allows faster image acquisition and multiplanar and 3D reconstruction. Imaging uses both the vascular and parenchymal phases of contrast material enhancement to provide a combined angiographic and organ-directed study (3). MR imaging including MR cholangiopancreatography (MRCP) and MR angiography also provide a comprehensive evaluation of the transplant-ed liver including its vascular structures and bile ducts. An important consideration is the relatively low toxicity of its contrast agents and the lack of associated radiation exposure. Invasive procedures such as conventional angiographic and cholangiographic studies are now generally reserved for nonsurgical treatment of certain complications.

The transplant hepatic artery

Vascular mechanical complications occur most frequently in the transplanted hepatic artery and may be divided into steno-occlusive and nonocclusive. Steno-occlusive is a collective term describing arterial obstruction including hepatic artery thrombosis, stenosis and kinking.
angiography if thrombolysis is followed by formal hepatic artery vascular patency and parenchyma angiography may be used to evaluate flow. Newer techniques such as CT angiography may be used to evaluate vascular patency and parenchyma followed by formal hepatic artery angiography if thrombolysis procedures are contemplated (Fig. 2). Treatment options include retransplantation or revascularisation via surgical exploration with thrombectomy or anastomotic revision, transcatheter thrombolysis or systemic anticoagulation. Transcatheter thrombolysis is controversial due to the high risk of intra-abdominal bleeding reported in the limited number of case studies on this procedure (8). The majority of patients will require retransplantation (5). If conservative management is employed radiological intervention can be used to treat secondary complications of ischaemia as they occur, namely biliary necrosis requiring percutaneous transhepatic cholangiography and liver parenchymal breakdown and abscess formation requiring percutaneous drainage.

Hepatic artery stenosis

Hepatic artery stenosis occurs in approximately 5% of liver transplants, most frequently at the anastomotic site (9). Causes include clamp injury, intimal injury due to perfusion catheters, or anastomotic ischaemia. It is classified based on the anatomical relationship to the anastomosis as proximal, anastomotic or distal (intra-hepatic or extra-hepatic). Digital subtraction angiography is the gold standard diagnostic modality (Fig. 3). Both Doppler US and multidetector CT angiography may also be used to accurately depict areas of hepatic artery stenosis.

The consequences of haemodynamically significant hepatic artery stenosis (>50% stenosis) are essentially identical to those of hepatic artery thrombosis. However, in contrast to hepatic artery stenosis, reestablishment of arterial flow is of value even in cases of established ischaemia. Treatment should be instigated before the onset of biliary necrosis. Treatment options include anticoagulation, surgical revascularisation and re-transplantation. Revascularisation techniques require a multidisciplinary approach including endovascular and open surgical management. First line interventional radiological procedures are used to treat amenable stenoses and percutaneous transluminal angioplasty can maintain hepatic arterial patency in 60-70% of cases. Access is obtained using a 6-7 Fr vascular sheath and 3000-5000 IU of Heparin are given prior to crossing the stenosis with a 0.014-0.035 inch guidewire (Fig. 4). Angioplasty is performed distal to proximal using a 4-6 mm balloon for adult patients and a 2-2.5 mm balloon for paediatric patients. The rate of intraprocedural complication occurrence is 7-10%, with more complex lesions, including kinked, tortuous, or multiple lesions, incurring an increased risk of complications and a higher failure rate (10, 11). Open surgical techniques are employed to treat technical failures or complications of endovascular techniques as well as treating complex lesions de novo.
Hepatic artery kinking

Hepatic artery kinking refers to an acute arterial bend of the hepatic artery (Fig. 5) and occurs in 0.4% of transplant recipients. It is generally due to redundancy of donor or recipient vessels, and infrequently occurs because of external compression from surgical drains. Treatment depends on the cause. If kinking is secondary to arterial redundancy, surgical revision is advised. Endoluminal management of hepatic artery kinking is largely inadvisable due to the high risk of arterial dissection or subsequent thrombosis (11).

