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New Jersey Medical School
DEPARTMENT OF SURGERY

10th Annual Update on Liver Disease: A Multidisciplinary Approach

Session: Liver Failure

The Surgeon (Transplant)

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Disclosures

- I have no financial disclosures to report



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Introduction

Background

- Orthotopic liver transplant is the removal of a patient's native liver and replacement with a whole or partial liver from a donor
- It is a treatment option for patients with decompensated end-stage liver disease, acute liver failure, and certain liver malignancies
- Liver transplant provides life-saving therapy that confers a mortality benefit for select patients

Liver Transplant by the Numbers – 2022

- Waiting List
 - 13,180 additions
 - 1,032 died waiting
 - 1,109 were too sick to transplant
 - 1,057 improved and removed from waitlist
- Transplants
 - 8,925 deceased donor liver transplants
 - 603 living donor liver transplants

10,618 remaining on the waiting list

Acute Liver Failure

- Severe acute liver injury
- Hepatic encephalopathy
- Coagulopathy
- No pre-existing liver disease

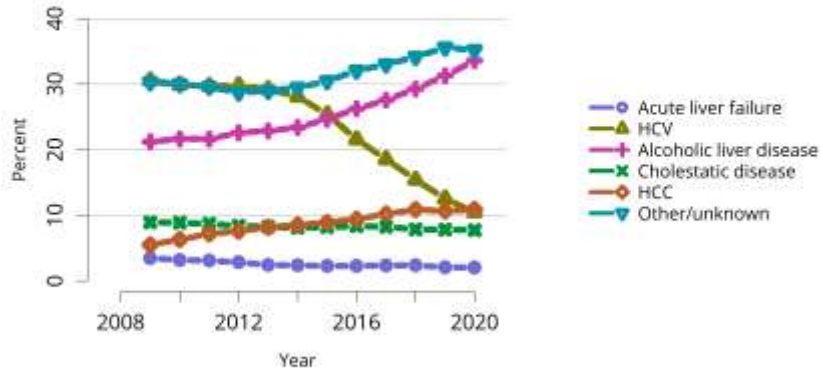
- 40% of patients may spontaneously recover
- Ideally managed at a center with an active liver transplant program
 - Early recognition and early transfer are critical to successful outcome
 - Patients quickly become too sick for transfer

Acute Liver Failure

- Potential etiologies
 - Autoimmune hepatitis
 - Wilson Disease
 - Acute hepatitis B infection or other viral hepatitis infections
 - Tylenol or other drug toxicity
 - Mushroom poisoning
 - Budd-Chiari syndrome
 - Acute liver failure in pregnancy
 - Herpes simple virus infection
 - Idiopathic/unknown etiology

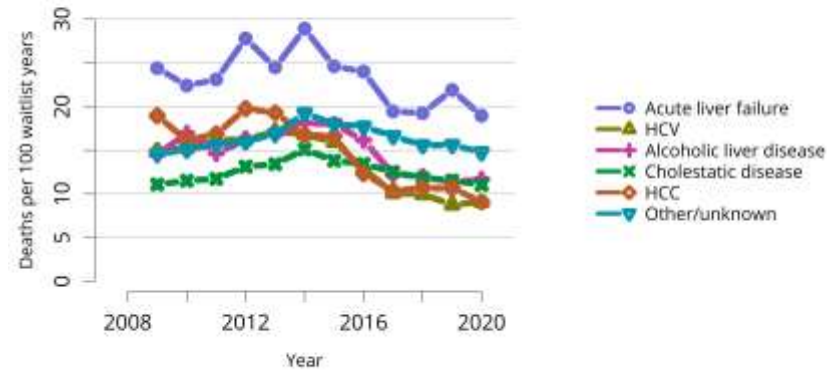
Acute Liver Failure

Figure 6. Distribution of adults waiting for liver transplant by diagnosis



OPTN/SRTR 2020 Annual Data Report

Figure 28. Pretransplant mortality rates among adults waitlisted for liver transplant by diagnosis



OPTN/SRTR 2020 Annual Data Report

Case Study

18M reports 2 weeks of fatigue and progressive yellowing of his eyes. Initially presented to urgent care but referred to local ER for abnormal liver function tests.

