Patient Selection and Survival

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Clarian/IU Digestive Disease Center
An Indiana University School of Medicine & Clarian Health Partnership

Potential Conflicts

- Consulting agreements with many pharma companies
- Clinical trials with Lilly, Debiovision, Gilead

Do not represent conflicts for this presentation

Outline

- Definitions
- Indications
- Contraindications
- Evaluation process
- Management while waiting
- Survival

Liver transplantation

- Orthotopic vs. auxiliary
- Adult vs. pediatric
- Cadaveric vs. living related
- Living related – right lobe or left lobe
- Domino transplant
- Re-transplantation

When to refer a patient to transplant center?

- Acute liver failure
  - Acetaminophen: renal failure, acidosis, encephalopathy
  - Non-APAP: encephalopathy, increasing INR, ↑ bilirubin
- New complication in a stable cirrhotic
- Newly diagnosed decompensated cirrhotic
- Abnormal hepatic imaging
- Patient/family request

Indications

- Fulminant liver failure
- Complications of cirrhosis/liver disease
- Systemic complications of liver disease
- Metabolic disorders

Indications: Fulminant Liver Failure

- Acetaminophen toxicity, idiosyncratic drug induced liver injury, HBV, Wilson's disease
- King's college criteria
- IV N-acetyl cysteine may have a role
- Cerebral edema, infection and multi-organ failure are frequent causes of death
- Status 1
- One year survival may be lower

Indications: Complications of Cirrhosis

In general, decompensated cirrhosis is an indication for liver transplantation

- Ascites
- Encephalopathy
- Recurrent variceal bleeding
- HCC
- Intractable itching
- Recurrent cholangitis or liver abscess in PSC

Liver transplantation for HCC

- Milan criteria: single lesion < 5 cm or max 3 lesions with no lesion exceeding 3 cm PLUS no evidence of extrahepatic or vascular invasion
- UCSF criteria [single lesion < 6.5 cm or three lesions < 4.5 cm with total < 8 cm]
- Tumor downsizing may be beneficial
- Biopsy may not be needed
- Survival can be excellent, depending on patient selection

Systemic Complications

- Hepatopulmonary syndrome
- Portopulmonary syndrome
- Hepatic osteodystrophy

Liver transplantation for Metabolic disorders

- Primary hyperoxaluria
- Familial Primary Amyloidosis
- Urea cycle defects

Potential for Domino transplantation exists

Contraindications

Absolute

- Active extrahepatic malignancy
- HCC with metastasis or vascular invasion
- Uncontrolled infection outside liver
- Active drug or alcohol abuse
- Severe cardiopulmonary ds
- Poor psychosocial status
- Technical barriers
- Brain death

Relative

- Age
- BMI
- Cholangiocarcinoma
- HIV
- Previous malignancy
- Previous psychiatric illness
- Poor social support
- Non-compliance

Evaluation Process

- To establish that liver disease is severe enough
- To establish that there are no contraindications
- Center-specific algorithm
- Labs, cardiopulmonary evaluation, hepatic imaging, general health assessment, transplant surgery, anesthesia, psych, social work, nutrition and financial

MELD forms the basis for listing

- 3 variables: total bili, INR and creatinine
  $0.936 \times \text{Log}_e$ (creatinine [mg/dl]) + $0.378 \times \text{Log}_e$ (total bilirubin [mg/dl]) + Log_e(INR) + 0.643
- Minimal MELD for listing: 15

Recipient listing status

- Status 1A: ≥ 18 years of age and FHF or primary non-function or hepatic artery thrombosis following recent liver transplantation
- Status 1B: MELD > 25 and mechanical ventilation or ongoing GI bleeding or dialysis/hemofiltration or Glasgow coma score < 10 within 48 hours of listing
- Regular listed status according to MELD score
- Upon listing, MELD score is periodically reevaluated; status 1 or MELD > 25 (every week), MELD 19-24 (every month) and MELD 11-18 (every 3 months)

MELD exceptions

Hepatocellular carcinoma
Recurrent hepatic encephalopathy
Hepatopulmonary syndrome
Portopulmonary syndrome
Familial amyloidosis
Cystic fibrosis
Polycystic liver disease
Primary oxaluria
Recurrent cholangitis
Unusual tumors (metastatic carcinoid)

- In these instances, an appeal can be made to the regional boards to assign additional points to their MELD scores.

Wait list activity and Patient status at 6, 12 and 18 months from listing (listed in 2006)

	Total listed (n=11,037)		
	6 months	12 months	18 months
Alive on list	43%	31.5%	25%
Died on list without OLT	7%	8.7%	10%
Removed from the list	3%	4%	4.5%
Cadaveric transplant	36.5%	37.7%	27.7%
Living related donor LT	1.5%	1.6%	1.3%

Managing while on the list

- High attrition and complication rate
- Judicious management of complications
- Avoidance of nephrotoxic agents, including contrast studies
- Screening for HCC and varices
- Vaccination against hep A and B, pneumovax and influenza
- Monitoring bone health
- Attention to routine screening tests

Graft and Patient Survival in Adults 0/7/01/2005 through 12/31/2007

	1 month	1 year	3 years
Graft survival	93.8%	83.38%	72.93%
Patient Survival	96.48%	87.85%	77.8%

Individual center's results are available at the UNOS website (www.UNOS.org)

Factors affecting survival

- Immediate post-op: pre-op condition, renal failure, procedural complications, prolonged intubation and systemic infections
- Short-term: Acute rejection, biliary and vascular complications, infections and HCV recurrence
- Long-term: Recurrent HCV, **coronary artery disease**, **renal failure**, diabetes, obesity and malignancy

Re-transplantation

- Primary non-function or hepatic artery thrombosis accounts for up to 75% early re-transplantation
- Recurrence of primary disease (HCV mainly) and chronic rejection are common reasons after first year
- 3-year survival is ~ 50% for re-transplantation

Organs from non-heart-beating donors

- Organs from controlled non-heart-beating donors are a potential source
- Outcomes are probably inferior to heart-beating donors
- Organ from a non-heart-beating donor is one of the risk factors in the “Donor Risk Index”
- May have limited role for those with very high MELD scores

Summary

- Over the last three decades, the art and science of orthotopic liver transplantation has evolved significantly and is continuing to improve
- For carefully selected patients, liver transplantation not only prolongs survival but can dramatically improve their quality of life