Selection and Evaluation for Transplantation

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Disclosures:

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We have some material to cover in the next 20 minutes

MELD/PELD scoring systems
MELD/PELD exceptions
Multi-organ candidates
Co-morbidities
Impact of active infection, malignancy and malnutrition
Psychosocial issues

- § 121.8 of the Final Rule states that allocation policy should be based on "objective and measurable medical criteria, for patients or categories of patients who are medically suitable candidates for transplantation to receive transplants"
- Patients should be rank ordered from most to least medically urgent on the waiting list

Adult candidate assignments

- Adult status 1A
- Calculated MELD-Na score
- Exception MELD score
- Inactive status

Pediatric candidate assignments

- Pediatric status 1A
- Pediatric status 1B
- Calculated MELD/PELD score
- Exception MELD/PELD score
- Inactive status

Policy 9: Allocation of Livers and Liver-Intestines

https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf

Adult status 1A requirements (1)

1. Fulminant liver failure in ICU, no pre-existing liver disease
   - HE within 56 days of onset AND *one* of:
     - Ventilator dependent or
     - On HD, CVVH, CVVHD or
     - INR > 2.0
2. Anhepatic
3. Primary non-function of allograft within 7d of txp
   - AST ≥3000 IU/L AND *one* of:
     - INR ≥ 2.5
     - Arterial pH ≤ 7.3
     - Venous pH ≤ 7.25
     - Lactate ≥ 4 mmol/L

OPTN Policy 9, effective 5/21/20

Adult status 1A requirements (2)

4. HAT within 7 days of txp
   - AST > 3000 IU/L AND *one* of the following:
     - INR ≥ 2.5
     - Arterial pH ≤ 7.30
     - Venous pH ≤ 7.25
     - Lactate ≥ 4 mmol/L
5. Acute decompensated Wilson disease

Pediatric status 1A requirements (1)

1. Fulminant liver failure, no pre-existing liver disease
   - HE within 56 days of onset AND *one* of:
     - Ventilator dependent or
     - On HD, CVVH, CVVHD or
     - INR > 2.0
2. Primary non-function of allograft within 7 d of txp
   - AST ≥2000 IU/L AND *one* of:
     - INR ≥ 2.5
     - Arterial pH ≤ 7.3
     - Venous pH ≤ 7.25
     - Lactate ≥ 4 mmol/L

Pediatric status 1A requirements (2)

3. HAT within 14 days of txp
4. Acute decompensated Wilson disease

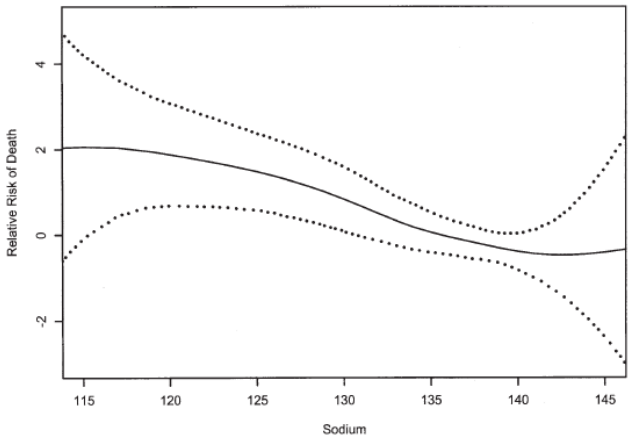
Pediatric status 1B requirements (1)

1. Hepatoblastoma without metastatic disease
2. Organic acidemia or urea cycle defect and has had an approved PELD exception for metabolic disease for > 30 days
3. Chronic liver disease with calculated MELD/PELD of greater than 25 AND *one* of:
   - Mechanical ventilation
   - GI bleeding with >30 mL/kg RBC transfusion in 24 hours
   - HD, CVVH, or CVVHD
   - Glasgow coma score of < 10, 48 hours prior to status 1B assignment

