41b. Indications for Liver Transplantation

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41b.1. General Considerations

Candidates for OLT must have irreversible acute or chronic end stage liver disease (table 41b.1). Virus or alcohol-induced liver cirrhosis constitute the most common disease indications in adults [1] (fig. 41b.1). In our department 28% of cirrhotic liver transplant recipients are transplanted for hepatitis C virus (HCV)-related liver disease and 26% undergo OLT for alcohol-related liver disease. Other indications include cholestatic liver disorders [primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), biliary atresia], hepatitis B virus (HBV) infection, autoimmune hepatitis, cystic fibrosis, inherited metabolic diseases (Wilson's disease, hemochromatosis, alpha-1-antitrypsin deficiency), nonalcoholic steatohepatitis, nonmetastatic hepatocellular carcinoma, and acute virally-, toxin-, or drug-induced hepatic failure. The most common indications in children comprise biliary atresia and metabolic liver diseases.

Many attempts have been made to optimize the timing of liver transplantation for advanced chronic cholestatic liver diseases. A number of investigators have developed prognostic indices using clinical and laboratory parameters for prediction of survival in patients with PBC and PSC. The most popular model, the Mayo model, considers prognostic variables such as serum levels of bilirubin and albumin, age, prothrombin time, and the presence of peripheral edema including response to diuretic therapy. Apart from the prognostic model, the level of serum bilirubin is the most heavily weighted variable for prediction of survival. In patients with PSC, interventional endoscopic therapy may produce clinical and biochemical improvement and may prolong transplant-free survival.

Contraindications for OLT include active alcohol and drug abuse, extrahepatic malignancies, sepsis, uncontrolled pulmonary hypertension, and coexistent medical disorders such as unstable coronary artery disease, congestive heart failure, or severe lung disease.

OLT in patients with cholangiocellular carcinoma (CCC) reveals a high rate of recurrence and poor post-transplant survival. Concurrent illnesses that previously precluded consideration for OLT such as infection with human immunodeficiency virus (HIV), have been shown to be acceptable in selected cases with the introduction of potent antiretroviral therapy.

The patient status based on the Child-Pugh score (table 41b.2) and the length of time on the waiting list is still being considered in Europe. In 2002, the Organ

Table 41b.1. Reasons for acute or chronic liver failure potentially requiring liver transplantation.

- Chronic liver disease
  Post hepatitis cirrhosis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerotic cholangitis, Budd-Chiari syndrome, polycystic liver disease, Caroli's disease.
- Metabolic liver disease
  Wilson disease, hemochromatosis, Crigler-Najjar syndrome, α1-antitrypsin deficiency, Familial hypercholesterinemia, primary hyperoxaluria, haemophilia A, Tyrosinemia, Glycogenoses Type I and IV, Familial amyloidotic polyneuropathy, Gaucher's disease, Niemann-Pick disease, Erythropoietic protoporphyria.
- Acute liver failure.

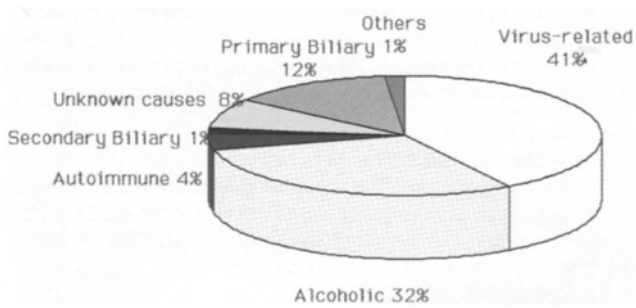

Fig. 41b.1. Indications for liver transplantation in cirrhotic patients (n = 31169) in Europe, during the period January 1988 to December 2004 (data kindly provided by European Liver Transplant Registry; http://www.eltr.org).

Table 41b.2. Child-Turcotte-Classification (Pugh-Modification).

• Points	1	2	3
Albumin (g/dl)	> 3.5	3.0-3.5	< 3.0
Bilirubin (mg/dl)	< 2.0	2.0-3.0	> 3.0
Ascites	no	manageable	refractory to therapy
Encephalopathy	no	light	severe
Quick-Value (%)	> 70	40-70	< 40
CTP-Score:	A (5-6)	B (7-9)	C (> 9)

Table 41b.3. Calculation of the MELD* Score.

$$\text{MELD Score} = 0.957 \times \text{Log}_e(\text{creatinine mg/dL}) + 0.378 \times \text{Log}_e(\text{bilirubin mg/dL}) + 1.120 \times \text{Log}_e(\text{INR}^{**}) + 0.643$$

* Model of end-stage liver disease.
** International Normalized Ratio.

Procurement and Transplantation Network (OPTN), along with the United Network of Organ Sharing (UNOS), developed a new system based on the model for end-stage liver disease (MELD, table 41b.3). The MELD score will soon be applied to transplant candidates in the Eurotransplant International Foundation organ procurement system.

A candidate is not considered for liver transplantation if his life expectancy is deemed greater without a transplant. Merion et al. reported that the adjusted relative mortality risk is significantly higher in transplanted patients than in those waiting for OLT with a MELD score of less than 152. Patients with MELD scores of 18 or higher derive significant survival benefit. Candidates with very high MELD scores have an extremely high waiting-list mortality whereas the post-transplant mortality risk seems to rise more gradually [2]. Those patients, whose calculated score is higher than 40 are aggregated with those whose MELD score is equal to 40.

