89 Liver transplantation

- USEFUL WEBSITES IN LIVER TRANSPLANTATION
- Vascular complications

Auxiliary liver transplantation

Auxiliary liver transplantation

Auxiliary LT involves implanting a healthy liver graft placed either heterotopically or orthotopically while leaving all or part of the native liver intact. Auxiliary heterotopic LT , where the graft is implanted below the native liver, was proposed as an alternative to orthotopic LT in the early era of transplantation when recipient hepatectomy was associated with massive blood loss and transfusion requirements. But the technique was marred with failures due to the heterotopic position of the graft resulting in poor venous drainage. More recently there has been a renewed interest in auxiliary LT for ALF and certain metabolic liver diseases. To overcome the previous technical di ffi culties, the procedure is now performed with a ient partial hepatectomy to create space for the graft (Figure 89.6). The procedure is therefore termed auxiliary partial orthotopic liver transplantation (APOLT). It is a technically - /uni25CF /uni25CF /uni25CF /uni25CF - /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF

Figure 89.6 Right lobe auxiliary partial orthotopic liver transplantation (APOLT) for acute liver failure due to yellow phosphorus poisoning. (a) Recipient left lateral section of the liver looking pale and fatty owing to yellow phosphorus poisoning; right lobe graft from the donor /uni00A0 implanted into the orthotopic position. (b) Hepatobiliary iminodiacetic acid (HIDA) scans done over the /f_i rst year after transplant in a left lobe APOLT. The scans show regression of the left lobe auxiliary graft and functioning native liver. TABLE 89.2 Extended criteria donors in liver transplantation. Type of extended criteria donor Primary risk to the recipient Advanced donor age Delayed graft function Macrovesicular steatosis Delayed graft function Donation after circulatory death Biliary complication organs Organ dysfunction at Delayed graft function, procurement: primary non-function ICU stay >7 days Hypernatraemia >165 /uni00A0 mmol/L Bilirubin >51 /uni00A0 µmol/L Elevated liver enzymes (AST, ALT) Vasopressor use Cause of death: anoxia, Delayed graft function, biliary cerebrovascular accident complication Disease transmission: Infectious risk Hepatitis B core antibody- positive donor Hepatitis B surface antigen- positive donor Hepatitis C virus-positive donor HIV-positive donor High-risk history (active drug abuser, etc.) Extrahepatic malignancy Delayed graft function, Cold ischaemia time >12 hours primary non-function (long storage of organ after procurement) ALT, alanine aminotransferase; AST, aspartate aminotransferase; HIV, human immunode /f_i ciency virus; ICU, intensive care unit.

native liver regeneration in ALF . The most important benefit of APOLT is the potential for immunosuppression withdrawal when the native liver fully regenerates, although outcomes have been suboptimal in less experienced hands. In metabolic liver diseases in children, APOLT is performed with the intention of keeping part of the native liver for future gene therapy .

Biliary complications

Biliary complications

The biliary complications usually present as bile leak, biliary anastomotic stricture (AS), biliary non-anastomotic stricture (NAS), bile duct sludge/stone/casts, biloma and duct loss (ductopenia) in patients with chronic rejection. Biliary compli - split LT cations following LT can be caused by the vulnerable vascular supply to the biliary tree (supplied by hepatic artery alone), the biliary epithelium being more liable to ischaemic injury than hepatocytes, suboptimal preserv ation of the peribiliary plexus - Summary box 89.6 - Complications after L T /uni25CF - /uni25CF /uni25CF /uni25CF - /uni25CF

Early complications (within 6 months) Graft Primary non-function Delayed graft function Surgical Bleeding Hepatic artery thrombosis Portal vein thrombosis Hepatic venous out /f_l ow obstruction Bile leak Biliary anastomotic stricture Medical Infections (bacterial, viral, fungal) Rejections Acute kidney injury Late complications (after 6 months) Graft Ischaemic cholangiopathy (non-anastomotic biliary strictures) Surgical Vascular stenosis (hepatic artery, portal vein or hepatic vein) Late HAT Biliary AS Incisional hernia Medical Infections (bacterial, viral, fungal) Rejections/chronic rejection leading to graft failure Renal impairment Disease recurrence Cardiovascular disease Metabolic and bone diseases Malignancy

sion injury . The incidence of biliary complications is higher in LDLT and other anatomical variant grafts than in whole-graft LT . T his is because of the small size of the ducts, multiple duct anastomoses and also cut surface leaks. Due to the morbidity involved with biliary complications, bile duct anastomosis is considered the Achilles’ heel of LT . The management of bile leaks usually involves bile duct reconstruction with Roux-en-Y hepaticojejunostomy in the immediate post-transplant period or endoscopic decompression of the bile duct and percuta neous drain insertion. For AS, the management involves endoscopic dilatation, stent insertion or surgical revision. The NAS or ischaemic-type biliary lesions (ITBL) are the most severe form of biliar y strictures, where there is widespread desquamation of biliary epithelial cells with formation of biliary casts, multiple segmental stenosis and a picture similar to PSC. This can happen within a few weeks, months or years after transplantation and the incidence is 25–30% with DCD grafts but is less common in DBD grafts. The management will include imaging to rule out HAT or stenosis, dilatation of dominant strictures, ursodeoxycholic acid to increase bile flow and lower the lithogenicity and antibiotic maintenance therapy to prevent recurrent episodes of cholangitis. Eventually most patients will require retransplantation.

CAUSES OF ALLOGRAFT DYSFUNCTION

CAUSES OF ALLOGRAFT DYSFUNCTION

Liver graft dysfunction can happen any time after transplanta tion; if not identified early and treated promptly , it can lead to graft loss. The most common presentation is an asymptomatic elevation of liver enzyme levels . Early after LT , acute cellular rejection is the most common cause of graft dysfunction and is usually treated by increasing the dose of immunosuppression, which includes pulsed-steroid therapy for 3 days or more depending on the degree of rejection. The other common reasons for graft dysfunction are the vascular complications, bile leak or bile duct obstruction, post-transplant infections and drug toxicity . Even if rejection is suspected, it is important to rule out any vascular or biliary complications by perform ing a Doppler ultrasound scan and, if there is any doubt, a contrast-enhanced CT scan. Liver biopsy is usually performed through a percutaneous route, but a coagulopathic patient might need transjugular liv er biopsy . LT patients are followed up more frequently in the first 3 months after transplant, as this is the time when presentation with graft-related issues is most common and also when mon itoring and optimisation of immunosuppression ar e crucial. The follow-up protocol varies between LT centres, but mostly includes once a week for the first 6 weeks after transplant and then once a f ortnight for another 6 weeks, before reducing the frequency of appointment. Late graft dysfunction is usually due to acute/chronic rejection, vascular issues such as hepatic artery stenosis or venous outflow obstruction, biliary obstruc tion, recurrence of primary disease such as hepatitis C (rare nowadays owing to viral clearance prior to transplant), auto immune diseases or NAFLD, and other opportunistic infec tions suc h as CMV or herpes simplex hepatitis.