MELD and MELD-Na

- MELD=0.957 x $\log_e$ (Cr mg/dL) + 0.378 x $\log_e$ (bili mg/dL) +1.120 x $\log_e$ (INR) +0.643
- Cr set to 4 mg/dL when:
  - Cr > 4.0 mg/dL
  - Two or more dialysis treatments in last 7 days
  - 24 hours of CVVHD in last 7 days
- MELD still used for candidates with MELD≤11

6 Month wait list mortality as a function of serum sodium



Biggins SW et al, Gastroenterology 2006;130:1652-1660

MELD-Na

- Used for allocation if MELD ≥12
- MELD-Na=$MELD_{(i)}$ +1.32 (137-Na) – [0.033x$MELD_{(i)}$x(137-Na)]
- Sodium values less than 125 mmol/L are adjusted to 125 mmol/L

PELD score

- Used for candidates <12 years old
- PELD=0.436(if age < 1 yr)-0.687x$\log_e$(albumin g/dL)+0.480x$\log_e$(bili mg/dL)+1.857xloge(INR)
- +0.667(growth failure)
- Growth failure=2 standard deviations below expected growth for age and gender

Major changes to MELD exceptions effective 2019

- No longer a q 3 month MELD escalator
- MELD scores provided for standard exceptions are based on Median MELD at Transplant (MMaT)
- MMaT is calculated for geographic areas every 180 days
- Most adult exception scores are MMaT-3

Standard MELD exceptions (1)

- HAT < 14 days MELD=40, if not Status 1
- Primary hyperoxaluria= MMaT (SLK, biopsy or mutation proven, GFR≤25mL/min by MDRD6)
  - 3 month escalator
- HCC= MMaT - 3 6 months after listing
- CCA=MMaT - 3
- FAP= (EF > 40%, ambulatory, identified mutation and biopsy proven)
  - MMaT - 3

Standard MELD exceptions(2)

- Cystic fibrosis= MMaT - 3 (FEV1 < 40%)
- HPS= MMaT – 3 (Evidence of shunt, PaO_2<60 mmHg, no underlying primary lung disease, clinical evidence of portal hypertension)
- PPH= MMaT – 3 (Post-treatment MPAP<35 mmHg, Post-treatment PVR < 400dynes/sec/cm^{-5}

Non-standard MELD/PELD exceptions

- Must go to National Liver Review Board
- Request a specific MELD/PELD score
- Justify why request is appropriate for score requested
- Majority vote of NLRB voters

Guidance to Liver Transplant Programs and the National Liver Review Board for:

Adult MELD Exception Review

https://optn.transplant.hrsa.gov/media/2847/liver_guidance_adult_meld_201706.pdf

Standard pediatric MELD/PELD exceptions (1)

- HAT < 14 days MELD=40, if not Status 1
- Primary hyperoxaluria= MMat + 3 points at listing (SLK, biopsy or mutation proven, GFR≤25mL/min by MDRD6)
- Urea cycle disorder or organic acidemia- MMaT
  - If no txp in 30 days, can go to Status 1B
- HCC=score of 40 points immediately
  - 3 month escalator, capped at 34
- CCA= MMaT
  - 3 month escalator

Standard pediatric MELD/PELD exceptions (2)

- CF= MMaT/MPaT
- HPS=MMaT/MPaT
- PPH=MMaT/MPaT

National Liver Review Board

- Implemented May 2019
- National anonymous review panels with waitlist mortality based guidance
- Expected to reduce non-standard exceptions
- Expected to eliminate regional variability in award of exceptions
- Each center may have two reviewers for adult non-HCC, peds and HCC boards

Simultaneous liver/kidney transplantation

- New policy in effect in August 2017 radically changed transplant options
- No real restriction on combined txp previously
- Rigorous rules in place now
- Safety net for recipients who do not undergo renal recovery after OLT

Simultaneous adult liver/kidney allocation requirements

Diagnosis to qualify	Subsequent documentation
Chronic kidney disease GFR < 60 mL/min > 90 consecutive days	Must have one of : -Initiated regularly scheduled RRT -GFR ≤ 30 mL/min at time of registration for KT or after registration for KT
Sustained acute kidney injury No pre-existing GFR requirement	Must have one, or combination of both, for at least 6 weeks: -On dialysis at least once a week every 7 d -calculated CrCl or GFR of less than 25 mL/min every 7 d
Metabolic disease	Hyperoxaluria Atypical hemolytic uremic syndrome