- PMH: history of mono
- PSH: none
- HM: none
- Allergies: none
- Social: college student, never used alcohol, never used tobacco
- Family: no liver or autoimmune history in family



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Listing

Transplant Evaluation Requirements for Listing

- Labs
 - CMP
 - CBC
 - PTT/INR
 - Blood type
 - ABG
 - Tumor markers
 - Infectious serologies
 - Autoimmune serologies

Transplant Evaluation Requirements for Listing

- Cardiopulm work-up
 - EKG
 - TTE
 - Stress test
 - RHC/LHC as indicated
 - CXR
 - PFTs as indicated
- GI Work-up
 - EGD screen for varices
 - Cross-sectional imaging to evaluate for liver malignancy

Transplant Evaluation Requirements for Listing

- Health Maintenance
 - Age-appropriate cancer screening (colorectal, breast, prostate, cervical)
 - Skin exam
 - Immunizations
- Psychosocial Work-up
 - Attend education session
 - Psychological evaluation
 - Social support evaluation

Transplant Evaluation Requirements for Listing

- Consults
 - Surgical evaluation
 - Pharmacy evaluation
 - Nutrition evaluation
 - Financial screening
- Optional Consults
 - Addiction medicine
 - Infectious disease
 - Critical care
 - Anesthesia
 - Other specialists depending on patient's medical history

Contraindications for Transplant

- Uncontrolled non-hepatic malignancy or without a long enough disease-free interval
- Hepatocellular carcinoma with metastases outside the liver
- Uncontrolled sepsis
- Unmanageable cardiopulmonary disease
- Anatomical reasons
- Acute liver failure with poor cerebral perfusion
- Persistent non-adherence
- Lack of social support

Model for End-Stage Liver Disease (MELD) Score

- Initial MELD(i) score equal to:
 $0.957 \times \text{Loge}(\text{creatinine mg/dL})$
 $+ 0.378 \times \text{Loge}(\text{bilirubin mg/dL})$
 $+ 1.120 \times \text{Loge}(\text{INR}) + 0.643$
- If initial MELD score > 11 , re-calculated with Na
 - $\text{MELD} = \text{MELD}(i) + 1.32 \times (137 - \text{Na}) - [0.033 \times \text{MELD}(i) \times (137 - \text{Na})]$

MELD	3mo Mortality Risk
>40	71.3%
30-39	52.6%
20-29	19.6%
10-19	6%
<9	1.9%

Wiesner R, Edwards E, Freeman R, Harper A, Kim R, Kamath P, Kremers W, Lake J, Howard T, Merion RM, Wolfe RA, Krom R; United Network for Organ Sharing Liver Disease Severity Score Committee. Model for end-stage liver disease (MELD) and allocation of donor livers. *Gastroenterology*. 2003 Jan;124(1):91-6. doi: 10.1053/gast.2003.50016. PMID: 12512033.

Status 1A Listing

- Age > 18 years
- Life expectancy < 7 days without liver transplant
- At least one of the following diagnoses:
 - Acute liver failure
 - Anhepatic
 - Primary non-function within 7 days of transplant
 - Hepatic artery thrombosis within 7 days of transplant
 - Acute decompensated Wilson Disease

Status 1A Listing – Acute Liver Failure

- Hepatic encephalopathy within 56 days of first sign or symptom of liver disease
- No pre-existing liver disease diagnosis
- Admitted to an ICU
- At least one of the following:
 - Ventilator dependent
 - Requires HD or CVVH
 - INR > 2

Case Study

Admission Labs

- Total bilirubin: 29.0
- Creatinine: 1.3
- INR: 5.4
- Sodium: 133
- AST: 889
- ALT: 1,158
- Albumin: 2.8
- Alk Phos: 138

MELD-Na Score: 41

Case Study

- Within 3 days developed worsening encephalopathy
- Transferred to ICU
- Started CVVH for volume management
- Total bilirubin: 36.6
- Creatinine: CVVH
- INR: 12.1
- Sodium: 132