CHALLENGES AND POTENTIAL FUTURE DEVELOPMENTS IN LI

CHALLENGES AND POTENTIAL FUTURE DEVELOPMENTS IN LIVER

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Domino liver transplantation

Domino liver transplantation

Domino LT involves transplanting a liver from a patient with metabolic disease who needs LT into a patient with end-stage liver disease with the expectation that the recipient will not develop the metabolic syndrome or the recurrent syndrome will have minimal e ff ect. Several hereditary metabolic diseases such as familial amyloid polyneuropathy (FAP), maple syrup urine disease and familial hypercholesterolaemia are caused by aberrant or deficient protein production in the liver, and these conditions can be cured with an orthotopic LT . Although their native livers eventually caused severe systemic disease in these patients, these livers are otherwise structurally and functionally normal, and hence used as domino into those with end-stage liver failure. A typical example of domino LT is the use of a liver from a patient with FAP to a patient who is outside transplant criteria for liver malignancy . Even if they develop amyloidosis, it would take 10–20 years for the disease to become symptomatic in these recipients. If they have no recurrence of tumour and become symptomatic from FAP in the future they can be o ff ered a retransplant without the risk of recurrence of malignancy .

FURTHER READING

FURTHER READING

Busuttil R, Klinymalm G (eds). Transplantation of the liver , 3rd edn. Philadelphia, PA: Elsevier-Saunders, 2015. Clavien P , Trotter J (eds). Medical care of the liver transplant patient, edn. Oxford: Wiley-Blackwell, 2012. Croome K, Muiesan P , Taner B (eds). Donation after circulatory death (DCD) liver transplantation: a practical guide . Springer, 2020. Fan ST (ed.). Living donor liver transplantation, 2nd edn. Singapore: World Scientific, 2011. Hadzic N, Baumann U, McLin V . Pediatric liver transplantation: a clinical guide . Philadelphia, PA: Elsevier, 2021. Hricik D (ed.). Primer on transplantation, 3rd edn. Oxford: Wiley- Blackwell, 2011. Garden OJ, Parks RW , Wigmore SJ (eds). Principles and practice of surgery, 8th edn. Elsevier, 2022. Oniscu G, Forsythe J, Fung J (eds) . Abdominal organ retrieval and transplantation bench surgery . Oxford: Wiley-Blackwell, 2013. Sutcli ff e R, Antoniades C, Deshpande R et al . Liver and pancreatobiliary surgery: with liver transplantation. Oxford: Oxford University Press, 2009. Definitions /uni25CF /uni25CF /uni25CF - /uni25CF /uni25CF /uni25CF /uni25CF - /uni25CF /uni25CF

Acute liver failure: complex multisystem illness that evolves quickly after a catastrophic insult to the liver, leading to coagulopathy and encephalopathy; based on onset of encephalopathy – hyperacute (within 7 days), acute (8–28 days), subacute (>28 days) Allograft: an organ or tissue transplanted from one individual to another Chronic liver disease: progressive deterioration of liver functions for more than 6 months, with in /f_l ammation, destruction and regeneration of liver parenchyma, leading to /f_i brosis and cirrhosis Heterotopic graft: a graft placed in a site different from that where the organ is normally located HLA: human leukocyte antigen, the main trigger to graft rejection MELD score: model for end-stage liver disease score; predicts prognosis in patients with chronic liver disease and is used to allocate liver for transplant NAFLD: non-alcoholic fatty liver disease; associated with metabolic syndrome (obesity, hyperlipidaemia and diabetes mellitus). Some patients develop non-alcoholic steatohepatitis (NASH), which leads to /f_i brosis and cirrhosis Orthotopic graft: a graft placed in its normal anatomical site UKELD score: United Kingdom model for end-stage liver disease score; predicts survival of patients listed for LT in the UK

Haemorrhage

Haemorrhage

Portal hypertension and coagulopathy of CLD are important causes of bleeding that are unique to LT procedures. A study of more than 12 /uni00A0 000 LTs showed 12.5% needing re-explorations during the same hospitalisation, of which 68% were for bleeding. Meticulous haemostasis during the transplantation operation is important in order to minimise the risk of early haemorrhage. Excessive haemorrhage is also common if the graft has sustained a severe reperfusion injury or if a marginal graft is used and the early graft function is poor. Ex situ can also have a high blood loss from the cut surface of the liver. This is not the case in in situ split LT and LDLT partial grafts where haemostasis is secured during the donor operation. It is standard practice to place two large drains behind the right and left lobes of the liver to monitor for bleeding and bile leak. It may be necessary , occasionally , to pack the peritrans plant ar ea for 24–48 hours to achieve adequate haemostasis when there is di ff use oozing despite correction of coagulopa thy . Evacuation of an extensive perihepatic haema toma may be required to avoid secondary infection.

IMMEDIATE POST-TRANSPLANT CARE

IMMEDIATE POST-TRANSPLANT CARE

Following LT , patients are monitored in an intensive care unit (ICU) and maintained on a ventilator, usually for less than 24 hours. If haemodynamically stable and awake with good early liver graft function and renal function they are extubated. Spontaneous correction of lactic acidosis and correction of coagulopathy (falling international normalised ratio [INR]) and low serum transaminases are indicators of good early graft function. A Doppler ultrasound is also performed prior to extubation to assess the patency of blood supply to the liver. Most patients with an uncomplicated postoperative course get moved to the high-dependency unit or ward after 2 days. During the ICU stay , there is close management of fluid and electrolytes, which could be significantly abnormal as a result of the prolonged operation and massive fluid shifts. Following transfer to the transplant wards, the patient is closely monitored by the transplant surgical and medical - (hepatology) team, as well as by pharmacists, nutritionists and physiotherapists. The liver and kidney function, the coagu - lation parameters and full blood count are monitored daily . Doppler ultrasound scans are performed at regular intervals to ensure that the blood vessels are patent and there are no other abnormalities. Dosages of immunosuppressive agents are adjusted according to blood levels and organ function during this period. Antibacterial, antiviral and antifungal prophylaxis are given to prevent infections, including those from opportunistic organisms, such as cytomegalovirus (CMV) and Pneumocystis carinii . Factors determining graft function after L T /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF

