AASLD November 13-16, 2020

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About the program:

Best of The Liver Meeting 2020 was created by the Scientific Program Committee for the benefit of AASLD members, attendees of the annual conference, and other clinicians involved in the treatment of liver diseases. The program is intended to highlight some of the key oral and poster presentations from the meeting and to provide insights from the authors themselves regarding implications for patient care and ongoing research.

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Paradigm change in liver transplant practice after the implementation of the new liver-kidney allocation policy

Aim

To evaluate effects of the new SLK policy on pre- and post-transplant practice in liver transplant alone (LTA) patients with kidney dysfunction

Methods

The OPTN/UNOS registry was used. The number of LTA registration, post-transplant outcome, the number of KT listing after LTA and KT waitlist outcome were evaluated in pre- and post-new policy eras.

Main Findings

The new SLK policy 1) significantly increased the number of LTA candidates on dialysis (0.95/day to 1.21/day, $P<0.001$), 2) did not affect the post-transplant survival of LTA patients with kidney dysfunction, 3) increased KT listing after LTA especially in those on dialysis (see Table), and 4) safety-net provided significantly better kidney waitlist outcomes to LTA patients (see Figure).
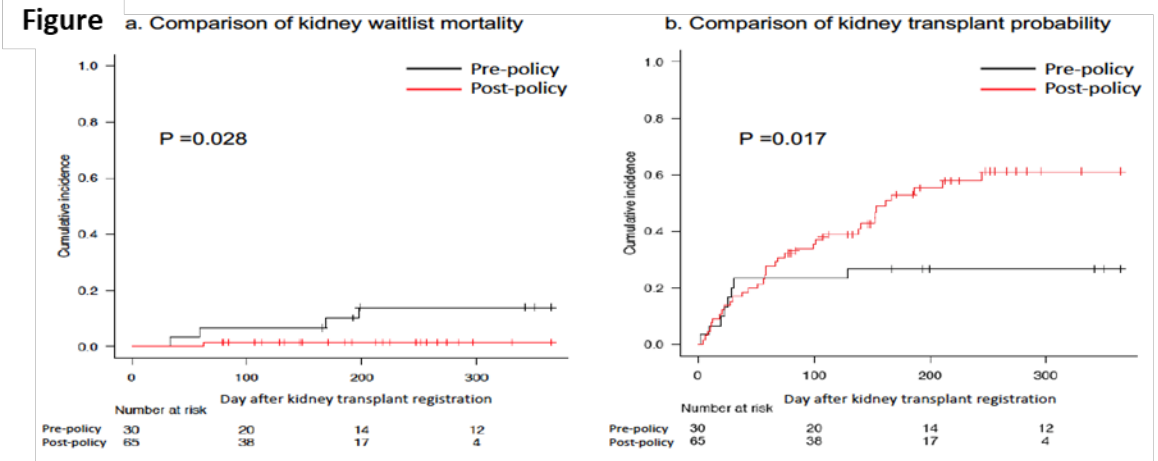
Conclusions

The new SLK policy successfully stratified patients with kidney dysfunction for LTA and provided KT opportunities to patients with post-LTA kidney failure.

Suzuki Y, Nagai S, et al., Abstract 1

Final kidney function		KT listing after LTA in 1 year	P value	OR (95% CI)
CKD 4	Pre-policy	6 / 367 (1.6%)	0.151	2.24 (0.74-6.76)
	Post-policy	7 / 195 (3.6%)		
CKD 5	Pre-policy	4 / 124 (3.2%)	0.300	-
	Post-policy	0 / 77 (0.0%)		
Dialysis	Pre-policy	16 / 784 (2.0%)	<0.001	4.38 (2.48-7.75)
	Post-policy	52 / 622 (8.4%)		
All	Pre-policy	30 / 1522 (3.9%)	<0.001	3.30 (2.12-5.12)
	Post-policy	65 / 1046 (6.2%)		

Figure

a. Comparison of kidney waitlist mortality

P =0.028

b. Comparison of kidney transplant probability

P =0.017

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Optimal timing of liver transplantation for acute-on-chronic liver failure grade-3 patients using a dynamic model

Aim

To create a Markov decision process model to determine optimal timing of LT among patients listed with ACLF-3, accounting for donor organ quality and organ failure recovery

Methods

- Data source: UNOS database, years 2005-2017
- Analysis of four patient groups listed with ACLF-3 and transplanted within 7 days: age < or ≥ 60 years; 3 OF or 4-6 OF at listing
- Markov decision process model created using Python 3.6

Main Findings

Survival benefit demonstrated with early LT, regardless of donor organ quality. Probability of pre-LT organ failure recovery is <10%. Two-way analyses based on center's expected post-LT survival and likelihood of receiving an organ offer can determine when to proceed with LT (see Figure).

Conclusions

Early transplantation is favored in patients listed with ACLF-3.

Zhang S, et al., Abstract 2
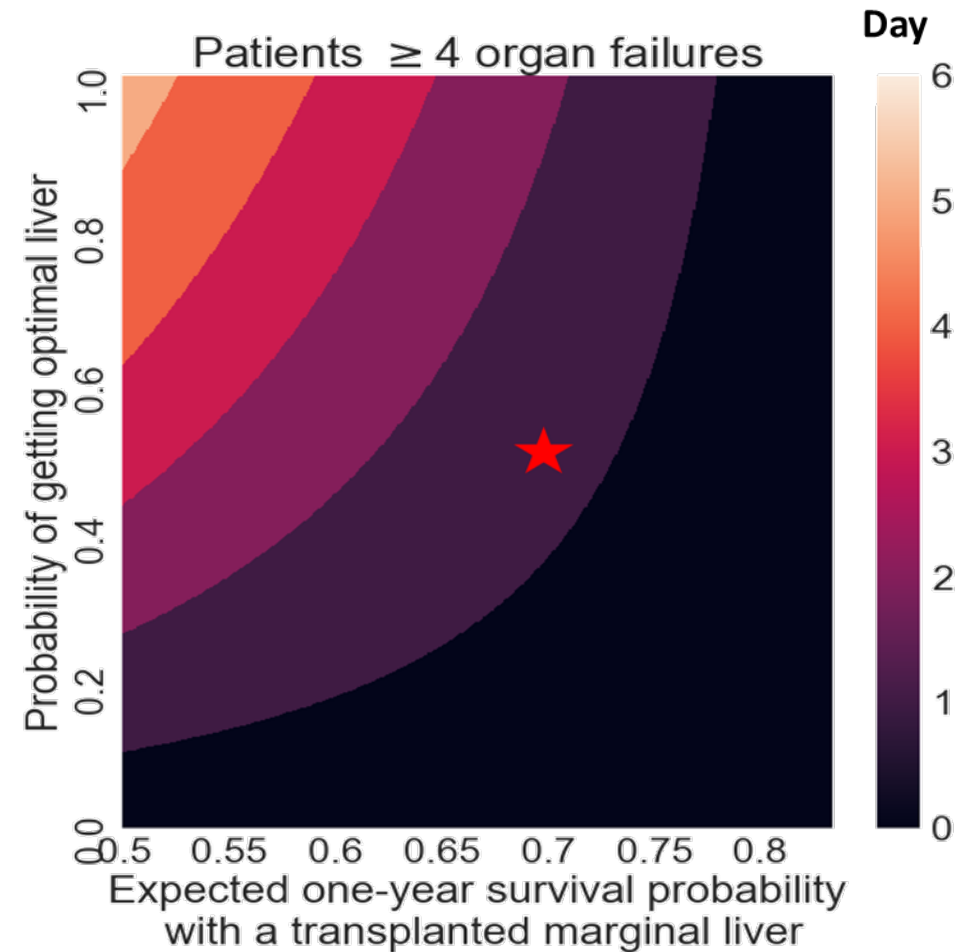
Use of neural network models to predict mortality/survival among patients on the liver transplant waitlist