Non-occlusive hepatic artery disease represents less than 5% of transplant artery complications. Examples include hepatic artery pseudoaneurysms and arteriovenous fistulae, and also non-occlusive diminished flow and arterial rupture.

Hepatic artery pseudoaneurysm

Hepatic artery pseudoaneurysm formation occurs in 0.4% of patients post liver transplantation. They are classified as either intra-hepatic (30%) (Fig. 6) or extra-hepatic (70%) (Fig. 7, 8) and are considered as distinct clinical entities. Intra-hepatic hepatic artery pseudoaneurysm formation typically affects the right lobe of the liver and is related to percutaneous biopsy procedures and drain placement. It is usually asymptomatic and has no association with hepatic artery thrombosis and is managed conservatively with either transcatheter embolisation or percutaneous thrombin injection. Embolisation techniques utilize a coaxial microcatheter. Coiling of the aneurysm sac or selective embolisation of the distal or proximal aspect of the involved arterial branch is undertaken. There is an increased incidence of atrophy or necrosis of the involved hepatic segment relative to native livers. Extra-hepatic hepatic artery pseudoaneurysm formation is related to the surgical anastomosis and is considered to be the same clinical entity as mycotic pseudoaneurysm formation (arteritis). In contrast to intra-hepatic
hepatic artery pseudoaneurysms, they are frequently symptomatic and may present with fever, gastrointestinal bleeding related to haemobilia and biliary obstruction and are frequently associated with the development of subhepatic collections. Extra-hepatic hepatic artery pseudoaneurysm formation is associated with hepatic artery thrombosis in up to 44% of cases.

**Arterial steal syndrome**

Arterial steal syndrome is a recently described complication of orthotopic liver transplantation characterized by arterial hypoperfusion of the graft resulting from a shift in blood flow into other arteries that originate from the same trunk. The pathogenesis of the steal is unknown. It is a separate entity to HAS and HAT; it causes hypoperfusion secondary to reduced blood flow through the hepatic artery rather than obstruction. It is thought to be an under-recognised cause of graft ischaemia. Most cases of steal are associated with the splenic artery. However, cases of gastroduodenal and left gastric steal syndrome have also been reported (12). Diagnosis can be made accurately using angiography and treatment options include embolisation of the ‘steal’ artery.

**The transplant portal vein**

Post-transplant portal venous complications, including stenosis and thrombosis, are relatively uncommon in comparison with arterial complications, yet they can be even more destructive (5). They occur more frequently in split liver and living related donor transplants. Stenosis usually occurs at the donor-recipient anastomosis and is most commonly seen in paediatric cases due to size mismatch between donor and recipient portal veins (13, 14). It most frequently occurs late following transplant (15). Most patients are asymptomatic, and are diagnosed on routine follow-up ultrasonography (Fig. 9). The diagnosis can also be made reliably using contrast enhanced CT (Fig. 10) or MRI. Patients with clinical evidence of portal hypertension require careful assessment to assess its significance. To measure portal venous pressure a right-sided percutaneous transhepatic approach is employed under ultrasound guidance and puncture of a second or third degree portal branch with a 22 guage needle.
is performed. The traditional management of portal vein stenosis has included reconstruction of the anastomosis, or retransplantation. However, percutaneous balloon angioplasty and tract embolisation has been shown to have a 71% patency at 24 months and improve survival in this population (13). Stent placement may be performed using a 10mm self-expanding stent in cases of residual or recurrent stenosis. The main complications that have been described with this procedure include haemoperitoneum and intrahepatic pseudoaneurysm (16).

Portal vein thrombosis has an incidence of 1-2% post liver transplant and most frequently occurs in the early post transplant period (5, 17). Presentation can be with elevated transaminases, with signs of portal hypertension or thrombosis can be detected incidentally on US (Fig. 11). Treatment options include retransplantation, systemic anticoagulation, transcatheter thrombolysis and port-systemic shunting. Several case reports have validated the safety and efficacy of transcatheter percutaneous balloon angioplasty and stent placement in recanalising the portal veins post OLT (18-20).

