AASLD 2023 Synopsis: Liver Transplantation

Παρασκευή Φυτιλή
Γαστρεντερολόγος- Ηπατολόγος
Πανεπιστημιακή Γαστρεντερολογική Κλινική
Γ.Ν.Α Λαϊκό

- 157 Abstracts Liver Transplantation
- 144 Posters
- 13 Oral Presentations
- 1 Late Breaking Abstract

Κατανομή οργάνων: δίκαιη, μέγιστη χρησιμότητα

Ενδείξεις: ALH, MASLD, ACLF3

BaylorScott&White HEALTH

Alcohol-associated Liver Disease: Transplant Triumphs and Challenges

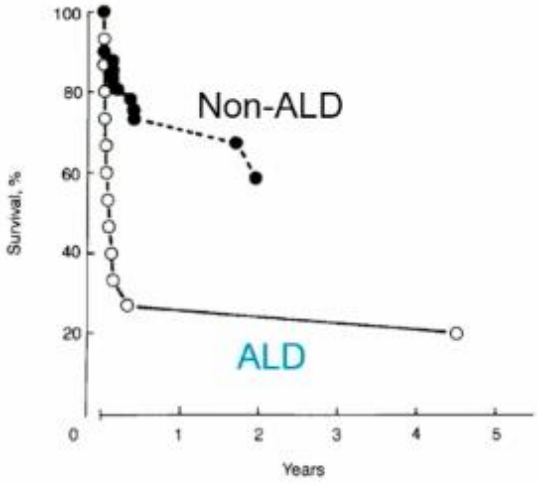
Thomas E. Starzl Transplant Surgery State of the Art

Sumeet Asrani MD MSc
Chief of Hepatology and Liver Transplantation
Baylor Dallas/Fort Worth

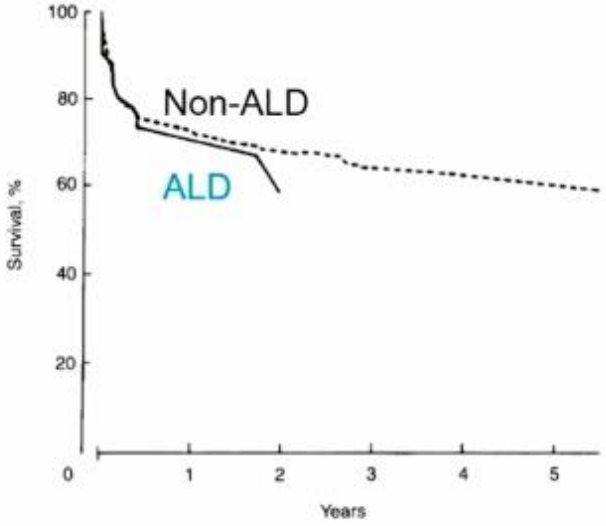
November 2023

1960s-1980s

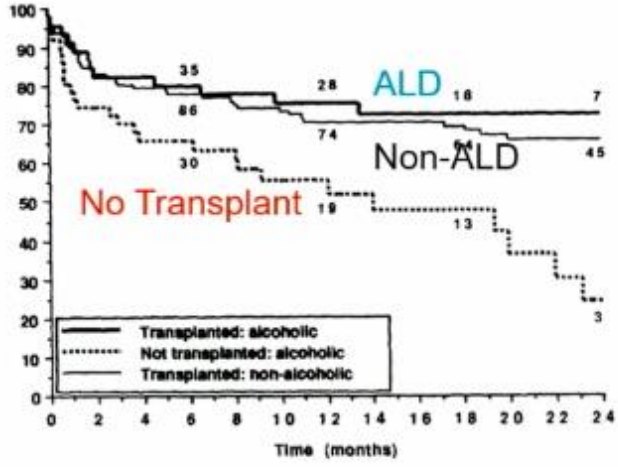
Pre-Cyclosporine
University of Colorado 1st 8 died