Aim

To develop neural network (NN) models that more accurately predict liver transplant (LT) waitlist mortality using the OPTN/UNOS

Methods

The OPTN/UNOS registry from 2002 to 2018 was used. To create NN prediction model, 44 pre-LT variables were selected. Model performance was evaluated using area under Area Under Receiver Operating Curve (AUC-ROC) and Area Under Precision-Recall curve (PR-AUC). Probability of 90-day mortality for given MELD score was mapped to compare the performance.

Main Findings

According to NN prediction models, the AUC-ROC for *90-Day mortality* was 0.928 and the PR-AUC was 0.730. The *90-Day Mortality* NN model outperformed MELD score for both AUC-ROC and PR-AUC (see Figure).

Conclusions

Prediction models using NN more accurately identified waitlist mortality, which outperformed MELD score. Using NN will lead to developing a more accurate and equitable allocation system.

Nagai S, et al., Abstract 3

Figure. Comparison of 90-Day Mortality NN Model Against MELD Score
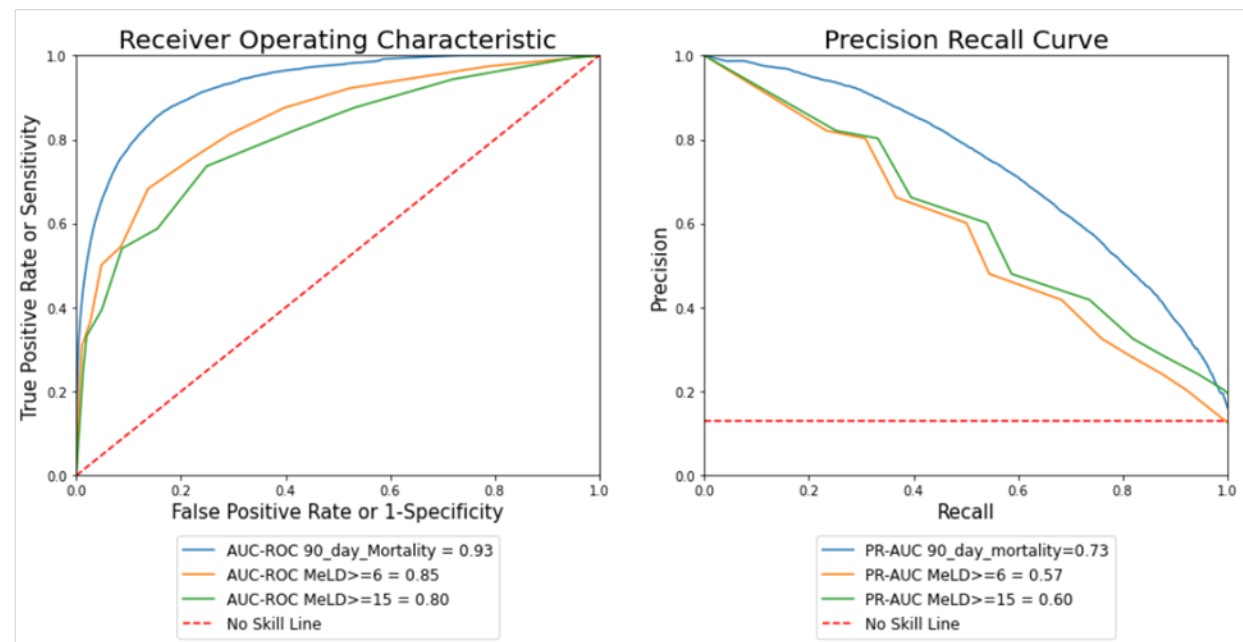
	NN 95% CL	MELD>=6, 95% CL	MELD>=15, 95% CL	*P*-Value, NN vs MELD>=6	*P*-Value, NN vs MELD>=15
AUC-ROC	0.928 (0.927-0.929)	0.846 (0.843-0.848)	0.805 (0.802-0.807)	<0.001	<0.001
PR-AUC	0.730 (0.725-0.734)	0.571 (0.566-0.576)	0.603 (0.598-0.608)	<0.001	<0.001

Normothermic machine perfusion of discarded human livers alleviates ischemia-reperfusion injury and promotes regenerative pathways

Objective

To characterize injury and repair mechanisms during normothermic machine perfusion that differentiate viable from nonviable human livers

Methods

6 discarded human livers from donation after circulatory death were assessed during normothermic machine perfusion; tissue transcriptome and perfusate proteome analysis was performed.

Main Findings

Viable livers demonstrated early innate immune activation followed by pro-autophagy and pro-survival signaling. Nonviable livers displayed persistent pro-inflammatory signaling without a robust repair response.

Conclusions

Activation of autophagy mechanisms during normothermic machine perfusion may lead to improved graft function in discarded or high-risk livers for transplant.