Donor characteristics Advanced donor age DCD donors Steatotic livers Small graft size in LDLT (‘small for size syndrome’) Procurement-related factors Warm ischaemic time Type of preservation solution Cold ischaemic time Recipient-related factor High MELD or UKELD score Severe portal hypertension Technical factors relating to implantation Haemodynamic and metabolic stability Massive transfusion of blood and blood-related products Immunological factors

IMMUNOSUPPRESSION FOLLOWING LIVER TRANSPLANTATION

IMMUNOSUPPRESSION FOLLOWING LIVER TRANSPLANTATION

Liver is considered to be an ‘immunoregulatory’ solid organ with specialised venous endothelial turnover, a high number of extramedullary haematopoietic stem cells and the ability to produce numerous immunoregulatory substances. The privileged state of liver in transplantation is highlighted by the relatively lower need for human leukocyte antigen (HLA) or blood-group matching. Compared with other organs, such as kidneys and lungs, the liver allograft has the advantage of demonstrating lower rates of acute and chronic rejection, a resistance to antibody-mediated rejection and a higher /uni25CF /uni25CF /uni25CF /uni25CF Harvey Williams Cushing , 1869–1939, Professor of Surgery , Harvard University Medical School, Boston, MA, USA. agents such as antithymocyte globulin (ATG), CD25 mono - clonal antibodies (basiliximab and daclizumab) or cluster of di ff erentiation (CD)52 monoclonal antibodies (alemtuzumab; Campath-1H), w hich routinely form part of kidney , pancreas and other organ transplants, are rarely used in L T . They are only considered in selected patients with a high immunolog - ical risk or renal compromise, in the latter case to delay the introduction of calcineurin inhibitors (CNIs). CNIs (tacrolimus and ciclosporin) are the mainstay of LT maintenance immuno - suppression, with mycophenolate mofetil (MMF), azathioprine and corticosteroids consider ed as the essential adjuncts to CNIs (Table 89.3). Mammalian target of rapamycin inhibitors (mTORi) such as sirolimus and everolim us have established roles in patients with worsening renal function and in those with LT for HCCs and incidental cancers on explant. The side e ff ects of prolonged immunosuppression are one of the limitations of long-term survival among LT recipients, espe - cially those due to immunosuppression-induced metabolic syndrome, cardiovascular disease, renal impairment and malignancy . Several studies have shown tha t 20% of LT patients can achieve operational tolerance, whereby there is long-term survival of the allograft in the absence of immunosuppression. However, there is a need for more research to understand this better and to identify the group of patients who will benefit from withdrawal of immunosuppression.

TABLE 89.3 Common immunosuppression medications after liver transplant. Drug Mechanism of action Calcineurin inhibitors Inhibit T-cell signalling, prevent (tacrolimus, ciclosporin) lymphocyte activation and block cytokine transcription Mycophenolate mofetil Inhibits T-cell and B-cell proliferation Azathioprine Purine analogue, impedes DNA and RNA synthesis Corticosteroids Decrease cytokine production Decrease lymphocyte activation and proliferation Decrease antibody production Decrease phagocytosis and release of proteolytic enzymes mTORi

(sirolimus/everolimus) Mammalian target of rapamycin inhibitor

INDICATIONS AND PATIENT SELECTION

INDICATIONS AND PATIENT SELECTION

The indications for liver transplantation (LT) fall into four groups: 1 chronic liver disease (CLD); 2 acute liver failure (ALF); 3 metabolic liver disease (including liver-based inborn errors of metabolism); 4 primary hepatic malignancy (hepatocellular carcinoma [HCC], hepatoblastoma). The most common indication for LT is decompensated CLD (Table 89.1). In adults the most common causes are alco holic liver disease, non-alcoholic fa tty liver disease (NAFLD), chronic viral hepatitis (hepatitis B virus [HBV] and hepatitis C virus [HCV]), autoimmune liver diseases (primary biliary cirrhosis, primary sclerosing cholangitis , autoimmune hep atitis and overlap syndromes) and cirrhotic metabolic liver diseases (Wilson's disease). The specific frequencies of these aetiologies depend on geographical variations. In the last tw decades hepatitis-related CLD (HBV and HCV) was the most common indication for LT . However, with universal vaccina tion for HBV and newer treatment options for HCV and with increasing obesity in a ffl uent countries, NAFLD is projected to become the most common indication for LT in the future. In children, who account for around 10–15% of all LTs, bili ary atresia is the most common indication for transplantation. ALF requiring transplantation on an urgent basis accounts for approximately 10% of LT activity and is usually drug induced or viral (e .g. paracetamol overdose in the UK). There are a variety of non-cirrhotic metabolic diseases for which trans plantation o ff ers the prospect of cure, including urea cycle Samuel Alexander Kinnier Wilson , 1878–1937, Professor of Neurology at King's College Hospital, London, UK. He described hepatolenticular degeneration in his gold medal winning MD dissertation of 1912 titled 'Progressive lenticular degeneration', which led the disease to be named after him as Wilson's disease. defect, oxalosis and familial hypercholesterolaemia. Primary hepatic malignancy is more common in patients with cirrhosis, especially viral-induced liver disease and NAFLD, and may be best treated by transplantation when advanced liver disease precludes liver resection because of the risk of postoperative liver failure or when the tumour is multifocal as a result of field changes in the cirrhotic liver that predispose to recurrence or further primary malignancies. LTs are usually performed between ABO blood group-compatible donor–recipient pairs. Histocompatibility matching, as in kidney transplantation, has not been neces - sary in LT as the liver is consider ed a more immunologically privileged organ. In countries where living donor liver trans - - plantations (LDLTs) are performed in large numbers because of a lack of deceased donor or gans, there has been a recent increase in the number of ABO-incompatible LT s when there is no blood group-compatible donor available. However, there - is an increased risk of infection owing to a higher immunosup - pression protocol and a higher incidence of antibody-mediated rejection with this type of transplantation. o Potential candidates undergo a comprehensive multi - disciplinary assessment, including hepatologists, transplant sur - - geons, anaesthetists, specialist n urses in LT , drug and alcohol rehabilitation services, dietician, psychologists and specialists from other clinical disciplines where indicated. Thr ee under - lying

principles dictate which patients should be referred for, - and potentially undergo, LT . First, the recipient should have irreversible liver disease (acute or chronic) tha t is expected to be fatal without transplantation. Second, the patient should have su ffi cient reserve to survive the operative and periopera - tive period. Finally , the candidate should be expected to have - significant survival (>50% at 5 years) and quality of life benefit from LT .

