

# The role of imaging in liver transplantation

**Key words:** liver transplantation; pre-transplant assessment; post-transplant complications

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## Abstract

Liver transplantation is the accepted treatment for patients with irreversible hepatocellular failure and in selected patients with hepatocellular carcinoma. Survival rate has continued to improve as a result of careful patient selection, as well as improvements in graft preservation, surgical techniques and immunosuppression. Radiology is an essential part of a successful transplant programme; assessment of the transplant candidate, recognition of post-transplant complications, interventional treatment and follow-up of transplant recipients require accurate diagnostic imaging and interventional radiological input.

## Introduction

The first human liver transplant that resulted in prolonged survival was carried out by Starzl in 1967.<sup>1</sup> Since then, more than 50,000 liver transplants have been carried out worldwide. With careful patient selection, improved graft preservation and surgical techniques, as well as a better understanding of rejection and immunotherapy, the survival rate by 1993 was 83% at 1 year and 74% at 4 years.<sup>2</sup> Liver transplantation is now the accepted treatment for patients with irreversible hepatocellular failure and in selected patients with hepatocellular carcinomas (HCC). Transplantation is a dynamic field of innovative surgery where new radiological challenges in diagnosis and intervention continue to arise.

Progressive irreversible hepatocellular failure in established chronic liver disease is the most common indication for transplantation. Primary biliary cirrhosis, chronic active hepatitis, sclerosing cholangitis and alcoholic cirrhosis are the common causes in adults. In children, biliary atresia and metabolic disorders are the principal indications. Acute liver failure caused by viral or toxin-induced hepatitis provides the greatest challenge, as these patients are likely to have multi-organ failure. Increasing evidence suggests that with careful patient selection, liver transplantation is the treatment of choice in patients with small HCCs

or a small number of HCCs. In a recent study of 122 patients with single tumours <5 cm or less than three tumours  $\leq 3$  cm, the 5-year survival was 80%.<sup>3</sup>

A variety of transplant techniques have been developed depending on the indication for transplantation and the availability of whole, reduced, segmental, auxiliary, split or living donors. In auxiliary transplantation, part or the entire native liver is left in the recipient, so that it can be used in reversible acute liver failure where the graft provides temporary function (Figure 1).



Figure 1. Contrast-enhanced CT showing a fatty native left lobe and right

On recovery of the native liver with restoration of function, immunosuppression can be withdrawn, with subsequent atrophy of the graft. An auxiliary transplant can also be used in non-cirrhotic in-born errors of metabolism such as Crigler-Najjar syndrome. Split liver transplantation is the splitting of a whole liver into two grafts, the left lateral segment for a child (Figure 2) and the residual right lobe for an adult.



Figure 2. Contrast-enhanced CT of left lateral segment graft in a child.



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Living donor transplantation began with parents donating left lateral segments for their children, but now right lobe grafts are also used in the adult population. Living related liver transplantation increases the number of organs available for transplantation and allows surgery to be carried out on an elective basis.

### Pre-transplant imaging

The role of imaging in pre-transplant assessment is predominantly recognition of the sequelae of chronic liver disease or developmental anomalies that may alter the surgical approach or contra-indicate transplantation. Fifteen per cent of patients with end-stage cirrhosis have portal vein thrombosis,<sup>4</sup> and although this is no longer considered an absolute contra-indication to transplantation, it requires surgical modification. A venous conduit may be constructed from the junction of the splenic and superior mesenteric veins (SMV), which means that SMV patency must be assessed. In end-stage cirrhosis, colour Doppler ultrasound (CDUS) assessment of the portal vein may be difficult because of the high reflectivity of the cirrhotic liver, fatty change and slow flow in portal hypertension. Ultrasound contrast agents can be used to improve the colour and spectral Doppler signal, and if doubt remains, indirect portography or magnetic resonance (MR) portal venography is indicated. Biliary atresia, the most common indication for elective paediatric transplantation, may be associated with other developmental anomalies including situs inversus, portal hypoplasia, polysplenia and caval interruption; such features may require surgical modification.