Raigani S, et al., Abstract 4
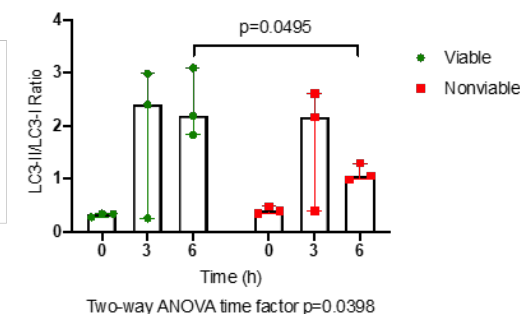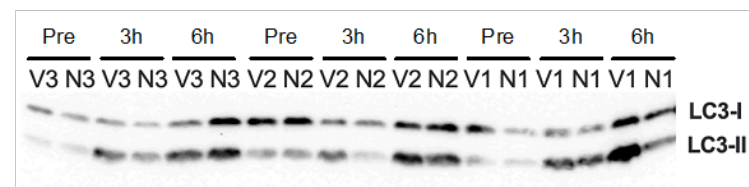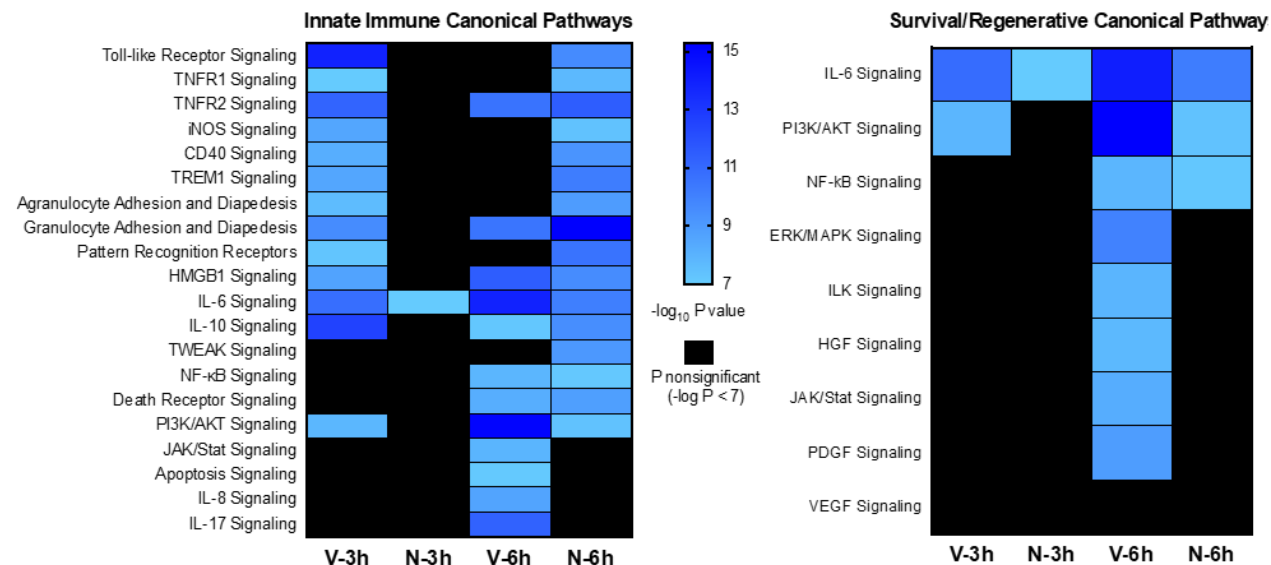
Early liver transplantation for severe alcoholic hepatitis: results of the QuickTrans study

Aim

Evaluate the 2-year relapse rate in patients transplanted for severe alcoholic hepatitis (AH) vs those transplanted for alcohol-related cirrhosis (6 months of abstinence)

Methods

Prospective study evaluating the non-inferiority of alcohol relapse after liver transplantation between the 2 groups
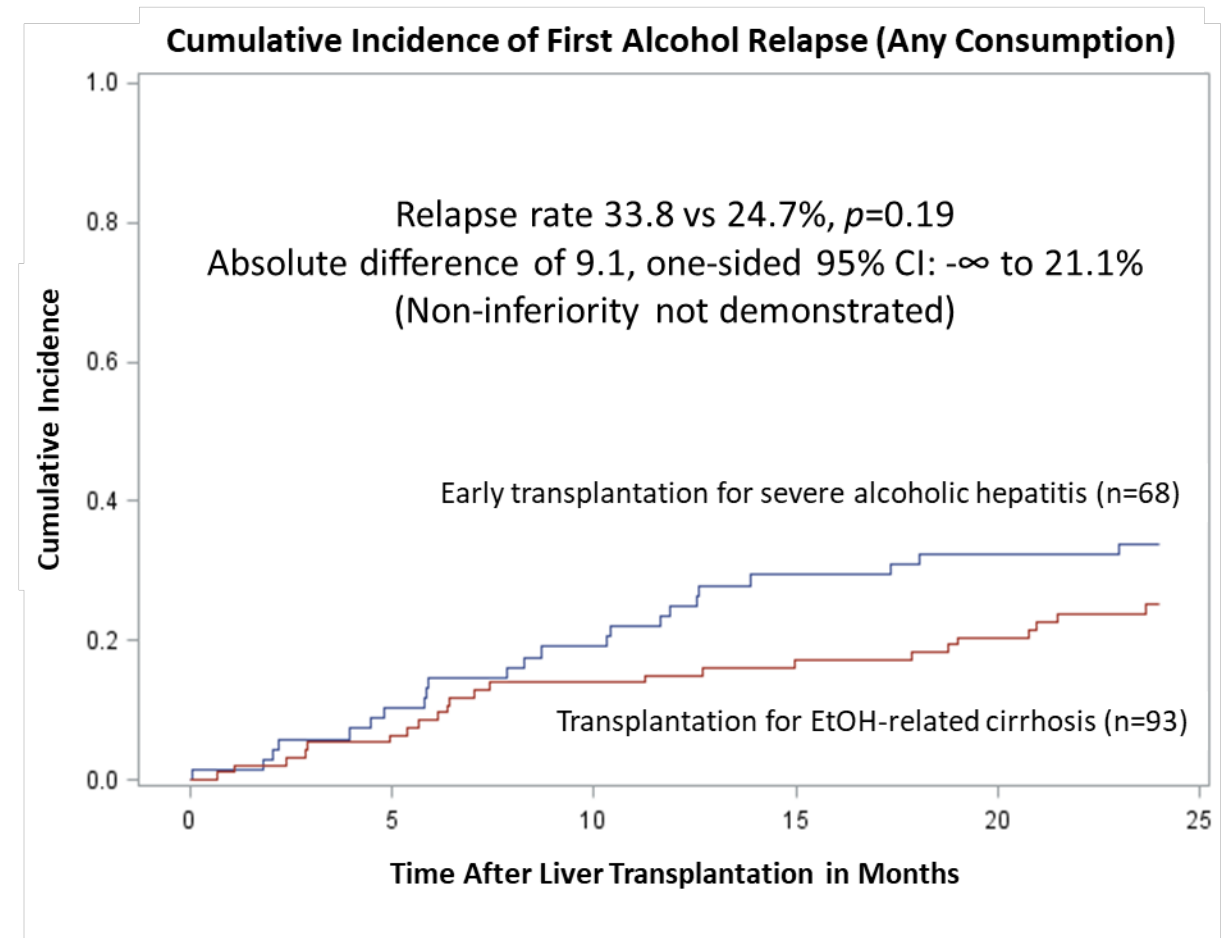
Main Findings

- In addition to relapse rate (see Figure), survival at 2 years was similar in the two groups: 89.7 vs 88.1%, p=0.8.
- Patients with AH who were transplanted had a better survival than those who were not: 82.8 vs 28.2%, p<0.0001.