The complications after liver transplantation • Living donor and paediatric liver transplantation • The causes of liver graft dysfunction • Liver graft preservation techniques •

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Aetiology in adult Acute liver failure Drugs (paracetamol overdose) Hepatitis A and E (severe acute impairment of liver Acute Wilson’s disease function with encephalopathy that Autoimmune hepatitis occurs within 8 weeks of the onset Acute fatty liver of pregnancy of symptoms and no recognised underlying chronic liver disease) Fatty liver disease: alcohol or non-alcohol Chronic liver disease related (any diseases that cause cirrhosis Chronic viral hepatitis B, C, D and its associated complications) Autoimmune liver diseases: primary biliary cirrhosis, primary sclerosing cholangitis, overlap syndromes Genetic haemochromatosis Wilson’s disease -antitrypsin de /f_i ciency 1 Secondary biliary cirrhosis Variant syndromes Intractable pruritus Hepatopulmonary syndrome (metabolic liver disease with Familial amyloidosis life-threatening extrahepatic Primary hypercholesterolaemia complications in children) Hepatic epithelioid haemangioendothelioma Recurrent cholangitis Nodular regenerative hyperplasia Hereditary haemorrhagic telangiectasia Glycogen storage disease Ornithine transcarbamylase de /f_i ciency Primary hyperoxaluria Maple syrup urine disease Porphyria Amyloidosis Hepatocellular carcinoma Liver tumours Rarely – cholangiocarcinoma, neuroendocrine tumours, colorectal liver metastasis

Introduction

Introduction

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LIVER TRANSPLANTATION FOR HEPATIC MALIGNANCY

LIVER TRANSPLANTATION FOR HEPATIC MALIGNANCY

As a general rule, malignancy in a solid organ is not an indication for transplantation. This is because of the risk of recurrence with immunosuppression post transplant; immuno suppression suppresses not only the host’s immunity preventing rejection of the transplanted graft but also the host’s immunity against cancer, which may cause rapid pr ogression of disease after transplantation. However, LT is one area where a total hepatectomy in selected patients can remove the entire disease en bloc and give patients a full chance of cure. LT is widely Jacques Caroli , 1902–1979, Professor of Medicine, St Antoine Hospital, Paris, France, described the disease in 1958. Daniel Alagille , 1925–2005, Eminent Professor of Paediatric Hepatology , Hôpital Bicêtre, Paris, France, first described this condition in 1969. George Budd , 1808–1882, Professor of Medicine, King’s College Hospital, London, UK, described this syndrome in 1845. Hans Chiari , 1851–1916, Professor of Pathological Anatomy , Strasbourg, Germany (Strasbourg was returned to France after the end of the First World War, in 1918), gave his account of this condition in 1898. John Fielding Crigler , 1919–2018, American pediatrician, described the rare inherited disorder Crigler–Najjar syndrome in 1952. Victor Assad Najjar , 1914–2002, Lebanese–American pediatrician and microbiologist, described the rare inherited disorder Crigler–Najjar syndrome in 1952. /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF α /uni25CF indicated as a curative treatment for selected patients with HCC, haemangioendothelioma and hepatoblastoma. Because of its association with CLD, up to 25% of LTs in the UK are in patients with HCC. Using the siz e and number of HCCs on pretransplant imaging, there are a number of criteria that - aim to select patients who have HCC with favourable tumour biology and hence a good outcome following LT . The two main staging criteria of HCC for the indication of LT are the Milan and the University of California San Francisco (UCSF) criteria. With recent advances in diagnostic modalities and chemo - therapeutic agents, LT has been carefully expanded to patients

Aetiology in children Drugs and toxins Hepatitis A and E Acute Wilson’s disease Biliary atresia - antitrypsin de /f_i ciency 1 Autoimmune hepatitis Sclerosing cholangitis Caroli’s syndrome Wilson’s disease Cystic /f_i brosis Progressive familial intrahepatic cholestasis Alagille’s syndrome Glycogen storage disease (types 3 and 4) Tyrosinaemia type 1 Budd–Chiari syndrome Any aetiology leading to hepatopulmonary syndrome or portopulmonary hypertension Crigler–Najjar syndrome Urea cycle defects Hypercholesterolaemia Organic acidaemias Glycogen storage disease type 1 Maple syrup urine disease Porphyria Unresectable hepatoblastoma (without active extrahepatic disease) Unresectable benign liver tumours with disabling symptoms

Evaluation of potential recipients for L T /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF with other primary or secondary malignancies of the liver. Cholangiocarcinoma (CCA) has been an uncommon indica tion for LT for nearly three decades. Recently there has been more interest with wider adaptation of the Mayo protocol, which involves strict patient selection, intensive pre-LT chemo radiation therapy , staging laparoscopy to assess tumour spread and then transplantation. Five-year survival has been reported in the range of 55–65% for hilar CCA in patients with primary sclerosing cholangitis (PSC), who get these cancers more com monly than de novo CCAs. Summary box 89.2 LT f o r h e p a t i c m a l i g n a n c y /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF The Mercedes-Benz sign takes its name from the insignia displayed on the bonnet of a Mercedes-Benz car.

Evaluation is undertaken by a multidisciplinary team, including a transplant surgeon and hepatologist Determine the presence of physical and mental health comorbidities Exclude malignancy and systemic sepsis Determine any contraindications Determine if the patient will bene /f_i t from LT with an acceptable quality of life Determine if the disease is suf /f_i ciently advanced to meet the minimal listing criteria for LT (e.g. UK end-stage liver disease [UKELD] score 49 or more) Determine the availability of family or social support and probable ability to cope psychologically with LT and comply with immunosuppression Optimise recipient condition before LT LT for HCC simultaneously treats the tumour and the underlying liver disease LT for HCC represents 15–50% of all transplants performed in most centres Milan criteria allow selection of HCC patients for LT, with improved overall and disease-free survival Milan criteria (one lesion ≤ 5 /uni00A0 cm, or three or fewer lesions ≤ 3 /uni00A0 cm each) UCSF criteria (one lesion ≤ 6.5 /uni00A0 cm, or three or fewer lesions ≤ 4.5 /uni00A0 cm each, with a total tumour diameter ≤ 8 /uni00A0 cm) UK HCC criteria (one lesion <5 /uni00A0 cm, or /f_i ve or fewer lesions all ≤ 3 /uni00A0 cm, or a single tumour >5 /uni00A0 cm and ≤ 7 /uni00A0 cm in diameter with no evidence of progression over a 6-month period) Tumour recurrence after LT for HCC ranges between 8% and 20% depending upon the criteria followed Primary malignant liver tumours constitute just over 1% of all childhood cancers The most common tumours that require LT in children are hepatoblastoma and HCC CCA, colorectal and neuroendocrine liver metastases are among the new indications for LT