The likelihood of relapse in patients transplanted for alcoholic liver disease is a major issue. It is our policy that patients with alcoholic liver disease must be abstinent for at least 6 months before liver transplantation. The Department of Psychosomatic Medicine and Psychotherapy at our university hospital established a group psychotherapy program with the aim of establishing alcohol abstinence and compliance of health behavior. Therapy consists of a 6-month program including 18 hours of group sessions. The alcohol concentration in the breath and alcohol metabolites in the urine is measured at every group session. Preliminary results presented by Erim et al (the 7th Annual Meeting of the European Association for Consultation Liaison Psychiatry and Psychosomatics and the 25th European Conference of Psychosomatic Research) suggest that structured cognitive-behavioral group therapy has a beneficial effect on the health behavior of these patients.

41b.2. Acute Liver Failure

The indication for liver transplantation in patients with acute liver failure must consider its etiology (table 41b.4). In principle, every chance should be given to allow recovery of liver function without liver transplantation, since acute liver failure frequently resolves with restitutio ad integrum, so avoiding a lifelong immune-suppression. If transplantation is deemed necessary, it must be performed without delay before prognosis worsens, hence patients with acute liver failure should be promptly transferred to a transplantation center.

The prognosis of acute liver failure is closely linked to the development of brain edema and a degree of encephalopathy. Therefore, the monitoring of intracranial pressure is of special significance. Beyond that, the general condition of the patient has a substantial influence on the success of a liver transplantation. Grade-IV encephalopathy, bleeding, as well as severe jaundice are considered particularly unfavourable. The great risk of septic complications following transplantation also accounts for high mortality. Furthermore, the duration of stay in the intensive care unit, intubation and the extent to which participation other organ systems are implicated (kidney failure, haemodynamic instability, ARDS etc.) are also of prognostic significance.

The necessity for a liver transplantation can be measured more closely by prognostic scores. The most important and most frequently used prognostic score

Table 41b.4. Reasons for acute liver failure.

- Viral disease
  Hepatitis A, Hepatitis B (with or without super infection with hepatitis D), Hepatitis C (extremely rare), Hepatitis E, other viral hepatitis (Herpes simplex viruses, Cytomegalovirus, Epstein Barr viruses, Varicella Zoster viruses, Para-influenza viruses).
- Toxicity/Idiosyncrasy
  Paracetamol, halo genius ores of hydrocarbons, Halothane, Isoflurane, Enflurane, INH, Rifampicin, Not steroid antirheumatics, Gold, Sulfonamides, Tetracycline, Ketoconazole, Mao Hemmer, tricyclic antidepressives, Allopurinol, Valproic acid, Phenytoin, Disulfiram, Methyldopa, Amiodarone, Propylthiouracil, Coumarin derivatives.
- Other causes
  Death cap (Amanita phalloides), acute pregnancy fat liver, Reye syndrome, Wilson's Disease, Budd-Chiari syndrome, Hyperthermia, Heat stroke.

Table 41b.5. King's College Criteria.

Patients with acute liver failure will also need a transplantation at security of bordering probability, if the following finding constellation is present.

In the case of paracetamol intoxication:

- pH < 7,3

or

- PTT > 100 sec and creatinine > 3.4 mg/dl and encephalopathy III° or IV°

In all other cases of acute liver failure:

- PTT > 100 sec (Quick < 7% or INR>6,7)

or at least 3 of the following criteria:

- Age < 10 years or > 40 years

unfavourable aetiology of the liver failure
(Cryptogenic hepatitis, halothane-hepatitis, intoxication with drugs)

- Jaundice > 7 days prior to the onset of encephalopathy

Table 41b.6. Clichy-Criteria.

By viral hepatitis:	Encephalopathy III° or IV° Factor V > 20% aged >30 Factor V < 30% aged < 30

in clinical practice is the "King's college criteria" (table 41b.5). This includes indices for liver transplantation, differentiating between acute liver failure due to paracetamol intoxication or due to other causes. A further score use to evaluate the necessity for transplantation in fulminant liver failure of viral genesis is "the Clichy criteria" (table 41b.6). This focuses on the age of the patient, the concentration of the coagulating factor V and the development of encephalopathy.

In patients with a transplant-worthy yet potentially reversible acute liver failure, the possibility of an auxiliary transplantation can be considered, in order to avoid lifelong immunosuppressive therapy. Favorable indications for an auxiliary transplantation may include fulminant hepatitis A, paracetamol intoxication as well as pregnancy fat liver. Auxiliary liver transplantation can be further discussed in fulminant hepatitis B (also with HDV co-infection) and halothane-induced acute liver failure. It should also be mentioned that particularly crucial to the consideration of auxiliary transplantation is the extent of liver cell necrosis and moreso the potential regeneration ability. However, since there are notable predictors for the latter, the practice of auxiliary liver transplantation nowadays has been virtually abandoned.

References

[1] Data from the European Liver Transplant Registry. http://www.eltr.org.

[2] Merion R, Schaubel D, Dykstra D et al. The survival benefit of liver transplantation. Am J Transplant 2005; 5: 307-313.