Conclusions

We cannot demonstrate non-inferiority of liver Tx for severe alcoholic hepatitis. Transplantation increases 2-year survival.

Louvet A, et al., Abstract 6

Cumulative Incidence of First Alcohol Relapse (Any Consumption)

Relapse rate 33.8 vs 24.7%, p=0.19
Absolute difference of 9.1, one-sided 95% CI: -∞ to 21.1%
(Non-inferiority not demonstrated)

Early transplantation for severe alcoholic hepatitis (n=68)

Transplantation for EtOH-related cirrhosis (n=93)

Cumulative Incidence

Time After Liver Transplantation in Months

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MELD subtypes and WL mortality:
Is a MELD score 25 driven by creatinine the same as a MELD score 25 driven by bilirubin or INR?

Aim

- Does the *same MELD score* driven by one dominant variable (eg, elevated creatinine) as compared to other variables (eg, elevated bilirubin) have different prognosis?

- Identify subsets of registrants on the WL with similar MELD scores that are creatinine dominant (MELDCr), bilirubin dominant (MELDBr), INR dominant (MELDINR), and assess WL mortality and LT rates by MELD dominance.

Methods

- Competing risks analysis to examine LT within 90 days
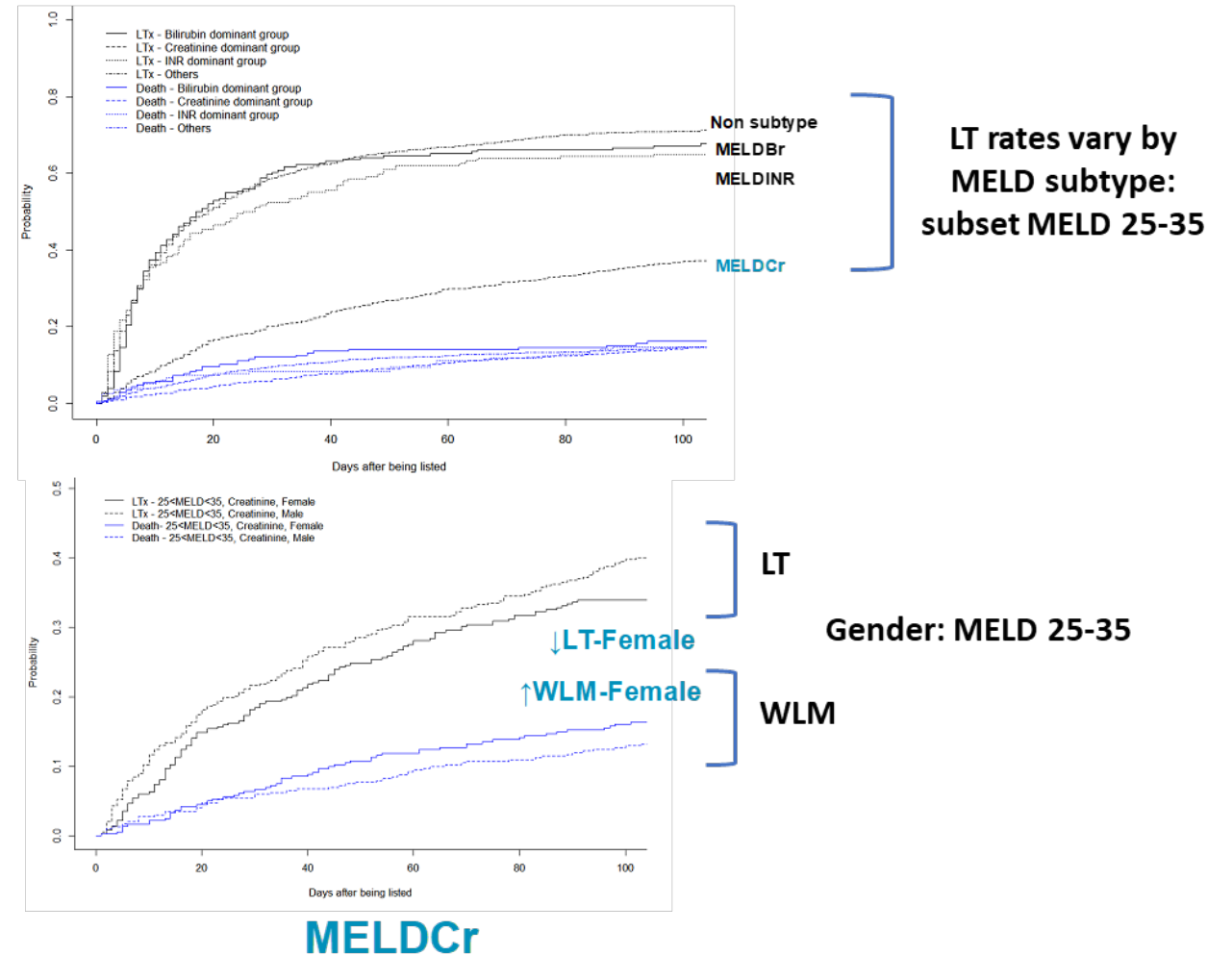- Patient population: SRTR, adult WL registrants 2016-2018

Main Findings

MELDCr subtype: lowest LT rates

Conclusions

All MELD is not created equal and WL mortality and LT rates vary by MELD subtypes.