LIVER TRANSPLANTATION

LIVER TRANSPLANTATION

Disease recurrence after LT has increased over the past decade, as many more patients are living more than 15–20 years with their liver graft. Disease recurrence after LT can be divided into four main groups: (i) malignant disease, (ii) viral disease, (iii) autoimmune diseases such as primary biliary cholangitis (PBC) and PSC, and (iv) lifestyle-related diseases such as NAFLD and alcoholic liver disease. The severity of recurrence varies from - mild to the development of progressive allograft failure. Despite strict morphological criteria in selecting patients with HCC for LT , tumour recurrence still occurs in 8–20% of cases, being associated with a median survival of 7–16 months after recurrence. The risk factor s for tumour recurrence are larger tumour burden (beyond the Milan criteria), poor tumour biology , microvascular invasion, higher AFP levels, viral aeti - ology and obesity in the recipient, percutaneous biopsy of the tumour leading to spillage of cells, longer waiting time to trans - plant, higher donor age, DCD transplants and higher burden of immunosuppression in the post-transplant period. HBV recurrence has been r eported in 10% of patients after LT . Howev er, new combinations of post-LT prophylaxis, includ - ing hepatitis B immunoglobulin and nucleos(t)ide analogues such as lamivudine, have reduced the recurrence rates and are part of most LT guidelines. HCV recurrence post LT leads to accelerated liver disease and cirrhosis, with reduced graft and patient survival. Factors associated with increased HCV risk or severity of recurrence after LT include older age, immuno - - suppression, HCV genotype 1 and high viral load at LT . The introduction of protease inhibitors in 2011 and direct-acting antiviral agents in 2013 has led to the reduction both of HCV complications requiring LT and of the consequences of recur - rent HCV infection after LT . A utoimmune diseases commonly recur after LT and may need retransplantation. This usually happens when corticosteroids are withdrawn, but patients usu - ally respond rapidly to the reintroduction of steroids with no adverse long-term impact. PBC and PSC can recur in 20% of patients at 5 years, some of which can be de novo secondary disease. Resumption of alcohol use post LT leads to recurrent - ALD and has an overall poor outcome. NAFLD can recur in patients with metabolic syndrome who continue with poor dietary habits post LT , leading to fibrosis in the graft and even - tually needing retransplantation. Prothrombotic conditions such as Budd–Chiari syndrome can recur in the transplanted liver, requiring retransplantation, but with dismal outcomes. - Summary box 89.7 Diseases that recur after L T /uni25CF /uni25CF /uni25CF /uni25CF - /uni25CF /uni25CF - /uni25CF - /uni25CF

Chronic hepatitis B and C PBC PSC Autoimmune hepatitis Alcoholic liver disease (recurrence alcohol consumption) NAFLD Budd–Chiari syndrome Malignant tumours (HCC, hepatoblastoma)

Learning objectives

Learning objectives

To know: The surgical principles of liver transplantation â€¢ Potential future developments in liver transplantation â€¢ To understand: The main indications and patient selection for liver â€¢ transplantation

Liver support devices

Liver support devices

ALF has a high mortality in the range of 50–80%. Extra corporeal liver support systems have the potential to provide temporary support to bridge patients with ALF to LT or spontaneous recovery . Artificial liver support devices function as ‘dialysis’ machines, which filter and adsorb toxic substances such as bilirubin, bile acids, metabolites of aromatic amino acids, medium-chain fatty acids and cytokines without significant loss of albumin from the circulation. Some examples of commonly available artificial liver support systems are the Molecular Adsorbent ® Recirculating System (MARS ; Gambro, Stockholm, Sweden) ® and Hepa Wash (Hepa Wash GmbH, Munich, Germany). Biological liver support uses whole animal or human liver, and the liver support–detoxification is achieved by portal and/ or artery perfusion. Some examples of commonly available biological liver support systems are the Extracorporeal Liver ® Assist Device (ELAD ; Vital Therapies Inc., San Diego, CA, ® USA) and the HepatAssist system (Alliqua Inc., Langhorne, PA, USA).

Living donor liver transplantation

Living donor liver transplantation

- In 1988, Silvano Raia in Sao Paolo, Brazil, was the first to introduce the concept of LDLT in a child. Although unsuc - - cessful, this was followed by a report of a successful outcome in paediatric LDLT by Russell Strong in Brisbane, Australia. The expansion of LDLT to the adult population began in 1993, when the Shinshu group in Tokyo performed the first success - ful adult-to-adult LDLT . However, adult-to-adult LDLT is not without risks to the donor, with the global mortality risk quoted at 1 in 300–500 for adult donors. Right lobe, left lobe or left lateral segments can be used as grafts depending on the size requirement f or the recipient. Right lobe grafts, which account for 60–70% of the total liver volume, are the most commonly used grafts for adult LDLT (Figure 89.4). The required graft volume is measured by either the graft weight to recipient weight ratio (GRWR) or the ratio of graft volume relative to the standard liver volume of the recipient (GV/ SLV). An ideal GRWR must be >0.8% and/or GV/SLV >35%. The assessment of volume of the graft in the donor is measured by marking the boundaries of the liver lobe on the donor computed tomography (CT) scan manually , but this can also be done more accurately using complex three-dimensional ® software such as MeVis (HepaVision , Bremen, Germany). The remnant liver mass in the donor must be kept to >30% of the whole liver, which allows for safe regeneration and prevents the risk of liver insu ffi ciency in the donor. LDLT is now undertaken in a number of transplant centres worldwide and is relatively common practice in some countries where deceased donation is not practised for cultural or religious reasons, notably in the Far East and South Asia. Over 90% of transplants in the East come from LDLT , whereas in the West over 90% of all LTs are DDLT . With increasing experience and innovation, the graft and recipient survival of adult-to adult LDLT now compare favourably with those of DDLT . If the recipient size is large, a right liver LDLT graft might not give an adequate GRWR. Similarly , if the donor remnant is small, it is not safe for the donation to proceed. To tackle T one innova the problem of inadequate graft size in LDL tive approach is ‘dual-graft liver transplantation’, done mostly in Korea and rarely in other LDLT countries; this approach is to transplant the recipient with two left lobe grafts or one right lobe and one left lobe graft from two living donors. With this approac h, donor safety is maintained and the recipient is transplanted with adequate graft volume. The procedure is technically very demanding and requires massive infrastruc ture where two donor hepatectomies and recipient LT surgery have to take place all at the same time. However, the ethical Claude Couinaud , 1922–2008, French surgeon and anatomist, described the segmental anatomy of the liver in his seminal book chirurgicales . issue of putting two donors at risk simultaneously for one recip - ient’s benefit is contentious. -