OPTN Policy 9.7.B

Other liver/SOT combinations

- No restrictions on simultaneous allocation
- Lung/liver transplantation
  - 2019-12 cases performed in US (largely CF)
- Heart liver transplantation
  - 2017-45 cases performed in the US (increasing, with more decompensated CHD with cirrhosis)
- All others liver combinations except liver intestine very rare

Comorbidities

- HIV
- Heart disease
- Pulmonary disease/tobacco abuse
- Skin malignancy
- Non-hepatic malignancy
- Frailty/sarcopenia
- Psychosocial support

HIV and liver transplantation

- Inclusion criteria:
  - CD4 count> 100 cells/uL without hx of OI
  - CD4 count > 200 cells/uL with prior resolved OI
  - Undetectable HIV viral load OR
    - Expectation of undetectable HIV viral load after txp
  - Documented compliance with ART regimen
  - Absence of chronic wasting/malnutrition
- HOPE Act permits HIV + organs into HIV + recipients at qualified centers

Blumberg E, et al. Am J Trans 2013;13:169-178
Fox AN, et al. Semin Liver Dis 2012;32:177-185

HIV and liver transplantation

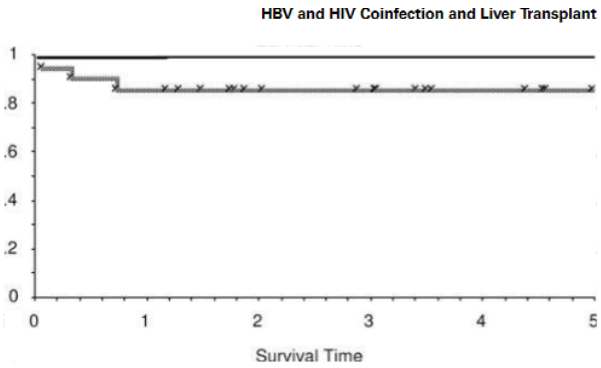


Figure 1: Cumulative patient survival, comparing HBV-HIV coinfected (N = 22) and HBV monoinfected (N = 20) transplant recipients. No significant differences were observed in patient survival between groups (p = 0.09, log-rank test).

Coffin CS, et al. Am J Transplant 2010;10:1268-1275

Predictors of outcome in HIV liver transplant

Predictor Multivariate Analysis	Hazard Ratio (95% CI)	P value
Dual Kidney-Liver	5.5 (1.8, 16.9)	0.003
HCV+ Donor	4.5 (1.8,11.2)	0.001
BMI at Listing <21	2.7 (1.0, 7.3)	0.05
Treated Acute Rejection	2.9 (1.2, 7.0)	0.02

Solid Organ Transplantation in HIV: Multi-Site Study (AI052748)

Cardiovascular testing

- Echocardiogram with bubble study
  - Assess RV and LV function
  - r/o HPS
  - r/o pulmonary HTN (beware RVSP > 35 mmHg)
- EKG
  - Assess for long QT, dysrythmia
- Pharmacologic stress testing
  - Largest data for dobutamine stress echo
- Cath as indicated by above (RHC or LHC, radial approach preferred in setting of coagulopathy)

Consensus recommendations for cardiac disease assessment

TABLE 1 Cardiac and pulmonary vascular disease contraindications to liver-alone transplantation: consensus recommendations[a]

Cardiac or pulmonary vascular condition	Absolute contraindications	Relative contraindications
Coronary artery disease	Nonrevascularized obstructive severe multivessel CAD	Nonrevascularized obstructive moderate CAD not involving left main or proximal LAD coronary arteries
Cardiomyopathy and heart failure	Left ventricular ejection fraction <40% Moderate to severe right heart failure	Left ventricular ejection fraction <50% Hypertrophic cardiomyopathy with resting left ventricular outflow tract obstruction
Portopulmonary hypertension	Severe pulmonary hypertension associated with right heart failure and/or not responsive to medical therapies	Moderate pulmonary hypertension with preserved right ventricular function not responsive to medical therapy
Cardiac arrhythmias	Recurrent ventricular arrhythmias	Recurrent unstable arrhythmias
Valvular heart disease	Severe irreversible valvular disease	Moderate pulmonary hypertension with preserved right ventricular function not responsive to medical therapy
Congenital heart disease	Congenital heart disease plus moderate to severe right heart failure not responsive to medical therapy	Congenital heart disease plus moderate pulmonary hypertension with preserved right ventricular function not responsive to medical therapy