Asrani SK, et al., Abstract 25

LT rates vary by MELD subtype: subset MELD 25-35

Gender: MELD 25-35

MELDCr

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Frailty, mortality, and healthcare utilization *after* liver transplantation

From the Multi-Center Functional Assessment in Liver Transplantation (FrAILT) Study

Objective

To evaluate the association between pre-transplant frailty and post-transplant mortality and healthcare utilization

Methods

- Prospective cohort study of 908 adult liver transplant recipients from 8 transplant centers in the U.S.
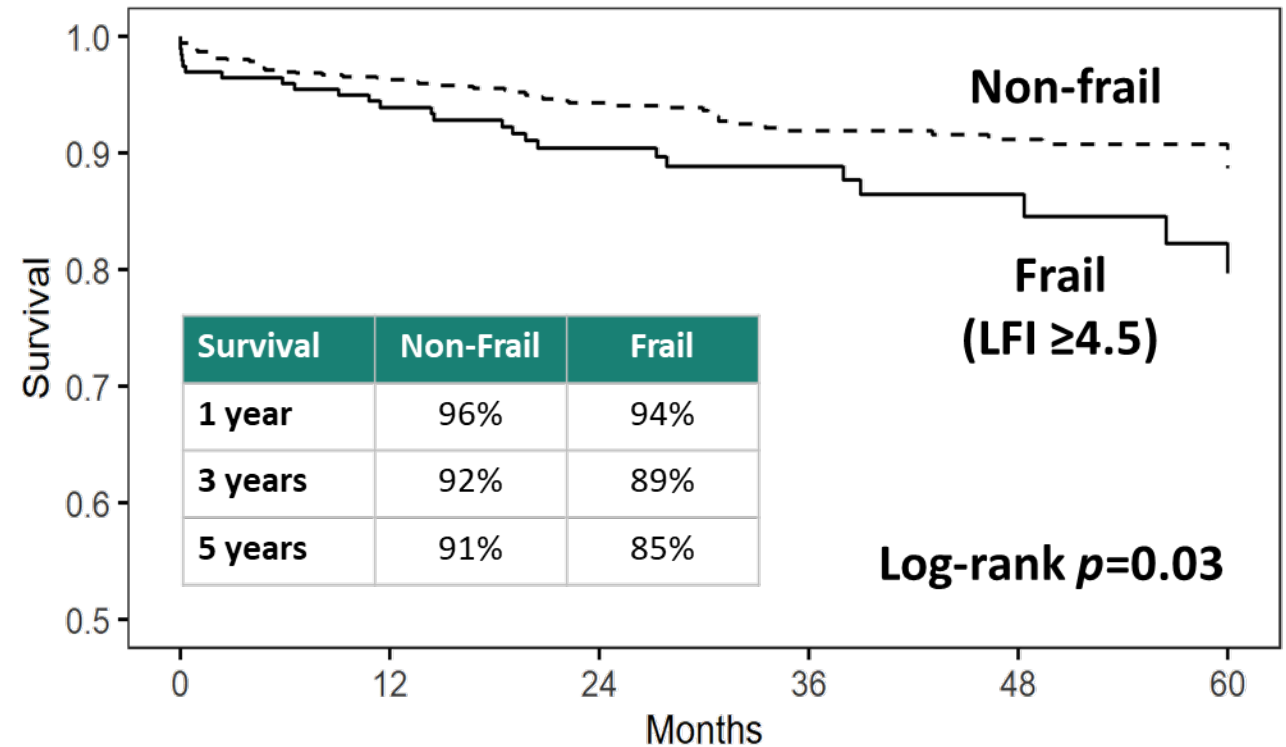- Metric of frailty: Liver Frailty Index

Main Findings

- Frailty was associated with 2.1x increased risk of post-transplant mortality (95% CI 1.3-3.4)
- And higher post-transplant length of stay, ICU days, hospitalized days within 90 days of transplant, non-home d/c

Conclusions

Frailty was associated with a 2-fold increased risk of post-transplant death and higher healthcare utilization, but post-transplant outcomes were acceptable even in frail patients.

Lai JC, et al., Abstract 29

Survival	Non-Frail	Frail
1 year	96%	94%
3 years	92%	89%
5 years	91%	85%

Non-frail

Frail
(LFI ≥4.5)

Log-rank p=0.03

A validated score to stratify and optimize use of liver graft for grade 3 acute-on-chronic liver failure patients

Aim

To develop a risk score predictive of post-LT survival in patients with acute-on-chronic liver failure (ACLF) grade 3.

Methods

- UNOS database (2002 to 2018) queried on adult LT recipients stratified to ACLF using modified EASL-CLIF criteria and study outcome was patient survival at one-year post-LT.
- Cohort of ACLF-3 (N=7166) was randomly split using a split sample validation technique into training and validation datasets.

Main Findings

- Of 54,874 LT recipients, 23,947 (43.6%) patients, had ACLF at the time of LT (14,414 with ACLF at listing).
- Variables predictive of 1-year mortality on Cox regression analysis of training dataset were recipient age, non-alcohol etiology, pulmonary failure, cardiovascular failure, and brain failure and these variables were used to derive the final risk score.
- 1-year patient survival for validation dataset, stratified to low-, medium-, and high-risk groups were 89%, 82%, and 80%, respectively (see Figure A), while observed and expected post-transplant survival showed excellent correlation (see Figure B).
- Improved survival was seen with good quality graft (donor risk index <1.5) in recipients within high-risk score group for both validation and whole datasets.
- Moreover, for 1268 recipients within the high-risk group and who received good quality graft, 1-year patient survival was similar comparing recipients waiting on LT list for ≤30 days vs >30 days.

Figure A) Kaplan-Meier survival curves on 1-year patient survival among liver transplant recipients with acute-on-chronic liver failure grade 3 at the time of transplant comparing three risk levels: low risk with score <7.55 (blue line), medium risk with score 7.55-11.57 (red line), and high risk with score >11.57 (green line). **B)** Calibration in the validation dataset between observed versus expected one-year patient survival among liver transplant recipients with acute-on-chronic liver failure grade 3 at the time of transplantation, R coefficient of 0.92.