Accurate radiological staging in defining suitable candidates with HCC for transplantation is of the utmost importance. The rate of recurrence is influenced by:

- tumour size and number
- histological type and differentiation
- the presence of vascular and lymph-node involvement.

Magnetic resonance imaging (MRI) with a hepatocyte-specific contrast agent is more sensitive than computerised tomography (CT) in detecting small HCC, although CT remains more sensitive in detecting extra-hepatic disease.

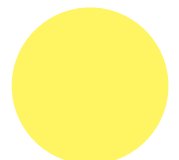
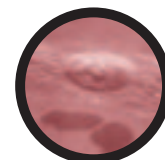
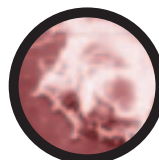
In living donor transplantation, pre-operative evaluation of the donor includes: MRI to detect focal liver lesions; accurate determination of liver volume, which is crucial to ensure adequate post-operative liver function for both donor and recipient; and MR cholangiography and digital subtracted angiography to demonstrate biliary and vascular anatomy for surgical planning.<sup>5</sup> In acute liver failure, radiology plays a limited role and is mainly used in diagnosing non-hepatic sequelae of cardiorespiratory, renal and in particular intracerebral complications that may present a neurological contraindication to transplantation.

### Intra-operative imaging

Intra-operative ultrasound is used to identify a plane for resection 1 cm lateral to the middle hepatic vein during donor right hepatectomy for living donor transplantation.

### Post-operative imaging

Post-operative imaging has two main functions: to document regeneration of liver volume in auxiliary and living donor transplantation, which can be performed using CT and MR; and to assess patients with suspected complications, for which a variety of techniques can be used. Early recognition and treatment of complications results in improved graft survival. In the early post-operative period, poor graft function is usually the result of one of four causes: primary graft non-function, sepsis, vascular insufficiency or acute rejection.



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The main contribution of radiology at this stage is confirming the integrity of the vascular anastomoses.

## Hepatic artery

Hepatic artery thrombosis is the most common vascular complication, reported in 5% of adult and 9–18% of paediatric transplants.<sup>6,7</sup> In addition, despite an increase in portal venous flow in the immediate post-operative period, the reciprocity of flow between the portal vein and hepatic artery can diminish – and surgery can also disrupt – collateral arterial pathways.

Correct interpretation of the imaging (or radiological) findings depends on the knowledge of the surgical technique used. When the donor hepatic arterial anatomy conventionally arises from the coeliac axis, an end-to-end anastomosis with the recipient hepatic artery is used. If the arterial supply is partially or completely from the superior mesenteric artery (SMA), bench re-fashioning of the vasculature is required to effect a single hepatic artery for anastomosis. An infra-renal arterial conduit using the iliac artery of the donor is usually constructed where segmental grafts are implanted (Figure 3).

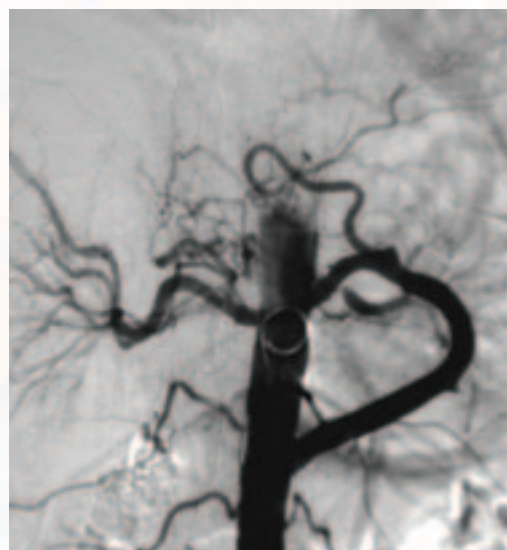


Figure 3. Flush aortogram demonstrating a patent infra-renal conduit with an incidental finding of left renal artery stenosis.

