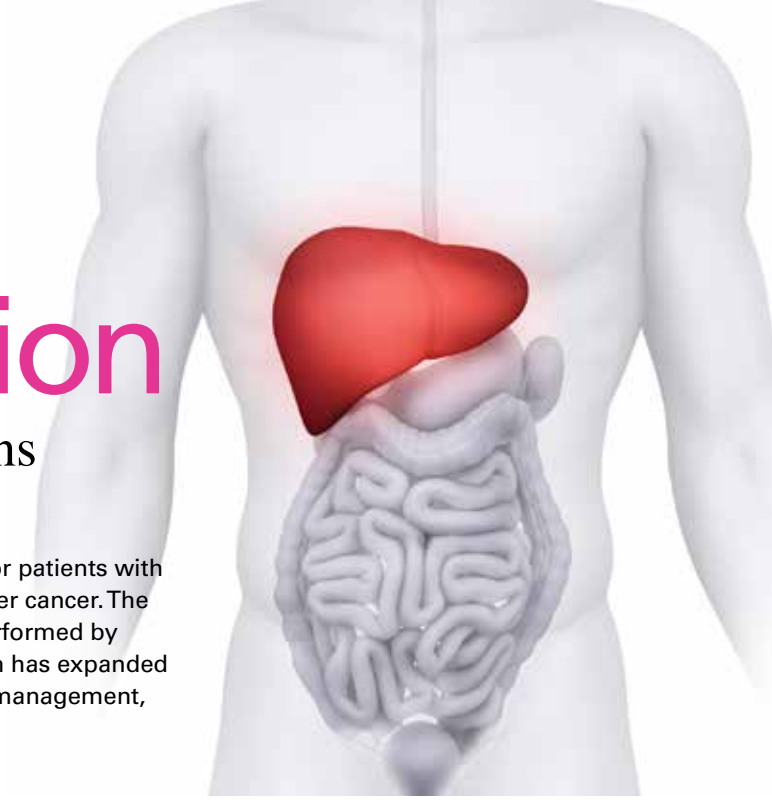
Liver Transplantation

by Dr Cheah Yee Lee

Evolution and current indications



Liver transplantation is an important treatment option for patients with chronic liver disease, acute liver failure and primary liver cancer. The first successful liver transplantation in humans was performed by Thomas Starlz in 1967. Since then, the field of transplantation has expanded due to improvements in surgical techniques, peri-operative management, preservation solution and immunosuppression regimens.

Indications for Liver Transplantation

Liver transplantation is indicated in the treatment of acute and chronic liver failure not responsive to maximum medical management. The presence of cirrhosis per se does not necessitate liver transplantation. Cirrhotic patients who develop complications from cirrhosis (e.g. ascites, gastrointestinal haemorrhage, hepatic encephalopathy) may benefit from liver transplantation especially those patients with poor prognosis. **Table 1** shows the common indications for liver transplantation based on guidelines by the American Association for the Study of Liver Diseases and the American Society of Transplantation 2013.[1]

The Model for End-stage Liver Disease (MELD)

Traditionally, the Child-Pugh score has been used to assess extent of chronic liver dysfunction and prognosis of cirrhosis but its main limitation is the inclusion of subjective criteria (namely the presence of ascites and encephalopathy). Currently, the Model for End-stage Liver Disease (MELD) score is more commonly used. It is a calculation which incorporates the serum creatinine, total bilirubin and international normalised ratio of prothrombin time (INR) levels. MELD score calculators are widely available online.[2]

The MELD score is on a continuous scale from six to 40, which corresponds to a three-month survival of 90% to 7%, respectively. Therefore, the higher the score, the higher the likelihood that the patient will succumb to their liver disease within the next three months. The risk of liver transplantation in patients with a MELD score of ≤ 15 outweighs its benefits.[3]

There are some groups of patients with low MELD scores who may still benefit from liver transplantation. One important group consists of patients who develop hepatocellular cancer associated with hepatitis B or cirrhosis from other causes. Surgical resection is considered the primary mode of treatment for hepatocellular carcinoma. The high risk of complications