Conclusions

- LT provides survival benefit to select patients with ACLF, however, post-transplant survival remains suboptimal for recipients with ACLF-3 at LT.
- In a cohort of ACLF-3 patients, we developed a novel score to predict post-transplant survival and match recipients with donor quality, with improved survival using better quality graft in high-risk patients, irrespective of waitlisting time.
- Utilization of this novel score is intended to optimize use of donor pool and improve post-transplant outcomes among recipients who at the time of LT are in ACLF-3.
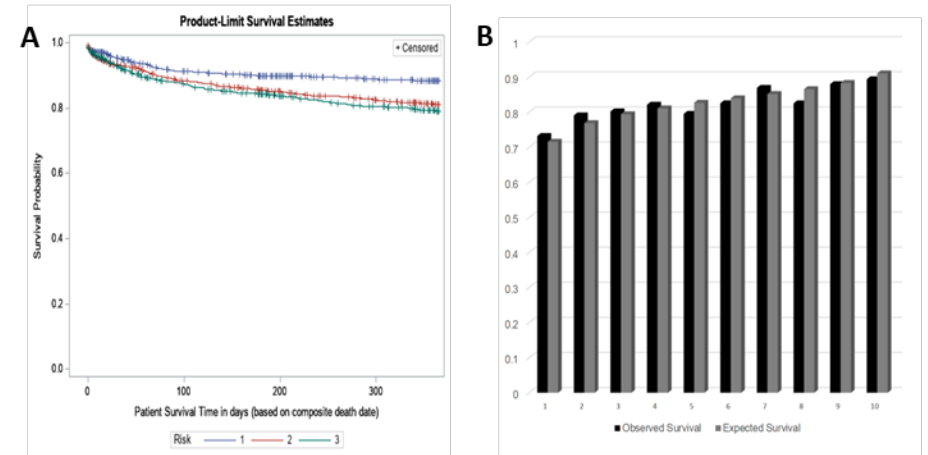
Waleed M, et al., Abstract 49

Long-term outcomes of "hard-to-place" LT recipients: a single-center experience over 7 years

Aim

Evaluate outcomes for offer number >50 ("hard-to-place") grafts

Methods

Retrospective cohort study of adults who received LT at Duke with match-run >50 from 1/2010 to 7/2017; f/u for 2 years

Main Findings

- Mortality at 2 years was ~11% (4/36), comparable to national data of all recipients.
- No association with magnitude of match-run number and mortality (see Figure), graft failure, length of stay, nor hospitalizations up to 2 years.

Conclusions

Increased scrutiny/consideration of "hard-to-place" grafts may present an opportunity to increase center-level access to LT without worsening outcomes.

Patel YA, et al., Abstract 51

Match Run Number by Outcome

P=0.19

Match Run Number

■ Alive ■ Dead
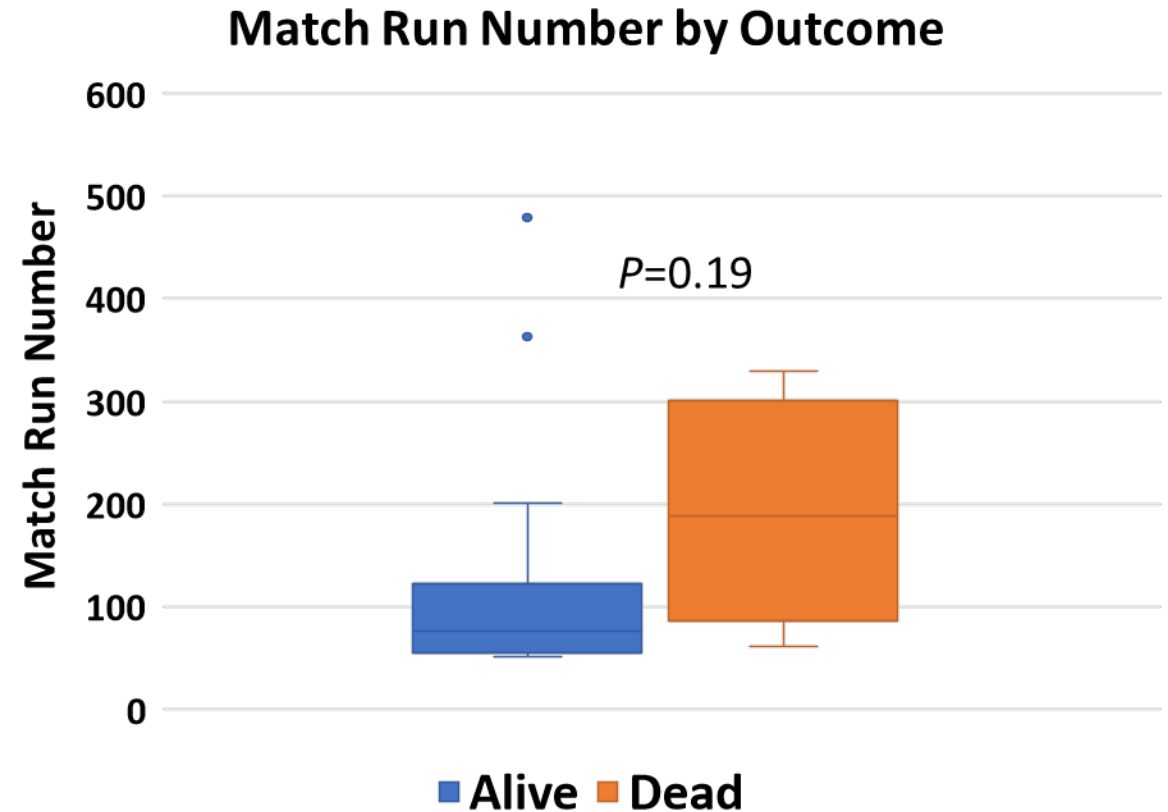
*Alive recipient outliers with match run 5534, 5422, and 2437 not depicted.

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Fate of liver and kidney transplant candidates before and after simultaneous liver-kidney transplant allocation policy change

Aim

To investigate the impact of the simultaneous liver and kidney transplantation (SLK) policy change on outcomes in SLK candidates

Methods

The OPTN/UNOS registry was used. Patients were stratified into the two eras: Era 1 (pre-policy era): January 1, 2015-July 31, 2017, Era 2 (post-policy era): September 1, 2017-March 31, 2019. Waitlist outcomes, type of transplant (SLK or LT alone [LTA]) were evaluated and post-transplant outcomes were compared according to transplant type using Cox regression model.

Main Findings

- The daily number of waitlisted patients for SLK significantly decreased in Era 2 (3.25/day to 2.89/day, P=0.013)
- Significantly higher proportion of LTA in SLK candidates was observed in Era 2 (see Figure 1).
- Among SLK candidates, liver graft survival was significantly worse in LTA group than SLK group (see Figure 2).

Conclusions

The decision on transplant type for patients who were initially listed for SLK (SLK candidates) needs careful assessment, because their outcomes were significantly worse than SLK.