Colour Doppler ultrasound is >90% sensitive and up to 100% specific for hepatic artery patency.<sup>8</sup> Failure to demonstrate an arterial signal in the early post-operative period is an indication for arteriography (Figure 4).



Figure 4. Selective coeliac arteriogram showing hepatic artery thrombosis at the site of the anastomosis.

Early surgical re-vascularisation may rescue the graft, obviating the need for re-transplantation. The degree of parenchymal ischaemia can be assessed with contrast-enhanced CT. In children, neovascularisation can occur with collaterals forming from the SMA and splenic artery, which may develop and protect the graft from ischaemic complications. Delayed presentation of hepatic artery thrombosis with biliary strictures, leaks and recurrent sepsis usually requires re-transplantation despite stenting and drainage procedures.

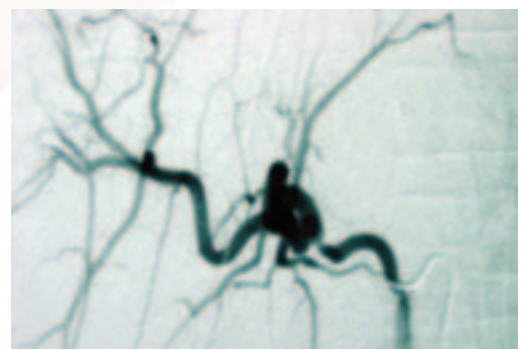
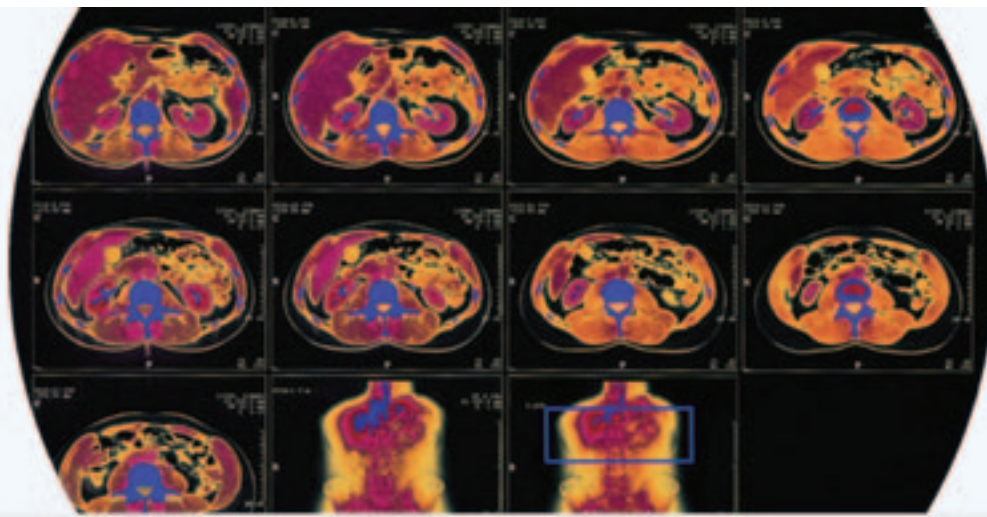


Figure 5. Selective hepatic arteriogram demonstrating a stenosis at the anastomosis.

Hepatic artery stenosis is less common and typically occurs at the surgical anastomosis. Stenosis can be



inferred on CDUS if the systolic acceleration time is  $>0.08$  seconds and the resistive index is  $<50\%$ .<sup>9</sup> The finding is confirmed with angiography (Figure 5).

