15th Annual Liver Update: 
LIVER TRANSPLANTATION

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Functional Assessments: Measures of Sarcopenia and Frailty & Patient Outcomes on the Liver Transplant Wait List
Determining Futility for Transplantation: Adjuncts to the MELD Score

Case I
- 55 y/o M with HCV-Cirrhosis, c/b ascites, non-bleeding EV and minimal HE
- Working part-time/active, listed MELD 19
- Admitted w/ severe SBP and develops HRS
- ICU on CVVH, not intubated
- INR 2.5 Bili 7.5 Na 133 → **MELD 38**

Case II
- 55 y/o M with HCV-Cirrhosis
- Similar decompensation
  - **MELD 38**, ICU with sepsis and renal failure
- Past 1 year: 6 hospitalizations

![Trajectory of decline](image_url)
Is it futile to transplant a MELD>40 patient?

<table>
<thead>
<tr>
<th>Probability of Restoration</th>
<th>Medical Need</th>
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Is it futile to transplant a MELD>40 patient?

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<td>Low, Futile?</td>
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<tr>
<td>High</td>
<td>Wait, Proceed</td>
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- Low Medical Need: Futile? (Futile? indicates uncertainty)
- High Medical Need: Proceed
Sarcopenia and Outcomes for Wait-Listed Patients

Abstract 1: Elizabeth Carey et. al: A multi-center study to define sarcopenia in patients with ESLD: from the Fitness, Life, Enhancement, and Exercise in Liver Transplantation (FLEXIT) Consortium

Background & Methods

• Study of sarcopenia (muscle depletion) & wait list mortality for cirrhotic patients

• Multi-Center Study (5 NA LT Centers)

• Newly listed patients (calendar year 2012)

• Recent CT scan (w/i 3 months)

• Radiologic assessment of muscle mass (total cross-sectional area of abdominal skeletal muscles at L3) using image analysis software
  • psoas, para-spinal, abdominal wall
Skeletal muscle index (cm$^2$/m$^2$): measured at L3 and normalized for height

Skeletal Muscle Index = total muscle area/ht sq
Sarcopenia and Outcomes for Wait-Listed Patients

• Outcome: weight list mortality (WLM)
  • Death prior to LT
  • Delisting for clinical deterioration

• Results
  • 396 patients
  • Median age 58
  • 70% M / 30% F
  • Median MELD 15
  • Median SMI 47.6 (41.8 – 53.6)
    • Male 50.0 (44.2 – 55.2)
    • Female 42.0 (36.1 – 46.7)
Sarcopenia and Outcomes for Wait-Listed Patients

• Median follow-up: 8.8 months
• Wait List Mortality was met in
  • 25% men
  • 36% women
• SMI was lower in those with WLM vs those without WLM
  • 45.6 vs 48.5 (p<0.001)
SMI cut-offs to define sarcopenia (based on waitlist mortality)

**Men: SMI<50 cm²/m²**

**Women: SMI<39 cm²/m²**

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<th>SMI cut-off</th>
<th>% Increase in WLM</th>
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**Men (n = 277):**
- SMI < 49 : 78% increase in WLM

**Women (n = 119):**
- SMI < 39: 343% increase in WLM

Source: liverlearning.aasld.org
Frailty, in liver transplantation

Source: liverlearning.aasld.org

Adapted from Lai JC et al. AJT 2014.

**Background & Methods**

- To establish objective set of criteria to define frailty which correlates with patient outcomes on the liver transplant wait list
- Consecutive cirrhotic patients were enrolled in the outpt setting
- Listed for Liver Transplantation, without MELD exceptions
- Evaluated for physical frailty measures
A Liver-Specific Frailty Index

- Grip
- Chair stands
- Balance

Takes <60-90 seconds to complete in the clinic setting!