CAD, coronary artery disease; LAD, left anterior descending.
[a]Expert consultation with a cardiologist or pulmonary hypertension specialist familiar with liver transplantation surgery is recommended prior to decision making in all situations.

VanWagner LB, et al., Am J Transplant 2018;18:30-42

Lung disease pre-OLT

- Tobacco consumption should be prohibited in OLT candidates
  - Increased CV mortality
  - Increased risk of hepatic artery thrombosis
  - Increased risk of lung and oropharyngeal cancer post-OLT
- Impact of COPD not studied with FEV1<30%
  - Risk of death not worse with lesser degree of impaired FEV1
- No published precise guidelines about COPD
  - Presence of obstructive or restrictive lung disease associated with longer intubation and ICU but not post-op mortality

Martin P, et al., Hepatology 2014;1144-1165. Krowka MJ, et al., J Hepatol 2013;367-374.
Leithead JA, et al., Liver Transpl 2008;14:1159-1164.
Pungpapong S, et al., Liver Transpl 2002;582-587. Kia L, et al., Liver Transpl 2016;22:805-811

Skin malignancy pre-txp

Skin malignancy	Appropriate treatment pre-txp	Wait time before txp
Low risk squamous cell cancer (SCC)	Excision with clear margins	No delay
High risk SCC	Excision with clear margins	2 years
w/perineural invasion or ≥ 2 risk factors	Excision with clear margins +/- radiation therapy	2-3 years
SCC with nodal disease	Excision/LN resection/XRT	5 years
SCC with distant mets	Oncology	Not eligible for OLT
In situ melanoma	Wide local excision	No delay, f/u 3 mos post-txp
Stage Ia melanoma	Wide local excision	2 years
Stage Ib/IIa melanoma	Wide local excision +/- sentinel node biopsy	2-5 years
Stage IIb/IIc melanoma	Wide local excision +/- sentinel node biopsy	5 years
Stage III or IV melanoma	Oncology	Not eligible for OLT

Zwald F, et al. Am J Transpl 2016;16:407-413

Non-hepatic malignancy

- Age appropriate cancer screening recommended
  - Colonoscopy, mammography, Pap smear, prostate ca
- Candidates with prior extra-hepatic cancer should have definitive therapy with expected adequate tumor free survival
  - Oncology communication
  - Israel Penn International Transplant Tumor Registry
    - www.ipittr.uc.edu

Frailty, sarcopenia

FrAILT
Functional Assessment in Liver Transplantation

Liver Frailty Index

Inputs: For instructions, see ⓘ below.

1. Gender: ○ Male ○ Female
2. ⓘ Dominant hand grip strength (kg):
   attempt 1: attempt 2: attempt 3: Avg: kg
3. ⓘ Time to do 5 chair stands: sec
4. ⓘ Seconds holding 3 position balance:
   Side: SemiTandem: Tandem: Total: sec