The transplant venous outflow tract

Venous outflow complications are relatively uncommon. Stenosis occurs more frequently in living donor and split liver transplants and hepatic vein stenosis occurs more commonly than inferior vena cava (IVC) stenosis (21). Hepatic vein stenosis may present with weight gain, ascites, hydrothorax, varices and may mimic portal hypertension. In the acute setting it generally arises from technical problems such as tight anastomosis, abnormal intimal flap or twisting of the veins. Stenosis presenting in delayed fashion is more likely to be secondary to perivascular fibrosis or intimal hyperplasia. Doppler ultrasound interrogation demonstrates decreased mean velocities in the hepatic veins and portal vein with accelerated flow and aliasing distal to the anastomosis and can be confirmed using venography. In one study of 26 patients suspected of having hepatic vein stenosis on Doppler ultrasound, only 20 (77%) had an abnormal gradient at subsequent venography (22). IVC stenosis occurs in <2% of liver transplants and usually occurs above the hepatic vein anastomosis, thus presenting in an identical fashion to hepatic vein stenosis. Isolated IVC stenosis below the hepatic veins is unusual and may present with lower limb oedema and ascites without hepatic dysfunction or hepatomegaly. CT with intravenous contrast can also accurately depict IVC stenosis post liver transplant (Fig. 12). Endovascular repair with balloon angioplasty or stent placement is safer than surgery and gives good results, although re-stenosis is frequent (22, 23). Angioplasty can be achieved via a transjugular, transfemoral, or direct transhepatic approach.

The transplant biliary tract

The most frequent mechanical complication of orthotopic liver transplantation occurs within the transplant biliary tract; strictures and bile leaks occur in 10-35% of transplant patients (24). The majority occur in the first six months post transplantation. Biliary strictures may occur at the anastomotic site secondary to scar tissue causing retraction and narrowing of the common bile duct at the suture site (Fig. 13). Bile duct strictures occurring secondary to ischaemia involve only the biliary tree of the graft, starting at the hilum and progressing to the intra-hepatic bile ducts. These nonanastomotic strictures are associated with prolonged allograft cold time (25). Methods of imaging the transplant biliary tract include ultrasound, T-tube cholangiography, MR cholangiography and invasive procedures such as endoscopic retrograde cholangio-pancreatography (ERCP) or percutaneous transhepatic cholangiography (PTC). Ultrasound is not the optimal imaging modality.
to investigate for biliary strictures as many liver transplants do not develop bile duct dilatation even in cases of high grade stenosis (26). MRCP has been shown to be a reliable technique for detecting post transplant biliary complications as it can provide information about the biliary tract that is nearly as diagnostic as that offered by invasive procedures (27). The majority of strictures can be managed by percutaneous dilatation (Fig. 14) with or without transhepatic biliary drainage. Bile leakage carries a significant morbidity and most commonly occurs at the site of T-tube placement. Small bile leaks may close spontaneously although surgical revision of the anastomosis is often necessary. Bile collections are easily visualised on ultrasound or CT (Fig. 15) and may be managed with percutaneous catheter placement and drainage.

**Post-transplant malignancy**

Liver transplant recipients are at increased risk of developing malignancy, especially non-Hodgkin’s lymphoma (Fig. 16) and squamous cell carcinoma and a high index of suspicion is necessary in evaluating these patients. Epstein Barr virus has been associated with post-transplantation lymphoproliferative disease in patients receiving cyclosporine therapy. In addition, recurrence of a primary malignancy e.g. hepatocellular carcinoma may occur in the transplanted liver.

**Conclusion**

Liver transplantation is a successful treatment for a variety of
parenchymal liver diseases. Advances in surgical technique, postoperative care and immunological therapy have decreased the previously high mortality and morbidity associated with the procedure, leading to an increase in the number of procedures performed. Radiologists play a vital role in the postoperative care of this patient group and must be familiar with both normal and abnormal transplant appearances in order to identify and treat associated complications. Where possible, complications should be treated using minimally invasive interventional radiological techniques, avoiding retransplantation, as these techniques are associated with a significantly lower mortality rate.

References