Post Cyclosporine
University of Pittsburgh



First ALD pathway?
University of Michigan



Starzl TE JAMA 1988
Van Thiel Alcoholism 1989
Kumar S Hepatology 1990
Lucey Gastro 1992

Reflections from 30-40 years ago on LT for ALD

Alcoholism alone did not contraindicate transplant (Michigan court system)

6 month does not equate with prognostic indicators of AUD success (Beresford and Lucey)

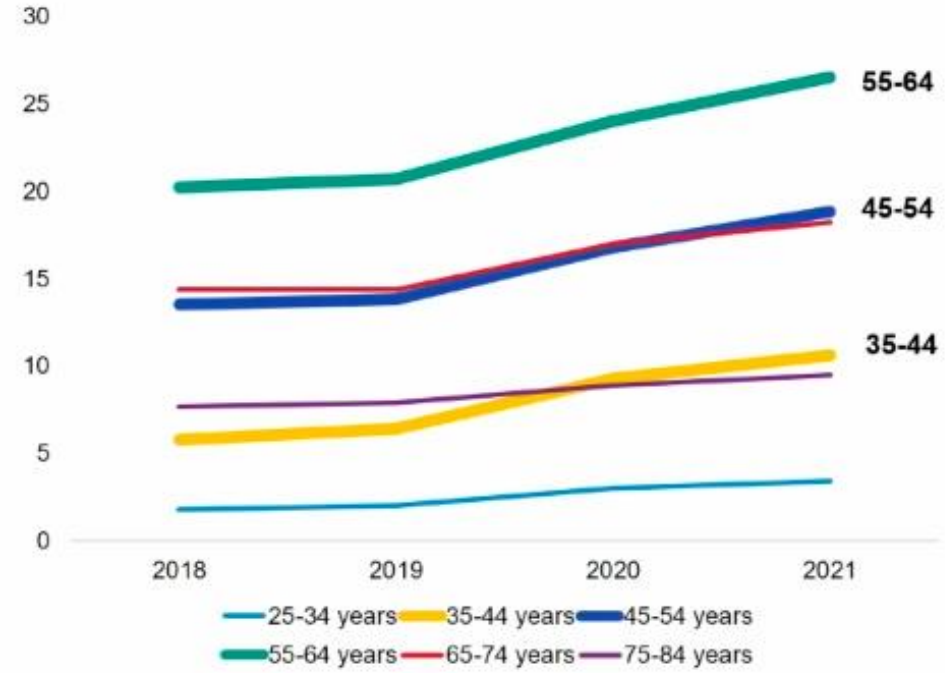
Objections are moralistic, undermine the modern understanding of alcoholism including recognition that this is a **treatable disease**, not a vice. (Van Thiel and Starzl)

The imposition of an **arbitrary period of abstinence** before going forward with transplantation would seem medically unsound or even inhumane. By waiting unnecessarily, reasonable candidates would be allowed to deteriorate to a poor-risk category, and those at poor risk from the outset would almost surely die during the interim.