***Table 1.* Indications for liver transplant**

Acute Liver Failure
Complications of Cirrhosis:
Ascites
Chronic gastrointestinal blood loss due to portal hypertensive gastropathy
Encephalopathy
Liver cancer
Refractory variceal haemorrhage
Synthetic dysfunction
Liver-based Metabolic Conditions with Systemic Manifestations:
α1-Antitrypsin deficiency
Familial amyloidosis
Glycogen storage disease
Hemochromatosis
Primary oxaluria
Wilson's disease
Systemic Complications of Chronic Liver Disease:
Hepatopulmonary syndrome
Portopulmonary hypertension

due to the presence of portal hypertension and liver failure, however, may preclude liver resection in many patients with cirrhosis.

The landmark paper by Mazzaferro et al in 1996 recommended limiting eligibility for transplantation to cirrhotic patients with solitary tumours of ≤ 5cm, no more than three tumour nodules with each being ≤ 3cm in diameter, and no macrovascular invasion, now collectively known as the Milan criteria. Since then many groups have expanded these criteria to include larger and more numerous tumours with no extra-hepatic spread.[4] Limits on expansion of these criteria are controversial due to the lack of donor organs.

Living Donor Liver Transplantation

Most of the initial experience with liver transplantation involved the use of donated livers from deceased donors. Due to the increasing number of patients on the waiting list coupled with a lack of deceased donor organs, the evolution to transplantation of partial liver grafts from living donors began with the first successful living donor liver transplantation in 1989. Donation of part of the liver is feasible due to the regenerative ability of the remnant liver. Living donor liver transplantation is particularly common in Asia due to low rates of deceased donor organ donation.

During a living donor liver transplantation, both the donor and recipient will undergo their respective operations simultaneously. A portion of the liver is removed from the donor (for an adult recipient, this is most commonly the right lobe of the liver) and placed in the recipient after the recipient's original diseased liver has been completely removed **[Figure 1]**. At least four anastomoses are performed between the donated graft and the recipient; namely the hepatic vein, portal vein, hepatic artery and bile duct anastomoses.

At the Asian American Liver Centre, prior to liver transplantation, the potential recipient will need to undergo an extensive evaluation process whereby their indications and fitness for the operation and post-operative care are examined. This will include consultation by numerous sub-specialists including hepatologist, transplant surgeon, cardiologist, respiratory physicians, infectious disease physician, dental surgeon, psychiatrist and transplant coordinators. Laboratory testing includes assessment of liver function, renal function, viral serologies, markers of other causes of liver disease, tumour markers, and ABO blood typing. Imaging of the liver is required to assess patency of vessels and presence of any tumours.

Potential donors who wish to donate part of their livers to save the lives of their loved ones also receive a thorough workup to ensure their suitability for liver donation. Their investigations mirror much of the above recipient's evaluation. 3-D imaging scans of the donor liver are performed to assess anatomy and ensure the volume of the liver is adequate for both recipient and donor **[Figure 2]**.

Donor safety is of paramount importance and our centre appoints an independent donor advocate (a doctor who is not involved in the treatment of the recipient) to ensure safe evaluation and care of donors. In Singapore, the donor and recipient pairing is also presented to the Ethics Committee, which is an independent body appointed by the Ministry of Health to ensure there are no ethical issues related to the proposed donation from the donor to the recipient.

Liver transplantation, particularly living donor liver transplantation, is a major surgical procedure with significant operative risks. The perioperative mortality rate of liver transplantation is 5%-10%, depending on the severity of liver disease and the presence of other comorbidities. Complications may occur in up to 30% of cases including bleeding, bile leak, acute rejection, primary graft non-function, vessel thrombosis and infectious complications.

Even though the donor hepatectomy operation has lower complication rates compared to the recipient operation, any risk is considered significant as the donor derives no benefit from their operation except for the emotional reward of a magnanimous gesture. The perioperative mortality rate of donor hepatectomy is up to 0.5% for right lobe donation whereas complication rates can reach up to 15% (bleeding, bile leak, infection). After initial recovery from the operation, however, liver donation does not shorten the donor lifespan or put them at increased risk of liver dysfunction compared to a person without liver donation.