Angioplasty may be successful in reversing or arresting the effects of ongoing graft ischaemia.<sup>10-13</sup>

Mycotic aneurysms occurring at sites of vascular anastomoses are rare, but rupture carries a high mortality. Intrahepatic aneurysms may develop following biopsy or as a result of mycotic emboli – they are usually asymptomatic and can be treated with coil embolisation. However, surgical excision of the infected component of intra-hepatic aneurysms is usually required.

#### **Portal vein**

Portal vein thrombosis after liver transplantation is uncommon, and occurs in  $<2\%$  of recipients.<sup>14</sup> In addition, portal hypertension is immediately relieved by liver transplantation. Variceal bleeding, ascites and interstitial oedema in the post-operative period indicate hindered portal venous flow, either by stenosis or thrombosis (Figure 6).

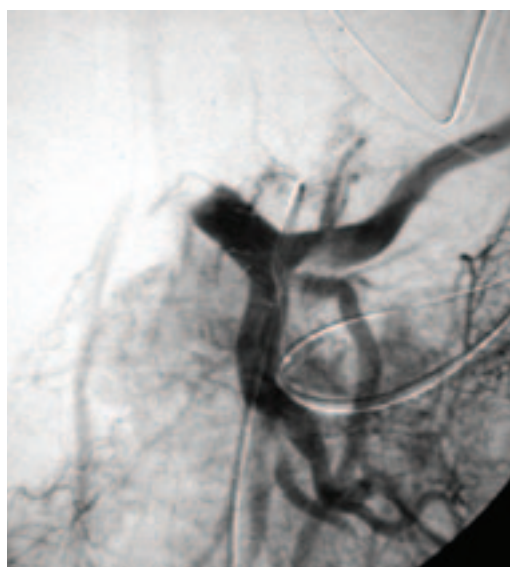


Figure 6. Venous phase of a selective superior mesenteric angiogram showing portal vein thrombosis.

Predisposing factors include:

- pre-existing thrombosis
- hypoplasia
- previous shunt surgery
- pro-thrombotic disorders.

If adequate collateralisation occurs, with development of a cavernoma and reduction of portal pressure, the graft survival may be unaffected. Stenosis of the portal vein is rare and is confirmed by portal pressure studies to determine the transanastomotic gradient; transplant portal venoplasty or stent insertion can be carried out<sup>15,16</sup> – long-term results indicate these to be a curative procedures.

#### **Inferior vena cava**

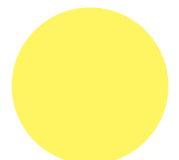
Occlusion or stenosis of the inferior caval anastomosis is rare and occurs in  $<1\%$  of recipients. Supra-hepatic caval stenosis results in hepatic venous outflow obstruction and presents as the Budd-Chiari syndrome, while infra-hepatic caval stenosis presents with peripheral oedema. Inferior venocavography with pressure studies is used to confirm the haemodynamic significance. As caval strictures are fibrotic, they may recur following venoplasty or stent insertion.

#### **Biliary tract**

Bile duct complications are an important cause of post-surgical morbidity and mortality. Three types of anastomosis exist: the duct-to-duct and Roux loop hepatico-jejunostomy types have earlier presentations than the now outdated stone-forming gallbladder conduit. The method of anastomosis, cold, ischaemia time and associated vascular insufficiency are factors that critically influence the frequency, development and type of complications.

Presenting features include:

- cholestasis
- cholangitis
- non-specific biochemical graft dysfunction
- biliary peritonitis from a leak.



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Sonographic findings may be misleading as biliary dilatation within the graft is a variable feature. More commonly, a high pressure/low volume biliary system develops proximal to the stricture. Magnetic resonance cholangiography is the investigation of choice, reserving the more invasive endoscopic and percutaneous cholangiography for when intervention is required.

An anastomotic stricture can be treated with dilatation and temporary stenting, or surgical reconstruction depending on the individual patient and the presence of other complications. The development of non-anastomotic strictures carries a worse complication as these represent a diffuse biliary injury with hepatic artery thrombosis (Figure 7), with prolonged ischaemia and ABO incompatibility as antecedent factors.