Figure 89.4 Adult right lobe living donor liver transplantation (LDLT). (V8) draining into the middle hepatic vein (MHV). (b) A right lobe LDLT graft after implantation showing the reconstructed V5 and V8 using a deceased donor iliac vein graft. (c) A well-perfused right lobe liver graft. Figure 89.5 Ex situ splitting of a donation after brain death liver. (a) Extended right lobe liver graft (Couinaud’s segments I and IV–VIII) prepared for implantation into an adult recipient; (b) left lateral seg ment graft (Couinaud’s segments II and III) prepared for implantation into a paediatric recipient. (a) Hepatic vein cuts showing the segment 5 vein (V5) and segment 8 vein

Machine perfusion

Machine perfusion

With the advances and improvements in outcomes in LT over the last four decades, there has been a focus on expanding deceased donor organs. Static cold storage (SCS) remains the standard-of-care preservation method in LT . This is achieved by cooling the liver to 4°C with preservation solution; this decreases cellular energy consumption by reducing the meta - bolic demand of the tissue. However, when these SCS organs are reperfused, there is a higher ischaemia–reperfusion injury owing to e ffl ux of accumula ted metabolic products formed during cold storage, resulting in a profound inflammatory immune response and causing damage to the hepatocytes and cholangiocytes, thereby leading to poor short- and long-term outcomes. One of the ways of reducing ischaemia–reperfusion injury is to perfuse the liver with cold solution (hypothermic machine perfusion; HMP) or warm blood (normothermic healthy endothelium, replenishing adenosine triphosphate (ATP) and thereby improving quality . This allows the organs to be preserved for a longer period prior to transplantation, thereby addressing the logistics of LT . Further studies will be needed to explore the ideal perfusion method with the aim of improving longer term outcomes and avoiding biliary complications such as ischaemic cholangiopathy and to study viability markers to identify livers that will not function in the recipient, allowing liver-directed therapeutic interventions on the machine. In other exciting technology – in situ normo thermic regional perfusion (NRP) – the blood supply to the abdominal organs after death is restored using extracorporeal circulation for a limited period bef ore organ recovery . This leads to superior liver outcomes in DCD livers compared with conventional organ recovery , and may be an answer to the problem of ischaemic cholangiopathy .

PAEDIATRIC LIVER TRANSPLANTATION

PAEDIATRIC LIVER TRANSPLANTATION

Paediatric LT has now been carried out for more than three decades and enjoys excellent success with good long-term outcomes. Split LT and LDLT have contributed to reduced waiting times in these children with improved outcomes (Figure 89.7). Contraindications to LT in children are uncommon, and usually include: (i) non-resectable extra- hepatic malignant tumour; (ii) concomitant end-stage organ failure that cannot be corrected by a combined transplant; (iii) uncontrolled sepsis; and (iv) irreversible neurological damage. Left lateral segment grafts usually su ffi ce for small children, but larger children will need left lobe or right lobe grafts. The left lateral segment graft donor operation involves removal of acceptable risk of donor complications. Monosegment grafts (transplanting isolated liver segments such as segment II or segment III for an infant) for small children (less than 5 /uni00A0 kg) is - a norm in experienced centres and can solve the problem of ‘large for size’ grafts in this age group. e very

Figure 89.7 Paediatric living donor liver transplantation. (a) Donor left lateral segmentectomy where the parenchymal transection is completed and the graft is ready to be taken out; (b) the left lateral segment graft implanted into a paediatric recipient.

POST-LIVER TRANSPLANT COMPLICATIONS Primary non-fu

POST-LIVER TRANSPLANT COMPLICATIONS Primary non-function

Primary non-function (PNF) is one of the most serious and life-threatening conditions in the immediate post-transplant period. It is defined as an aggravated form of reperfusion injury resulting in irreversible graft failure without detectable /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF

Major side effects Monitoring Blood trough levels Nephrotoxicity Hypertension Diabetogenic (tacrolimus) Gingival hypertrophy/hirsutism (ciclosporin) Increased susceptibility to infection No monitoring Leukopenia Increased susceptibility to infection and cancers Bone marrow suppression with cytopenias, No monitoring pancreatitis Steroid excess (Cushing’s syndrome) No monitoring Impaired wound healing, hyperlipidaemia, Blood trough levels proteinuria, hepatic artery thrombosis

is 4–8% and this is the most common indication for retrans plantation after LT . It is almost always a problem associated with DDLT , but can present in LDLT as well.

Paired-exchange programmes

Paired-exchange programmes

Liver paired exchange (LPE) allows liver donors and their intended incompatible recipients to exchange livers with another donor–recipient pair so that a compatible transplant can be performed. The advantage is that it allows the two transplant recipients to be removed from the deceased donor waiting list, thereby shortening the waiting for other patients who remain on the list, decreasing waiting list mortality . ABO blood group incompatibility , size incompatibility (small donor liver into large recipient or vice versa) or anatomical considerations (multiple arteries or bile ducts to reconstruct) are common reasons for non-acceptance of otherwise suit able donors in LDLT . In all these circumstances, donor and recipient pairs who are not optimally matched might benefit from a better match through LPE. At times, these LPEs can be initiated by a non-directed anonymous living donor (i.e. a domino pair ed exchange), where a person e ff ectively donates a portion of their liver to the pool of patients on the deceased donor transplant waiting list. Compared with kidney paired exchange, LPE is inherently more complex owing to the greater morbidity and mortality risks to the donor and to the logistics involved, hence it is not widely practised. Christian Johann Doppler , 1803–1853, Professor of Experimental Physics, Vienna, Austria, enunciated the Doppler principle in 1842. Strategies to overcome the shortage of livers for transplantation /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF

Increasing the donor pool Implementing an organ donation opt-out system (introduced in the UK in Wales – December 2015; England /uni00A0 – May 2020; Scotland – March 2021) Use of marginal DBD deceased donors Use of DCD deceased donors Increased use of split LT Increased living donor LT Use of HCV-positive donor grafts Improve the preservation and assessment of quality of donor grafts Use of machine perfusion systems (normothermic/ hypothermic machine perfusion) Maximise post-transplant long-term survival Reduce or avoid immunosuppression after LT to minimise side effects