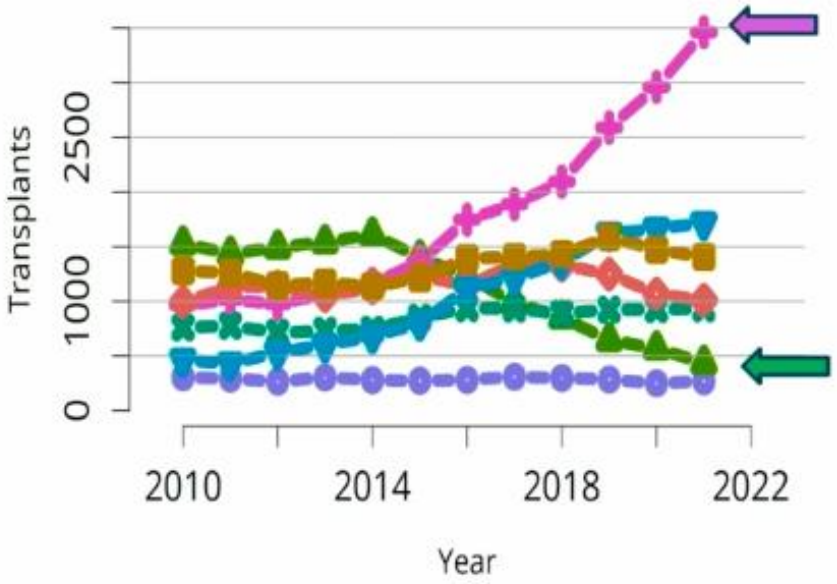
Beresford 1990
Beresford and Lucey Alcoholism 1992
Van Thiel Alcoholism 1989
Kumar S Hepatology 1990