Shimada S, et al., Abstract 54
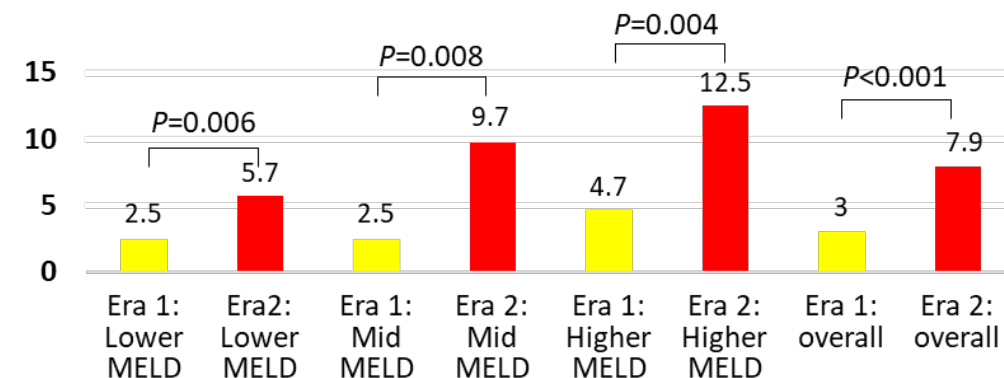

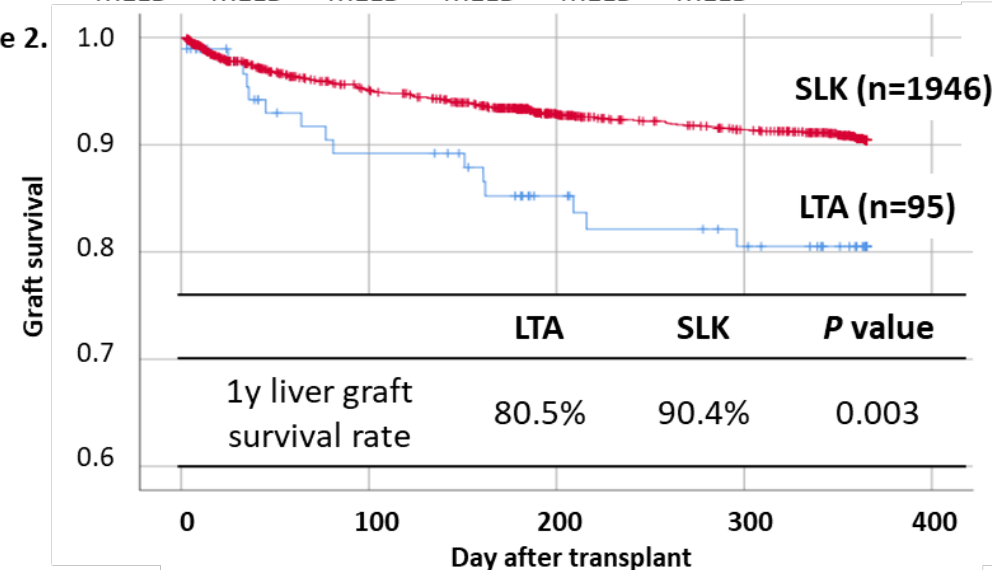Figure 1. The Rates of LTA in SLK Candidates

Figure 2.

	LTA	SLK	P value
1y liver graft survival rate	80.5%	90.4%	0.003

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Improved transplant-free survival following MARS therapy in acute liver failure: a multicenter propensity score-matched study

Aim

The *molecular adsorbent recirculating system* (MARS) removes water-soluble and albumin-bound toxins and may be beneficial for acute liver failure (ALF) patients. Rates of 21-day transplant-free survival (TFS) in ALF patients receiving MARS therapy and patients receiving standard medical therapy were compared.

Methods

Propensity score (PS)-matched analysis using all patients treated with MARS at 3 North American transplantation centers (n=104) and ALF controls from the *United States Acute Liver Failure Study Group* registry (n=416). Primary outcome was 21-day transplant-free survival.

Main Findings

Using multivariable conditional logistic regression adjusting for ALF etiology (acetaminophen (APAP): n=248; versus non-APAP: n=272), age, vasopressor support, international normalized ratio, *King's College Criteria*, and PS (*main model*), MARS was significantly associated with increased 21-day TFS (OR: 1.90; 95% CI: 1.07-3.39; *p*=0.030).

Conclusions

Treatment with MARS was independently associated with improved 21-day TFS in ALF. Following MARS therapy, improvements in biochemical parameters and hemodynamics were observed, particularly in APAP-ALF.
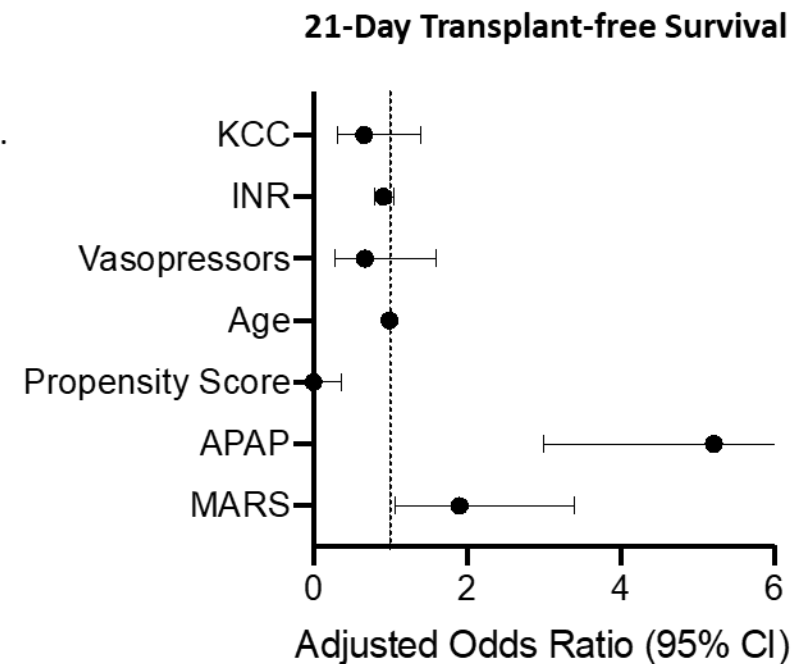
MacDonald AJ, et al., Abstract 132

21-Day Transplant-free Survival

Figure. Adjusted associations with 21-day transplant-free survival in 520 propensity-score matched ALF patients: *main model*

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Burnout among transplant hepatologists: a national survey

Aim

To describe the prevalence and predictors of burnout among practicing transplant hepatologists in the U.S.