Split and reduced-size liver transplantation

Split and reduced-size liver transplantation

Split LT is a valuable option for making the best use of - good-quality deceased donor liver grafts, by splitting the graft into a left lateral segment (segments II and III) for a paediatric recipient and an extended right liver lobe (segments I and IV–VIII) for an adult recipient. Not so commonly , the whole liver can be split as anatomical right and left lobes, the latter being used for a larger child or a smaller adult. The splitting ex situ , where the whole organ is procedure can be done - retrieved and split on the back-bench along the anatomical planes, so as to preserve the inflow and outflow vessels to both in situ splitting, liver transection is grafts (Figure 89.5). In performed during the donor procedure, similar to procuring a living liver donor graft. The major advantage of in situ splitting in contrast to ex situ bench splitting is that haemostasis on the cut surface can be obtained during the donor procedure with less blood loss from the cut surface during reperfusion in the recipient. In situ splitting also facilitates prompt transportation of the liver to transplant centres if the two split lobes are to be used in two di ff erent centres far away from each other, thereby reducing the cold ischaemic times for both organs. Although technically demanding, split LT is a safe pro - cedure resulting in an increased number of LTs, increased feasibility of LT in children and a reduced waitlist mortality . Short- and long-term outcomes and survival with these grafts are similar to those with whole-graft LT . Reduced-size LT is orerunner of split LT and involves ex vivo resection of a full the f liver into an appropriate size liver to fi t a small adult, with the rest of the reduced-size portion being discarded. Reduced-size LT , unlike a split technique, does not produce an additional graft. It is therefore not widely practised and is reserved for situations where a small adult or adolescent patient requires an urgent transplant and a whole liver or an extended right lobe is too large for the abdominal cavity . Le Foie: Études anatomiques et

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Using grafts from ECDs is a strategy to address organ shortage in LT . An ECD graft has been described as an organ with an increased risk of poor graft function (liver from older donors or fatty livers) and/or transmission of disease (i.e. infection or malignancy) to the recipient because of unfavourable donor characteristics (Table 89.2). In comparison with DBD, DCD LTs have been associated with higher rates of biliary complica tions and graft loss, historically limiting their use. Worldwide, there is considerable variation in the contributions that DCD makes to deceased donation overall. While some countries have no DCD programmes whatsoever (suc h as India, where it is illegal to procure a DCD organ), in countries like the UK and Australia DCD accounts for 20–30% of all LTs. DCD livers reduce waiting list mortality (i.e. by taking patients o ff the LT waiting list) and there is survival advantage in accepting a DCD o ff er than waiting for a ‘better’ DBD liver, which is more pronounced in patients with advanced liver disease. Outcomes with ECD organs can be improved with careful recipient selec tion and possibly with machine perfusion of the donor

liver, so as to assess its function and quality , prior to transplantation.

TECHNIQUE OF LIVER TRANSPLANTATION

Deceased donor

TECHNIQUE OF LIVER TRANSPLANTATION Deceased donor liver transplantation

A reverse-L or a Mercedes-Benz (transverse abdominal inci - - sion with a midline extension) incision is usually made and the diseased liver is mobilised. As a result of portal hypertension, the recipient hepatectomy (removal of damaged liver) is often - the most di ffi cult part of the operation, especially if there has been previous upper abdominal surgery . The common bile duct is divided, as are the hepatic arteries. The inferior vena cava is mobilised above and below the liver; the portal vein is - clamped and divided, and the vena cava is divided above and below , allowing the recipient liver to be removed. This ‘classical’ technique (Figure 89.1a) allows quick removal of the recipient liver without the need to free the liver from the cava by tying all the short and named hepatic veins (i.e. caval ‘preservation’ technique). Occlusion of the vena cava and portal vein results in a reduction in cardiac output and may necessitate the use of venovenous bypass, albeit not commonly . The bypass circuit delivers blood from the inferior vena cava and/or portal vein, back to the heart via a cannula inserted into the internal jugu - lar vein. This improves venous return to the heart and provides haemodynamic stability during the operation. The portal limb of the bypass also reduces portal hypertension and congestion of the bowel during the implantation phase and potentially can reduce blood loss. After total he patectomy the implantation starts by plac - ing the liver graft in the orthotopic position. The supra- and infrahepatic caval anastomoses are the first to be performed. The liver is flushed through the portal vein with normal saline a t room temperature to remove the preservative solution with the e ffl uent draining out through the lower caval anastomo - sis, which is left incomplete until the flushing. The portal vein anastomosis is then completed and the graft is reperfused. The hepatic artery anastomosis can sometimes be done first to reperfuse the liver with arterial blood followed by the por - tal vein anastomosis . Figure 89.2 shows a cirrhotic liver and the deceased donor liver after transplantation. Finally , biliary drainage is re-established usually by a duct-to-duct anastomosis (Figure 89.3a). In recipients with biliary atresia where the bile duct is absent or in those with PSC where the bile duct is dis eased, the donor bile duct is reconstructed through a Roux en-Y hepaticojejunostomy (Figure 89.3b). An alternative and more commonly performed technique is the ‘caval preservation’ technique, which allows the recipient liver to be remo ved without cross-clamping the vena cava, thus avoiding venovenous bypass. The donor liver here is implanted using a ‘piggyback’ technique onto the confluence of the three Cesar Roux , 1857–1934, Professor of Surgery and Gynaecology , Lausanne, Switzerland, described this method of forming a jejunal conduit in 1908. hepatic veins in the recipient (Figure 89.1b) or using a side-to - - side cavo-cavoplasty (joining donor and recipient

cava side to - side) (Figure 89.1c). Optimal perioperative management is crucial to a success - ful outcome and presents a major challenge. These pa tients are often very sick preoperatively , especially those transplanted for ALF . Blood loss during and after the transplantation procedure can be very considerable , and management of coagulopathy is particularly important. Coagulation is assessed repeatedly