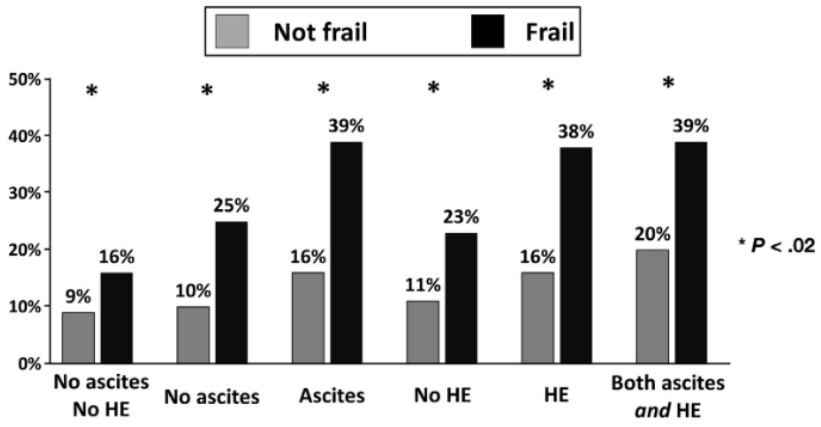
Results: refresh results

The Liver Frailty Index is _____

Decimal precision: 2

www.liverfrailtyindex.ucsf.edu

Waitlist mortality

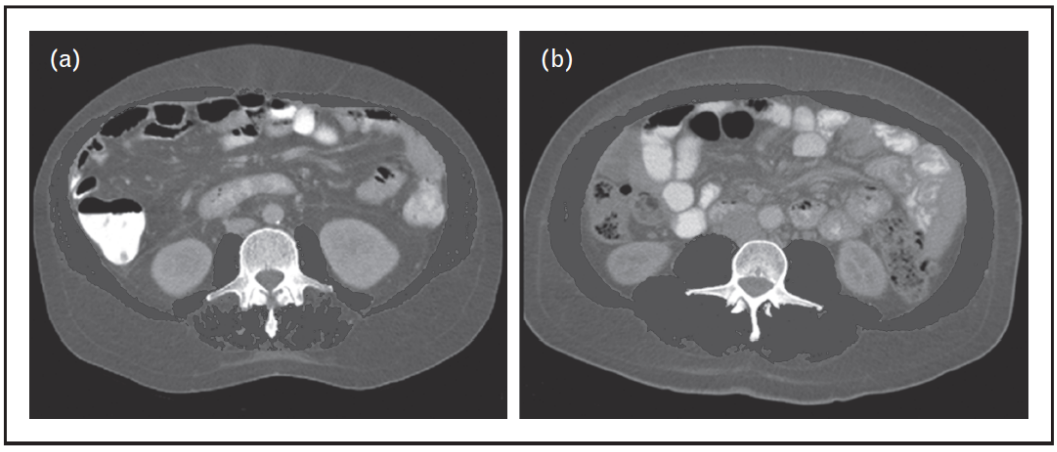


Lai, JC et al., Gastroenterology 2019;156:1682

Sarcopenia

- Better assessment of nutrition than BMI (ascites/edema)
- Predicts pre-transplant survival, post-OLT infection, LOS
- Failure to improve after transplant predicts mortality

Montano-Lopez AJ, et al., Liver Transpl 2014;20:640-648



Sarcopenic

Not Sarcopenic

Montano-Lopez AJ. Curr Opin in Clin Nutr & Metabol Care 2014;17:219-225

Psychosocial support

- Assessment of compliance
- Adequacy of support for perioperative recovery
- Absence of active psychiatric disease that could impact compliance, substance use
- Adequacy of financial coverage for post-operative care

Active infection and OLT

- Literature is sparse and observational
- Extrahepatic infection of more concern
  - Removal of infected PSC liver of low systemic risk
- SBP is a common issue
  - Waiting 48 hours from start of therapy reasonable
    - Negative blood cultures
    - Retap for evidence of improvement
- Bacteremia more challenging
  - Common recommendation for 48 hours of negative cultures and absence of deep seated infection (i.e. osteomyelitis, endocarditis, infected joint, etc.)

“Active” infection and OLT

- Less common organisms very difficult to manage, no clear guidelines, scattered case reports
- Cryptococcal meninigitis
- MAC pulmonary infections
- Latent tb can be managed post-OLT
- Transplant ID input essential

Contraindications to OLT

- Driven by likelihood of survival and futility tradeoff
  - No actual policy that defines absolute contraindication
- Frailty
- Uncontrolled infection
- Uncontrollable extrahepatic organ disease
  - Heart, lung, neurologic disease
- Presence of extrahepatic malignancy with low chance of treatment
- Absence of appropriate caregiving plan for support during recovery
- Absence of financial means for follow-up and immunosuppression