

Liver Transplantation

- It is the replacement of a diseased liver with a healthy liver allograft.
- Used technique is orthotopic transplantation, in which the native liver is removed and replaced by the donor organ in the same anatomic location as the original liver.
- Liver transplantation nowadays is a well-accepted treatment option for end-stage liver disease and acute liver failure.

History

- The first human liver transplant was performed in 1963 by a surgical team led by Dr. Thomas Starzl of Denver, Colorado, United States.
- The first short-term success was achieved in 1967 with the first one-year survival post transplantation.
- Despite the development of viable surgical techniques, liver transplantation remained experimental through the 1970s, with one year patient survival in the vicinity of 25%.
- The introduction of ciclosporin by Sir Roy Calne markedly improved patient outcomes,
- In 1980s saw recognition of liver transplantation as a standard clinical treatment for both adult and pediatric patients with appropriate indications.
- Liver transplantation is now performed at over one hundred centers in the USA, as well as numerous centres in Europe and elsewhere. One-year patient survival is 80–85%, and outcomes continue to improve

Indications

- Fulminant hepatic failure
- Complications of cirrhosis
 - Ascites
 - Encephalopathy
 - Synthetic dysfunction
 - Liver cancer
 - Refractory variceal hemorrhage
 - Chronic gastrointestinal blood loss due to portal hypertensive
- Systemic complications of chronic liver disease
 - Hepatopulmonary syndrome
 - Portopulmonary hypertension
- Liver-based metabolic conditions causing systemic disease
 - Primary oxaluria
 - Familial amyloidosis
 - 1-antitrypsin deficiency
 - Wilson's disease
 - Urea cycle enzyme deficiencies
 - Glycogen storage disease
 - Tyrosemia

Contraindications to Liver Transplantation

Absolute

- Active extrahepatic malignancy
- Hepatic malignancy with macrovascular or diffuse tumor invasion
- Active and uncontrolled infection outside of the hepatobiliary system
- Active substance or alcohol abuse
- Severe cardiopulmonary or other comorbid conditions
- Psychosocial factors that would likely preclude recovery after transplantation
- Technical and/or anatomical barriers
- Brain death

Relative

- Age
- Cholangiocarcinoma
- Portal vein thrombosis
- Chronic or refractory infections
- Human immunodeficiency virus infection
- Previous malignancy
- Active psychiatric illness
- Poor social support

Source of the graft

- Deceased donor
 - Brain dead
 - Cardiac dead
- Living donor
 - Right lobe
 - Left lobe
 - Left lateral segment
 - Posterior sector graft

King's college criteria for liver transplant in acute liver failure

Paracetamol-induced ALF

Arterial pH <7.30 after fluid resuscitation

OR all of the following features:

Prothrombin time >100 s (international normalized ratio >6.5)

Serum creatinine >259 µmol/l (3.4 mg/dl)

Grade 3 or 4 hepatic encephalopathy

Non-paracetamol-induced ALF

Prothrombin time >100 s (international normalized ratio >6.5)

OR any three of the following features:

Non-A, non-B viral hepatitis, drug-induced or indeterminate etiology of ALF

Time from jaundice to hepatic encephalopathy >7 days

Age <10 years, or >40 years

Prothrombin time >50 s (international normalized ratio >3.5)

Serum bilirubin >297.6 µmol/l (17.4 mg/dl)

Abbreviation: ALF, acute liver failure.

Parameter	1 point	2 points	3 points
Encephalopathy	None	Grade 1-2	Grade 3-4
Ascites	None	Medically controlled	Uncontrolled
Albumin, g/dL	> 3.5	2.8 – 3.5	< 2.8
Bilirubin, mg/dL	< 2	2 – 3	> 3
International normalized ratio	< 1.7	1.7 – 2.3	> 2.3

Child C (>10) is an indication for liver transplantation

MELD score

- MELD score = $0.957 \times \text{Loge}(\text{creatinine mg/dL}) + 0.378 \times \text{Loge}(\text{bilirubin mg/dL}) + 1.120 \times \text{Loge}(\text{INR}) + 0.643$.
- MELD >14 is an indication for liver transplantation
- It's used for patient listing

Living donor

Liver will regenerate up to 80% of its size after 14 days of removing 70 % of its mass.

Postoperative Details

ICU care

- Following LT, the function of the new liver is monitored closely in an ICU setting. Elevations of liver enzymes, notoriously transaminases (ie, aspartate aminotransferase, alanine aminotransferase), early on are reflective of preservation injury (cold preservation). On occasion, these enzyme levels rise sharply. If they are higher than 2000, the overall viability function of the liver should be monitored carefully to assess the need for retransplantation.
- Usually, the liver enzyme levels normalize very quickly, typically within a week of transplantation. The bilirubin level follows a similar pattern of early rise and delayed clearing. However, if the preservation injury is severe, this elevation can persist for 2-3 weeks and can be accompanied by a significant rise in alkaline phosphatase levels.
- Platelet counts usually decrease in the first week after LT and recover during the second week. This may be caused by platelet sequestration in the liver and spleen due to preservation injury. Once the liver has recovered, as manifested by the return of bilirubin to normal levels, the platelet count increases.
- Recovery in a typical patient is rapid, as is discharge to the floor, usually within 2-3 days.
- However, if the graft has suffered severe preservation injury, return to normality may lag.
- Treatment is mostly supportive, with the goal of maintaining stable hemodynamics while the liver recovers. In extreme cases, termed primary graft nonfunction, the new liver never recovers and urgent retransplantation is required

Floor care

- After the patient's medical condition has stabilized and graft function is stable, he or she is transferred from the ICU to the floor transplant unit. At this time, tests are performed to assure adequacy of the new connections.
- A duplex Doppler ultrasound helps check for patency of the vascular anastomoses and the presence of abnormal fluid collections leaks.
- During the patient's stay on the floor unit, his or her laboratory studies, medications, nutritional status, and exercise tolerance are monitored. As soon as patients are able, discharge instructions begin to prepare them for going home.
- Most patients with severe ESLD have a very low albumin level prior to transplantation. After successful LT, the albumin level slowly rises to normal levels. This explains the generalized edema that patients may experience following transplantation, which begins to disappear once albumin levels start to normalize.
- Patients should be kept on lifelong immunosuppressant to prevent rejection.

Post Liver Transplant Complications

Infections

- Bacterial; related to procedure →
 - Pneumonia; - biliary sepsis;
 - Wound infection; - catheter related,
 - C. difficile PMC
- Viral:
 - HSV stomatitis, - HCV,
 - Hepatitis B, if without prophylaxis
- Fungal:
 - Pneumocystis, - Aspergillus,
 - Cryptococcus, - Histoplasma,
 - Coccidioides
- Parasites:
 - Toxoplasma, - Strongyloides,
 - Leishmania, - Trypanosoma

Allograft dysfunction

- PNF in first two weeks
- Acute cellular rejection
- Small-for-size Syndrome

Biliary tract

- Bile leaks
- Anastomosis disruption
- Hepatic duct stricture/hepatic artery thrombosis

Disease recurrence

Rejection (acute and chronic)

Post-transplant lymphoproliferative disorder

Future and Controversies

- Xenotransplantation
- Hepatocyte cell transplantation
- Use of bioartificial liver devices (i.e. extracorporeal liver-assist devices)