(a) LHV Diaphragm Recipient IVC (b) LHV Donor IVC MHV RHV Diaphragm Recipient IVC Figure 89.1 Pictorial representation of inferior vena cava (IVC) reconstruction in a deceased donor live transplantation. replacement technique in which the recipient’s retrohepatic IVC is replaced with donor IVC. of the three hepatic veins in the recipient is used to anastomose with the top end of the donor IVC. the side of the donor IVC is joined with the side of the recipient IVC. LHV, left hepatic vein; MHV, middle hepatic vein; RHV, right hepatic vein. (a) Figure 89.2 Adult deceased donor liver transplantation. (a) Recipient cirrhotic liver; hepatic artery. MHV RHV Donor IVC Recipient IVC (c) LHV MHV Donor IVC Diaphragm Recipient IVC RHV (a) A ‘classical’ caval (b) A ‘piggyback’ technique in which the con /f_l uence (c) ‘Side-to-side cavo-cavoplasty’ in which (b) (b) whole liver graft after reperfusion with the portal vein and

throughout the transplantation period and corrected with appropriate clotting factors, if required. Many centres rou tinely use point-of-care ‘viscoelastic monitoring’ such as thromboelastography (TEG) or rotational thromboelastome try (ROTEM) to perform dynamic assessment of coagulation. The deceased donor liver transplant (DDLT) grafts come from either donation after brain death (DBD) donors or donation after circulatory death (DCD) donors. The latter are considered ‘extended criteria’ donors o wing to greater ischaemia associated with donor hypoxia/death, higher risk of graft dysfunction, higher risk of vascular and biliary complications and poor long-term outcomes. Although LT has established itself as a life-saving treatment, the limited availability of deceased donor liver grafts has urged the transplant community to devise newer techniques and strategies to reduce the gap between organ demand and supply . The various options to increase organ availability are: LDLT , split and reduced-size LT , use of extended criteria donors (ECDs), auxiliary LT , domino LT and the paired-exchange programme. Summary box 89.3 Types of L T (based on source of liver allograft) /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Silvano Raia , b. 1930, Emeritus Professor at the Faculty of Medicine, Sao Paulo, Brazil, performed the first living donor liver transplantation in a child. Russell Strong , contemporary , Emeritus Professor of Surgery , University of Queensland, Princess Alexandra Hospital, Australia. He successfully performed a living donor liver transplant of the left lateral segment of a Japanese mother’s liver into her 18-month-old son in 1989. Both were alive and well 27 years later (2016); the recipient graduated and is practising as a physiotherapist.

Liver Stomach Figure 89.3 Pictorial representation of the standard deceased donor liver transplant with a ‘classical’ caval replacement technique. graft after completion of all anastomoses, in order of performance: (1) suprahepatic cava; (2) infrahepatic cava; (3) portal vein; (4) hepatic artery; (5) bile duct. (b) A Roux-en-Y reconstruction where the donor bile duct is anastomosed to the loop of jejunum. The rest of the anastomoses and order of performance are the same. DDLT, which includes DBD (70–80%) and DCD (20–30%) LDLT – this can be adult to adult or adult to child Split and reduced-size LT ECDs Auxiliary LT Domino LT Paired-exchange programme Liver Inferior vena cava Portal vein Bile duct Hepatic artery (a) A liver

TRANSPLANTATION

TRANSPLANTATION

The allocation of liver grafts to patients with end-stage liver disease is dominated by three ethical principles: equity (need), utility (usefulness) and transplant benefit. The equity model gives prioritisation for sickest first, the utility prioritises the patient with the best expected outcome from transplantation and transplant benefit prioritises the patient with the greatest di ff erence in expected survival with and without transplanta - tion. The last balances both equity and utility and is expected to minimise mortality and maximise survival for the overall patients listed for transplant. TRANSPLANTATION

The outcomes after LT depend on the underlying liver disease; the best results are seen in patients with CLD. Patients undergo ing transplantation as a result of ALF have a higher mortality in the early post-transplantation period because of multiorgan failure, but those who make a satisfactory recovery hav good long-term liver allograft survival. In the UK, unadjusted 1-, 5- and 10-year patient survival for adult patients receiving their first elective transplant is 94%, 84% and 72%, respec tively . For super-urgent transplant, the survival is less: 90%, 82% and 70%, respectively (NHSBT Annual Report Septem ber 2020). Conversely , patients transplanted for tumour have a very good ear ly outcome but ultimately fare less well because of recurrent malignancy . As with other solid organ transplants, chronic imm unosuppression has its e ff ect on the LT recipient with increased risk of infections, metabolic syndrome and cancers. The common causes of death in post-LT recipients after 3 years of transplant are mostly non-transplant related, such as malignancy or cardiovascular disease, and are less due to chronic rejection and recurrent primary liver disease. TRANSPLANTATION

Donor shortage is the key issue in LT . The biggest challenge - ahead for the LT community will be to implement strategies that will overcome donor organ shortage, but at the same time maximise the long-term outcomes of the grafts transplanted. Reducing the waiting list mortality will involve bridging the gap between the demand and availability . Optimising the organ quality using newer technologies such as machine perfusion and ‘growing livers in the lab’ are exciting prospects that could overcome the chronic organ shortage.

USEFUL WEBSITES IN LIVER TRANSPLANTATION

USEFUL WEBSITES IN LIVER TRANSPLANTATION

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Vascular complications

Vascular complications

Hepatic artery thrombosis (HAT) is one of the most dreaded complications after LT , and may occur spontaneously or as a result of acute rejection; it is more common in children and in adults with PSC. The incidence of HAT has been reported to be in the range of 1–10% after LT . Anatomical variant grafts such as split, reduced and LDLT grafts have a higher risk of HAT when compared with whole-organ LT . Early HAT (within 4 weeks of LT) may present as a rise in serum transaminase levels, unexplained fever or bile leak. The risk factors for early HAT are not only related to technical factors such as vessel kinking, stenotic anastomosis and intimal dissection, but also to other factors such as elderly donors with calcified vessels, a hypercoagulable state in the recipient and rejection episodes. Doppler ultrasound or CT angiography is used to confirm the diagnosis, and urgent retransplantation is usually required. Endovascular interventions and thrombolysis are rarely successful. The UK super-urgent liver scheme allows listing of those patients who develop early HAT , up to 21 days after transplantation. Late HAT (after 4 weeks of LT) usually has an insidious course and can present as asymptomatic elevation of liver enzymes, bile duct strictures or liver abscess. The bile ducts su ff er the most ischaemic insult as they primarily depend on arterial blood supply with no portal venous blood supply . Retransplantation is usually reserved for those with severe biliary complications. Portal vein thrombosis and stenosis are rare and can pres ent with features of portal hypertension. The management usually involves endovascular interventions such as balloon dilatation or stent insertion, surgical bypass or retransplanta tion. Late portal vein thrombosis/stenosis manifests as portal - conservatively without risk of graft loss. Hepatic venous outflow obstruction often presents with increasing ascitic fluid losses over the postoperative period. A ca vogram with hepatic vein pressur e studies should be under - taken to confirm the diagnosis, and insertion of vascular stents, surgical correction or retransplantation may be required to treat the problem.