Source: liverlearning.aasld.org  Lai JC et al. Abstract #25, Transplant Plenary II @ 10:30AM.
RESULTS

• 536 cirrhotic patients listed for LT, *evaluated in the outpt setting*
• 59% M / 41% F
• Median Age 58y (50 – 63)
• Median MELD 18 (15 – 23)
• Median f/u of 11 months
  • Death/Delisting in 107 patients (20%)
RESULTS

• C-Statistic for correctly predicting 3 month waitlist mortality
  • MELD Na \textit{Alone} = 0.79
  • Frailty Index \textit{Alone} = 0.75
  • MELD Na + Frailty Index = 0.82

• By combining MELD Na with Frailty, 21% of patients were classified
  • 13% of deaths/delisting
  • 8% non-deaths/delisting

• Patients were classified as
  • Robust, if Frailty Index $\geq$ 75\%ile
  • Frail, if Frailty Index $\leq$ 25\%ile
A Liver-Specific Frailty Index better risk stratifies patients than MELDNa

Predicted probability of waitlist mortality:

By MELDNa alone

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[Graph showing survival probability over time for MELDNa 14 and MELDNa 23]
A Liver-Specific Frailty Index better risk stratifies patients than MELDNa

Predicted probability of waitlist mortality:

By MELDNa alone

MELDNa 14

MELDNa 23

By MELDNa + Frailty Index

MELDNa 14 Robust

MELDNa 23 Robust = MELDNa 14 Frail

MELDNa 23 Frail

Source: liverlearning.aasld.org Lai JC et al. Abstract#25, Transplant Plenary II @ 10:30AM.
Conclusions

• In a high MELD transplant environment, there are clear challenges in predicting which patients will have good post-transplant outcomes
• While MELD/MELDNa scores predict waitlist mortality, they only weakly predict post transplant survival
• High MELD/MELDNa scores alone are insufficient when deciding when transplant may in fact be futile
• Novel assessments of functional status, such as frailty and sarcopenia can help predict which patients are most fit for liver transplantation
• As these studies progress, it will be important to see how these functional assessments predict post-transplant outcomes in addition to wait list mortality
Prediction of HCC Recurrence post-OLT
Organ Allocation
A Liver-Specific Frailty Index better risk stratifies patients than MELDNa

Predicted probability of waitlist mortality:

By MELDNa alone

By MELDNa + Frailty Index

Lai J.C. et al. Abstract #5, Transplant Plenary II @ 10:30 AM.
Results. Of 366 LT candidates, 119 (30%) were women. Women vs. men were similar by age and race, but more likely to have NAFLD (15% vs. 11%) or cholestasis disease (24% vs. 5%) and less likely to have HCC (30% vs. 43%); they were shorter (182 vs 175cm), lighter (71 vs. 89kg), but had similar BMI (27 vs. 27 kg/m²) (p<0.05 for each).

Compared to men, women had similar median MELD (15 vs. 15, p=0.42), but lower creatinine (0.8 vs. 0.9 mg/dL; p=0.01). Median (IQR) SMI was 42 (36-47) cm²/1m² in women and 50 (44-55) cm²/1m² in men. By median 9 mo followup, 42(38%) women and 69(25%) men had WLM (p=0.02). In univariable competing risks regression, female vs. male sex was associated with 55% increased risk of WLM (HR 1.55, 95%CI 1.06-2.27; p=0.02). Adjustment for SMI completely mitigated this gender disparity (female sex HR 1.11, 95%CI 0.74-1.67; p=0.60), with no change after adjustment for MELD and Black race. Rates of WLM were significantly higher among sarcopenic women (59%) compared to non-sarcopenic women (29%).

Conclusions. Our multi-center data suggest that the presence of sarcopenia accounts for the gender disparity in LT waitlist mortality. Sarcopenic women are especially at risk for death on the waitlist and should receive targeted interventions to prevent or reverse sarcopenia while awaiting LT.

Figure. Unadjusted survival among men, non-sarcopenic, and sarcopenic women awaiting LT.
Defining Sarcopenia and Patient Outcomes

• Univariate Analysis
  • SMI was associated with WLD (HR 0.95, p<0.001)

• Multivariate Analysis
  • SMI remained significant after adjustment for black race and HCC

• Cutoffs
  • SMI = 49 (men)
  • SMI = 39 (women)
Defining Sarcopenia and Patient Outcomes

• Men, n = 277
  • 45% with SMI < 49
    • 78% increase in WLM

• Women, n = 119
  • 33% with SMI < 39
    • 343% increase in WLM
Frailty in liver transplant candidates

22% robust

61% pre-frail

17% frail (by Fried Frailty Index)

85 yo community-dwelling adults

17% will transition to frail