## **Rejection**

Acute rejection is cell mediated and characterised by lymphocytic infiltration. It is common in the early post-operative period and is usually successfully treated by manipulation of immunosuppression. Radiological findings are non-specific, and may include increased hepatic artery resistance on CDUS and periportal parenchymal changes on CT – the diagnosis is made on histological grounds. Chronic rejection is a process that is characterised histologically by arteriolar occlusive lesions and obliteration of bile ducts. It does not respond to alterations in immunosuppression and re-transplantation is the long-term treatment.

## **Malignancy**

Organ transplant recipients are at increased risk for the development of malignancy, at least in part caused by immunosuppression therapy. Four-to-five per cent of liver transplant recipients develop malignant tumours, and half of these develop post-transplant lymphoproliferative disorder (PTLD).<sup>17</sup> Liver transplant recipients have a four-fold increase in the incidence of lymphoma compared with the general population;<sup>18</sup> the majority of which are non-Hodgkin's lymphoma (NHL), mostly of the B-cell type related to Epstein-Barr virus infection. Post-transplant lymphoproliferative disorder can be polyclonal or monoclonal; the former responds to a reduction in immunosuppression while the latter requires chemotherapy. Most commonly, PTLD involves the lymph nodes, followed by the small bowel, the transplant graft, pulmonary nodules and the periventricular white matter. Skin malignancies (basal and squamous cell) are the most common sporadic malignancies.<sup>19</sup> Recipients with a history of long-standing inflammatory bowel disease and primary sclerosing cholangitis, appear to be at a higher risk of developing colorectal neoplasm.<sup>20</sup>

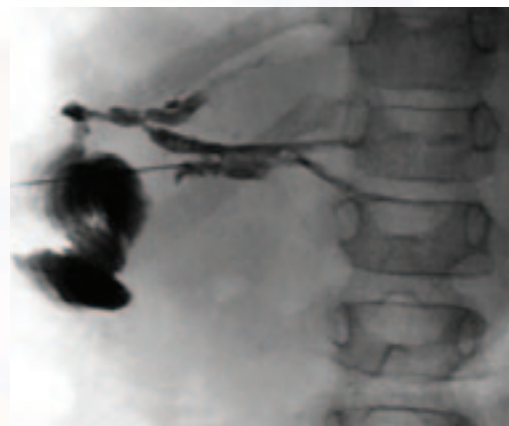


Figure 7. Percutaneous transhepatic cholangiogram showing non-anastomotic biliary strictures secondary to hepatic artery thrombosis.

Intraductal stones are a further complication with secondary septic cholangitis further damaging the biliary epithelium. Bile leaks from an anastomotic leak or resection margin of a reduced graft present with biliary peritonitis. Aspiration can be carried out under ultrasound or CT guidance. Direct cholangiography should be performed to demonstrate the site of the leak, and should be followed by stenting.



### Infection

The risk of infection by viral, fungal and bacterial agents is increased in transplant recipients as a result of immunosuppression. Improved antibiotics have decreased morbidity and mortality caused by bacterial infections, but the risk of opportunistic infections has increased. Cytomegalovirus (CMV) has become a major source of complications as the virus itself can induce immunosuppression, producing a flu-like illness at one end of the spectrum to myocarditis, pancreatitis and intestinal ulceration with fatal results at the other extreme. Transplant recipients who lack antibodies to CMV, receiving a graft from a CMV-positive donor, are at particular risk. Recurrent hepatitis B and C infections are also major sources of morbidity and mortality.

### Conclusions

Improved surgical and medical techniques have decreased the percentage of post-transplant complications. However, with an ever-increasing number of transplants carried out every year, the follow-up population is steadily growing. The radiologist needs to be aware of new surgical techniques, which present challenges for the imaging of and interventions for patients undergoing liver transplantation.

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