Methods

An electronic survey with 69-items, including the Maslach Burnout Inventory, was distributed via e-mail to transplant hepatologists nationwide from 10/2019-12/2019. We examined three subscales of burnout, with a focus on emotional exhaustion.
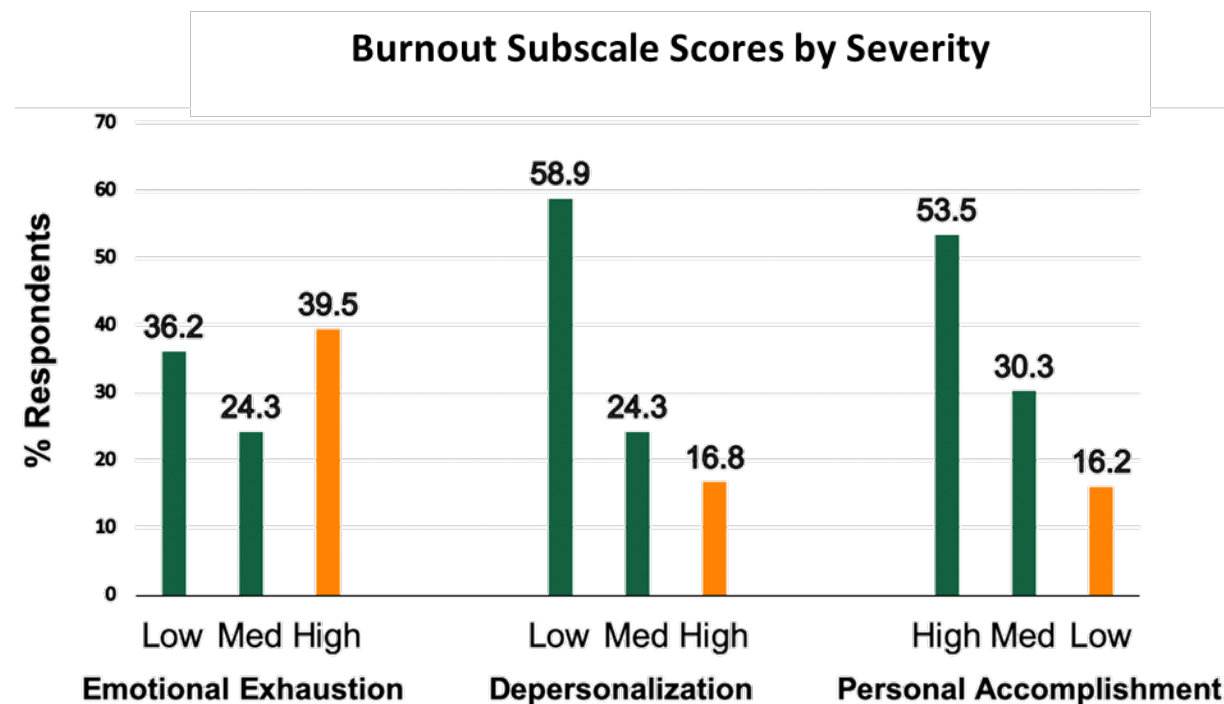
Main Findings

The prevalence of emotional exhaustion is 40%. Higher rates were observed among assistant professors, those with fewer colleagues, and those spending more time with direct patient care.

Conclusions

In this national study, we found a high rate of burnout among transplant hepatologists. Further analyses will investigate other key predictors, and future data collection will incorporate the effects of the SARS-CoV2 pandemic.

Pourmand K, et al., Abstract 152

Burnout Subscale Scores by Severity

	Low	Med	High
Emotional Exhaustion	36.2	24.3	39.5
Depersonalization	58.9	24.3	16.8

	High	Med	Low
Personal Accomplishment	53.5	30.3	16.2

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Affordable Care Act Medicaid expansion improved liver transplant waitlist placement and slowed racial disparities

Objective

To assess the association between early Affordable Care Act (ACA) Medicaid expansion and improvements in liver disease care and racial disparities in liver disease
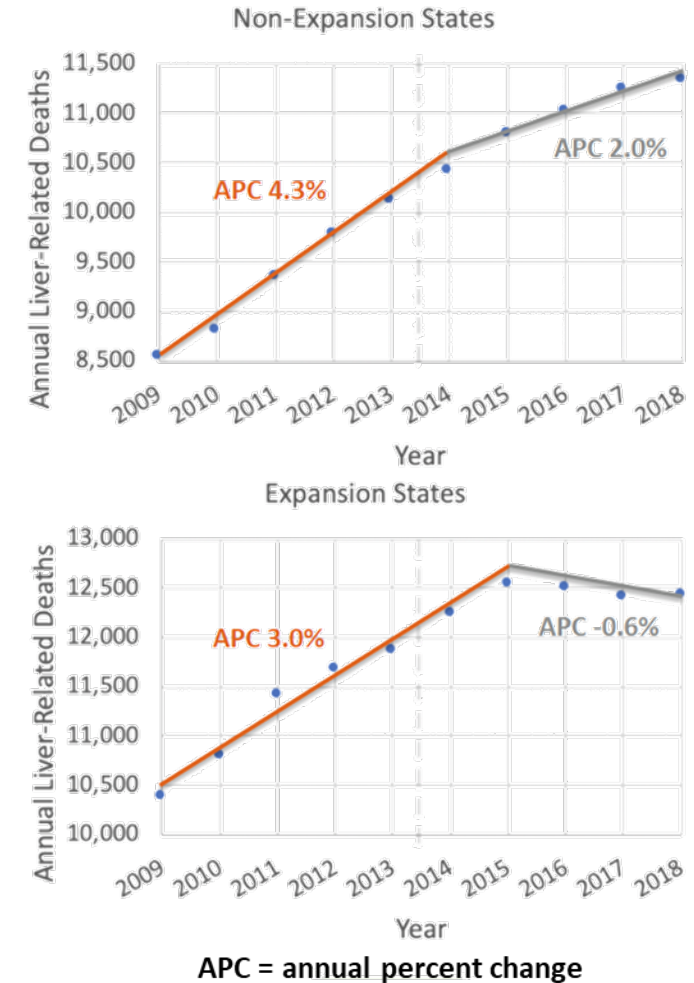
Methods

To compare changes in liver-related deaths, liver transplant listings, and listing-to-death ratio over time in states that expanded Medicaid early with states that did not expand Medicaid using joinpoint regression

Main Findings

Early Medicaid expansion through the ACA is associated with improvements in liver-related deaths (see Figure) and racial disparities in liver disease.

Conclusions

Expansion of government health care programs such as Medicaid may improve liver-related mortality and decrease the burden of liver patients needing transplant.

Wahid N, et al., Abstract 153

Non-Expansion States

APC 4.3%

APC 2.0%

Expansion States

APC 3.0%

APC -0.6%

APC = annual percent change

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