MELD-Na Score: 61



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Find a Donor Organ

Status 1A

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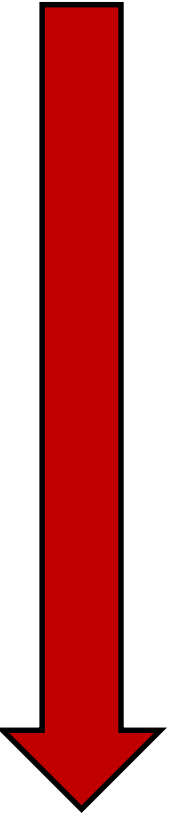
Standard Criteria Donor

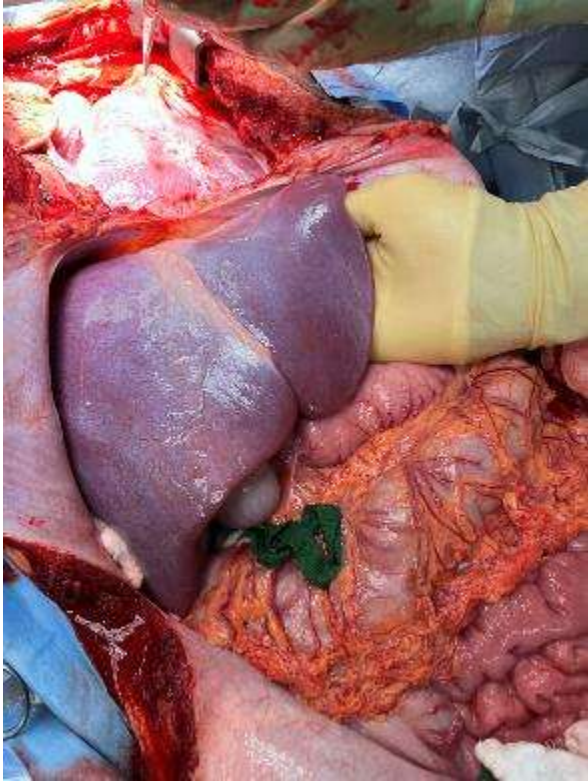
- Donor age 18-70
- Donation after Brain Death

Extended Criteria Donor

- Donor age over 70
- Macrosteatosis
- Donation after Cardiac Death
- Positive serologies (HBV, HCV)
- PHS high-risk donor

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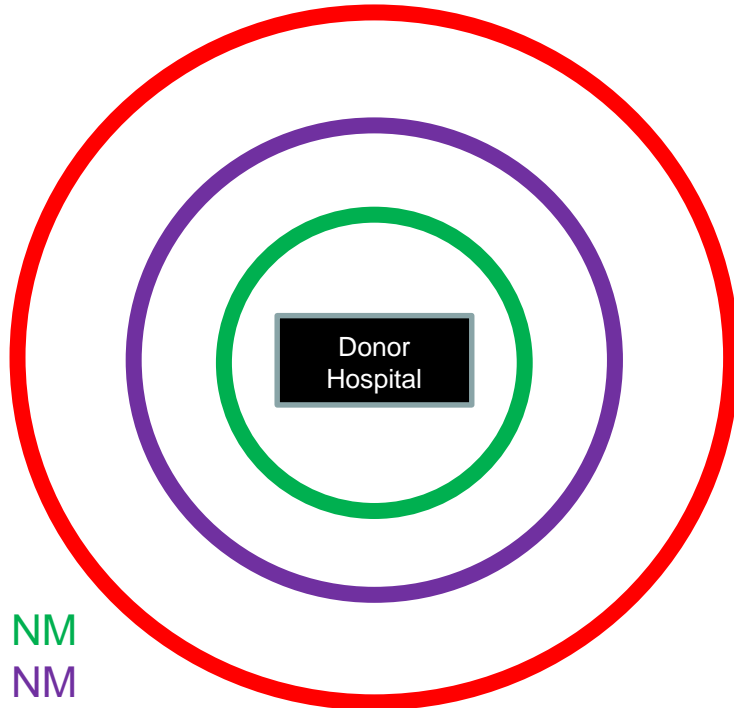








Acuity Circles



150 NM
250 NM
500 NM

- Status 1A within 500 NM
- MELD 40 → 37
 - 150 NM
 - 250 NM
 - 500 NM
- Repeat for MELD 33-36, 29-32, 15-28