Long-term outcomes from liver transplantation have improved since its inception and current five-year survival rates approach 78%. Long-term survival rates are lower for recipients who received a liver transplant for hepatocellular carcinoma due to risk of cancer recurrence. Liver transplant recipients will require life-long follow-up to monitor liver function, immunosuppression status, long-term complications including recurrence of original liver disease, development of certain cancers, and metabolic issues including hypertension and diabetes secondary to transplant medications.

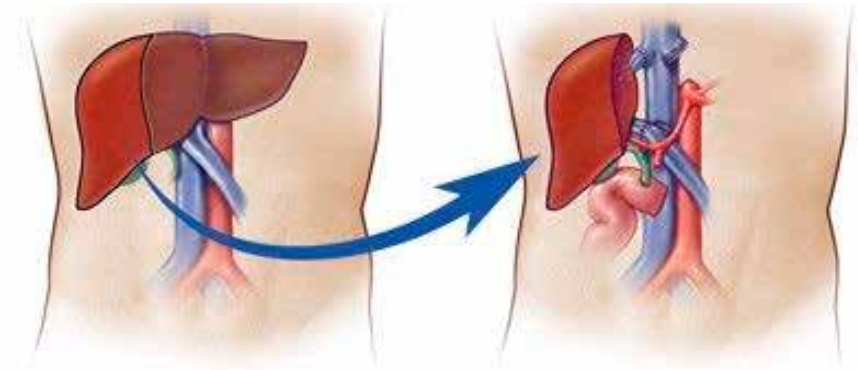


Figure 1. ***Right-lobe living donor liver transplantation. The right lobe of the donor is meticulously resected and transplanted into the recipient after the recipient's diseased liver has been removed.***

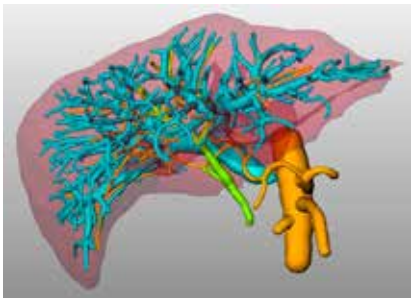


Figure 2. ***3-D reconstruction of donor liver anatomy demonstrating the relationship between the portal veins (blue), hepatic arteries (yellow) and biliary ducts (green).***

Case Example of Living Donor Liver Transplantation at Asian American Liver Centre

This is a 60-year old gentleman who has hepatitis B cirrhosis complicated by intractable ascites and several episodes of bleeding oesophageal varices. His preoperative MELD score was 24. He had an extensive workup for liver transplantation and his son was found to be an appropriate donor. The following are their intraoperative findings. Both donor and recipient are recovering well after their operations.

a) Recipient's cirrhotic liver.
b) Entire cirrhotic liver carefully dissected free and removed.
c) Donor's healthy liver with line demarcating right lobe from left lobe of liver (right lobe to be donated).
d) Donor's liver meticulously split along the border of right and left lobes leaving all vessels intact until ready for removal.
e) Right lobe of donor implanted into his father.

Conclusion

In conclusion, liver transplantation has grown and matured since the 1960s with the development of refined surgical techniques, improved medical management and expansion of indications for transplantation. Liver transplantation remains one of the most important life-saving treatment options for liver disease. MG

Dr Cheah Yee Lee is a liver transplant and hepatobiliary and pancreas (HPB) surgeon at the Asian American Liver Centre, Gleneagles Hospital. She treats patients with liver failure, and benign and malignant conditions of the liver, pancreas and bile ducts.

References:

1. Martin P, DiMartini A, Feng S et al. Evaluation for liver transplantation in adults: 2013 Practice Guideline by the American Association for the Study of Liver Diseases and the American Society of Transplantation. Hepatology 2014;59(3):1144-1165.
2. Organ Procurement and Transplantation Network Allocation Calculator. Available from: http://optn.transplant.hrsa.gov/converge/resources/MeldPeldCalculator.asp?index=98.
3. Merion RM, Schaubel DE, Dykstra DM, et al. The survival benefit of liver transplantation. Am J Transplant 2005;5:307-313.
4. Cheah YL, Chow PKH. Liver transplantation for hepatocellular carcinoma: an appraisal of current controversies. Liver Cancer 2012;1:183-189.