Selection for Liver Transplantation

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Key Issues in Liver Transplant

• Indications

• Organ Allocation

• Care of the Cirrhotic Patient

• Recurrent Disease
**Patient Selection Criteria for LT**

- Accepted indications for LT
  - Advanced chronic liver disease
  - Acute liver failure
  - Unresectable hepatic malignancy
  - Inherited metabolic liver disease
- No alternative form of therapy
- No absolute contraindication to LT
- Willingness to comply with follow-up care
- Ability to provide for costs of LT

**Stable cirrhosis in absence of complications**
(Fattovich, Gastroenterology 1997)

![Survival probability graph showing patients at risk](#)

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Platelets <115,000 > predictor
Stages of Cirrhosis and Annual Mortality

- Stage 1 compensated, no varices: 1%
- Stage 2 varices: 3.4%
- Stage 3 ascites: 20%
- Stage 4 GI Bleeding: 37%

Tsochatzis 2012

Evaluation Process

- Assessment of Liver Disease Severity and Prognosis
- Presence of Complications
- Comorbidities
- Psychosocial Issues and Support
**Evaluation Process**

- Routine Biochemical and Hematological Panels (CBC, Creat. INR, LFTs, ABO)
- Serological Screen (Hepatitis Panel, HIV, EBV, CMV)
- Imaging of Abdomen
- Medical Consultations and Evaluations as clinically indicated (e.g., ID, Cardiology)
- Age appropriate Cancer Screening

**Contraindications to LT: Absolute**

- Active alcohol or substance abuse
- Advanced cardiopulmonary disease
- Systemic sepsis, unresponsive to Rx
- Multiorgan failure; multiple pressors
- Extrahepatic malignancy
- Severe pulmonary hypertension
- Severe psychiatric disease likely to affect compliance
Contraindications to LT: Relative

- General debility
- Advanced age
- Extensive portal/mesenteric thrombosis
- Social isolation and limited support
- HIV seropositivity
- Cholangiocarcinoma

Indications for Liver Transplantation 2005 (UNOS Registry)
Listing and Allocation

Deceased Donor Liver Allocation

February 2002 Changes

CTP Score

- Ascites
- Encephalopathy
- Bilirubin
- Prottime INR
- Albumin

MELD Score

- Creatinine
- Bilirubin
- Prottime INR

MELD Score = 0.957 x Log_{10}(creatinine mg/dL) + 0.378 x Log_{10}(bilirubin mg/dL) + 1.120 x Log_{10}(INR) + 0.643.
MELD and Survival

Cumulative Percent Surviving

- 92.3%
- 90.7%
- 66.0%
- 35.8%

P < 0.001

Months from Listing

Deaths per 1000 Patient-years on the Waiting List: MELD

Era 1

Era 2

n=910
n=743
n=62
n=45

Deaths per 1000 Patient-years

Adult

Pediatric
Listing and Allocation Criteria

- Allocation of organs: local → regional → national
- Acute liver failure (status I): first priority
- End-stage liver disease
  - Listing: MELD >15
  - Allocation: MELD
- HCC
  - Milan criteria (modified stage 2)
- Metabolic and cystic diseases
  - Petition to Regional Review Board (RRB)

HCC: Liver Transplantation

**Standard = Milan Criteria**

- Cirrhosis with unresectable small HCC
  - 1 tumor <5 cm, or
  - 3 tumors, each <3 cm
- Post-LT actuarial survival: 75% at 4 yr
  - Meet criteria (n=35, 73%): 85%
  - Not meet criteria (n=13, 27%): 50%

Assigned MELD Points for HCC

- Initial listing: 22 (15% probability of death)
- 3 months later: 25 (+10% probability of death)
- Each 3 months: 28 → 29 → 31 → 33
- Takes time to acquire higher MELD score
- Refer early

HCC: Controversies

- Role of tumor ablation pretransplant
- Downsizing to meet Milan criteria
- Role of sirolimus to prevent HCC recurrence
- Introduction of sorafenib
Problems with MELD

- Unwieldy formula with log functions
- Sicker patients no longer kept in the hospital
- MELD score >25 not discriminatory
- Variability in assays for INR and creatinine
- What about other factors, e.g., older age, PSC, refractory ascites, refractory HE
- Does not address geographic variability or effect of blood type on access to donor organs
- Sodium-MELD may enhance accuracy at lower MELD scores

Liver transplantation

Anticipating Complications
Cirrhotic Complications Pre-LT

- Ascites, Hepatic Encephalopathy
- Variceal Hemorrhage
- Spontaneous Bacterial Peritonitis

Prevalence and Size of Esophageal Varices in Patients with Newly-Diagnosed Cirrhosis

Mortality 20%-30% at 6 weeks

Pagliaro et al., In: Portal Hypertension: Pathophysiology and Management, 1994: 72
Large Varices are more Likely to Rupture

- No Varices
- Small Varices
- Large Varices

2-year probability of first bleed:
- Small varices: 7%
- Large varices: 30%

*p<0.01*


Prophylaxis of Variceal Hemorrhage

Diagnosis of Cirrhosis

- Endoscopy

No Varices
- Follow-up EGD in 2-3 years*

Small Varices
- Follow-up EGD in 1-2 years*

Medium/Large Varices
- Beta-blocker therapy
- No Contraindications
- Contraindications or Beta-blocker intolerance

- *EGD every year in decompensated cirrhosis
- Stepwise increase until maximally tolerated dose
- Continue beta-blocker (life-long)

Endoscopic Variceal Band Ligation
Spontaneous Bacterial Peritonitis (SBP) is the Most Common Infection in Cirrhotic Patients

Fernández et al., Hepatology 2002; 35:140

Clinical Characteristics of Spontaneous Bacterial Peritonitis

Fever
Jaundice
Abdominal pain
Confusion
Abdominal tenderness
Hypotension
No signs or symptoms

0 20 40 60 80 100 %
Mortality Associated with SBP has been Decreased by Early Diagnosis and Treatment

Indications for Prophylactic Antibiotics to Prevent Spontaneous Bacterial Peritonitis

- Cirrhotic patients hospitalized with GI hemorrhage (short-term)
  - Norfloxacin 400 mg p.o. BID x 7 days

- Patients who have recovered from SBP (long-term)
  - Norfloxacin 400 mg p.o. daily, indefinitely

- Weekly quinolones not recommended (lower efficacy, development of quinolone-resistance)

- Patients with low albumin in ascitic fluid.
Incidence of Hepatitis C Infection and Obesity in the United States, 1982-2005


Frequency of Fatty Liver Disease as an Indication for Liver Transplantation at Mayo

**Reasons for Early Referral to Transplant Center**

- Timely, stepwise evaluation of candidate
- Patient and family education about LT
- Intervention for confounding issues
  - Chemical dependence
  - Obesity and other medical issues
- Financial counseling
- Program selection by patient
  - Center-specific results, facilities, relationships with staff, etc.

**Liver Transplantation 2012**

- Excellent outcomes the norm
- Recurrent HCV major challenge
- Expanding role in HCC
- NAFLD evolving indication
- Anticipating complications important in cirrhotic patients.