Case Study

- Urgently listed for liver transplant
- 48 hours later had a suitable donor offer
- Standard Criteria Donor: 58F, donor after brain death
- Whole liver with $<5\%$ macro





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Transplant

Operative Procedure

- 6-12 hours of surgery
- Removal of native liver
 - Dissect liver from all its attachments: diaphragm, vena cava, portal vein, hepatic artery, bile duct
- Preparation of donor liver – backbench procedure
- Implantation of donor liver
 - Vena cava outflow, portal vein inflow, hepatic artery inflow, biliary reconstruction
- Hemostasis
- Closure vs Temporary Closure/Planned Second Look

Anesthesia Concerns

- Monitoring
 - Central line
 - Swan-Ganz catheter
 - Arterial line
 - Coagulation profile
 - Thromboelastography
 - Rotational thromboelastometry
- Resuscitation
 - Products in room
 - RBC
 - FFP
 - Cryoprecipitate
 - Platelets
 - Vasopressors
- CVVH

Case Study

- Intraoperative CVVH
- Temporary abdominal closure
- Estimated Blood Loss: 3L

Path: Extensive necrosis of liver parenchyma with only a few areas containing viable hepatocytes. Extensive bile ductular reaction suggestive of an ongoing process. Differential diagnosis includes drug reaction or metabolic disease



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Outcomes

Short Term Outcomes

- Typical ICU length of stay ranges 1-3 days
- Typical hospital length of stay ranges 7-18 days
- Graft Failure
 - 5.9% at 6 months (94.1% graft survival)
 - 7.9% at 1 year (92.1% graft survival)
- Acute Rejection
 - 11.5% in the first year

Long Term Outcomes

- Graft Failure
 - 14.7% at 3 years (85.3% graft survival)
 - 20.7% at 5 years (79.3% graft survival)
 - 40.6% at 10 years (59.4% graft survival)

**Graft Survival \neq
Patient Survival*

- There are 98,842 liver transplant recipients alive in the US as of 6/30/2020

Outcomes after Transplant for ALF

- Multicenter prospective cohort of adult patients with ALF listed for liver transplant 1998-2018
- 624 patients listed
 - 398 (64%) underwent transplant
 - 100 (16%) died without transplant
 - 126 (20%) recovered spontaneously
- Etiologies for those receiving transplant
 - 22% indeterminate
 - 18% drug-induced liver injury
 - 16% Tylenol toxicity
 - 15% viral hepatitis

Karvellas CJ, Leventhal TM, Rakela JL, Zhang J, Durkalski V, Reddy KR, Fontana RJ, Stravitz RT, Lake JR, Lee WM, Parekh JR. Outcomes of patients with acute liver failure listed for liver transplantation: A multicenter prospective cohort analysis. Liver Transpl. 2022 Aug 18. doi: 10.1002/lt.26563. Epub ahead of print. PMID: 35980605

Outcomes after Transplant for ALF

- Survival after Transplant
 - 91% at 1 year
 - Most deaths that occur post-transplant are in the first month (67%)
 - 90% at 3 years
- Patients who died before reaching transplant
 - More severe multiorgan failure (vent dependent, pressor use, CVVH)
 - Older age, higher MELD score, higher grade encephalopathy
- Tylenol toxicity
 - Most common etiology for ALF requiring listing (29.3%)
 - Most common etiology in patients who died on waitlist (35%)
 - Most common etiology in patients who recover (66%)

Case Study

- Patient closed on POD 2
- Patient went back to OR for bleeding on POD 4
- ICU for 7 days
- Required CVVH → HD → renal recovery after 19 days
- Total hospital length of stay 20 days

- No readmissions or complications post-transplant

Summary

- Acute liver failure can end in timely transplant, death, or spontaneous recovery
- Early recognition and early transfer are critical to a successful outcome
- Liver transplant requires comprehensive work-up before listing
- Donor livers are allocated based on MELD score (sickest first)
- Not all donor livers are alike
- Liver transplant surgery and perioperative management are complex
- Short and long-term outcomes after liver transplant are excellent, including in acute liver failure



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Thank You

Questions?