Current landscape

Deaths related to ALD in the US

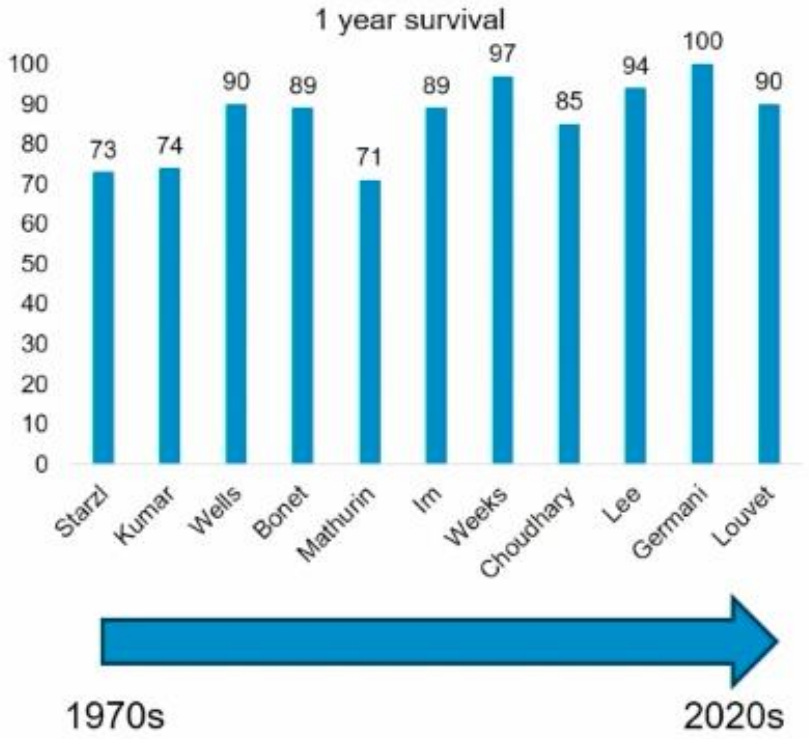


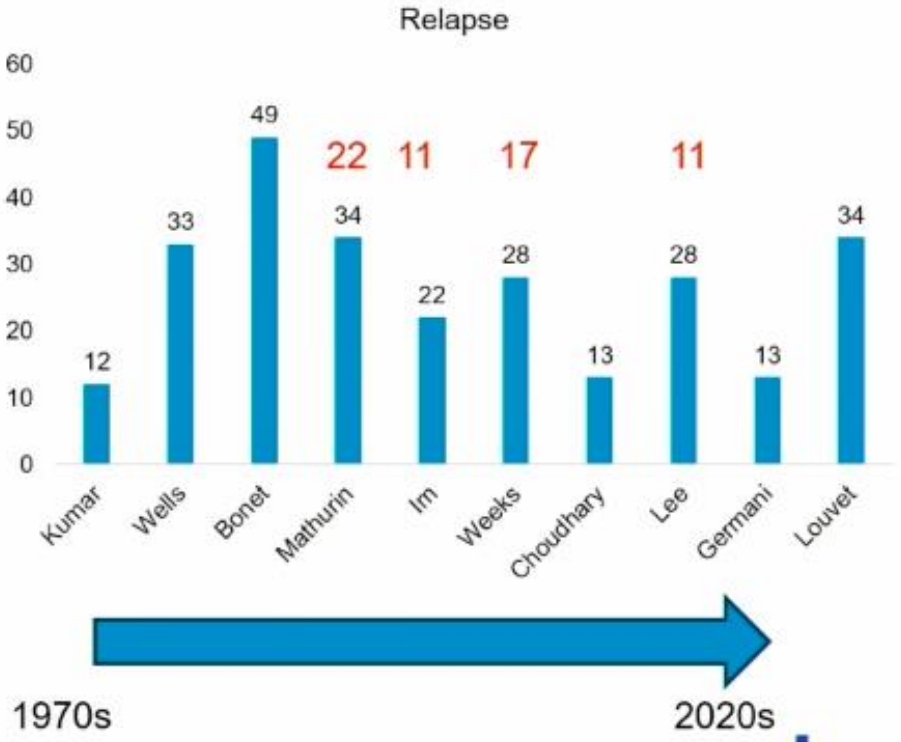
Liver Transplants related to alcohol in the US



CDC Wonder Accessed October 2023
SRTR Annual Report 2023

Survival and return to alcohol in LT for AAH



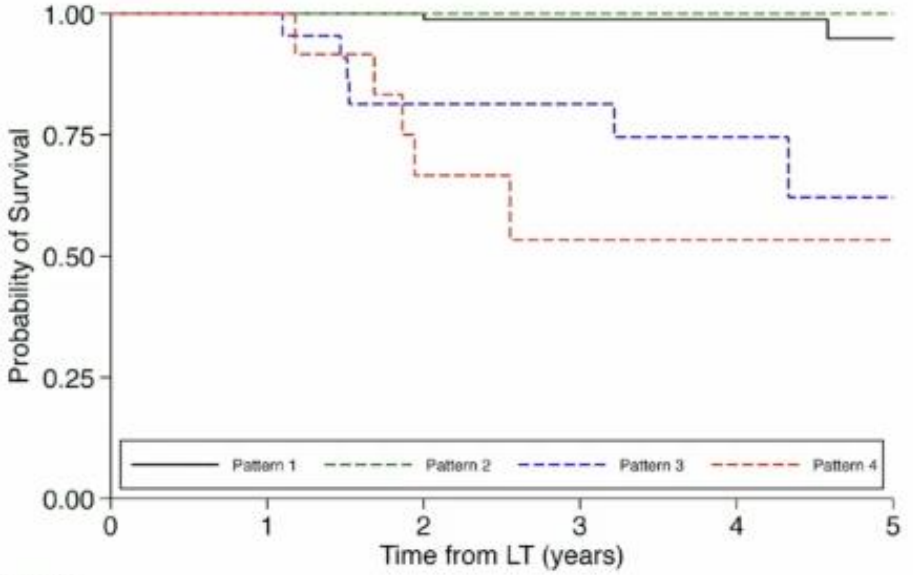


Germani J Hep 2023

LT for alcohol associated hepatitis-Wild Wild West

1. Responders vs non responders-hard to predict
2. Relapsers and pattern-hard to predict
3. Alcohol use disorder support is crucial-hard to obtain
4. Candidate selection is crucial-this is not standardized
5. LT for AH favors the well connected-women and minorities don't get a chance

Can we truly predict the pattern of alcohol use?



Number at risk

Pattern 1	103	98	84	51	36	18
Pattern 2	9	9	9	9	8	4
Pattern 3	22	22	15	12	8	2
Pattern 4	12	12	7	3	2	2

Lee BP et al Gastro 2018
Lee BP CGH 2020

The future of ALD and LT?

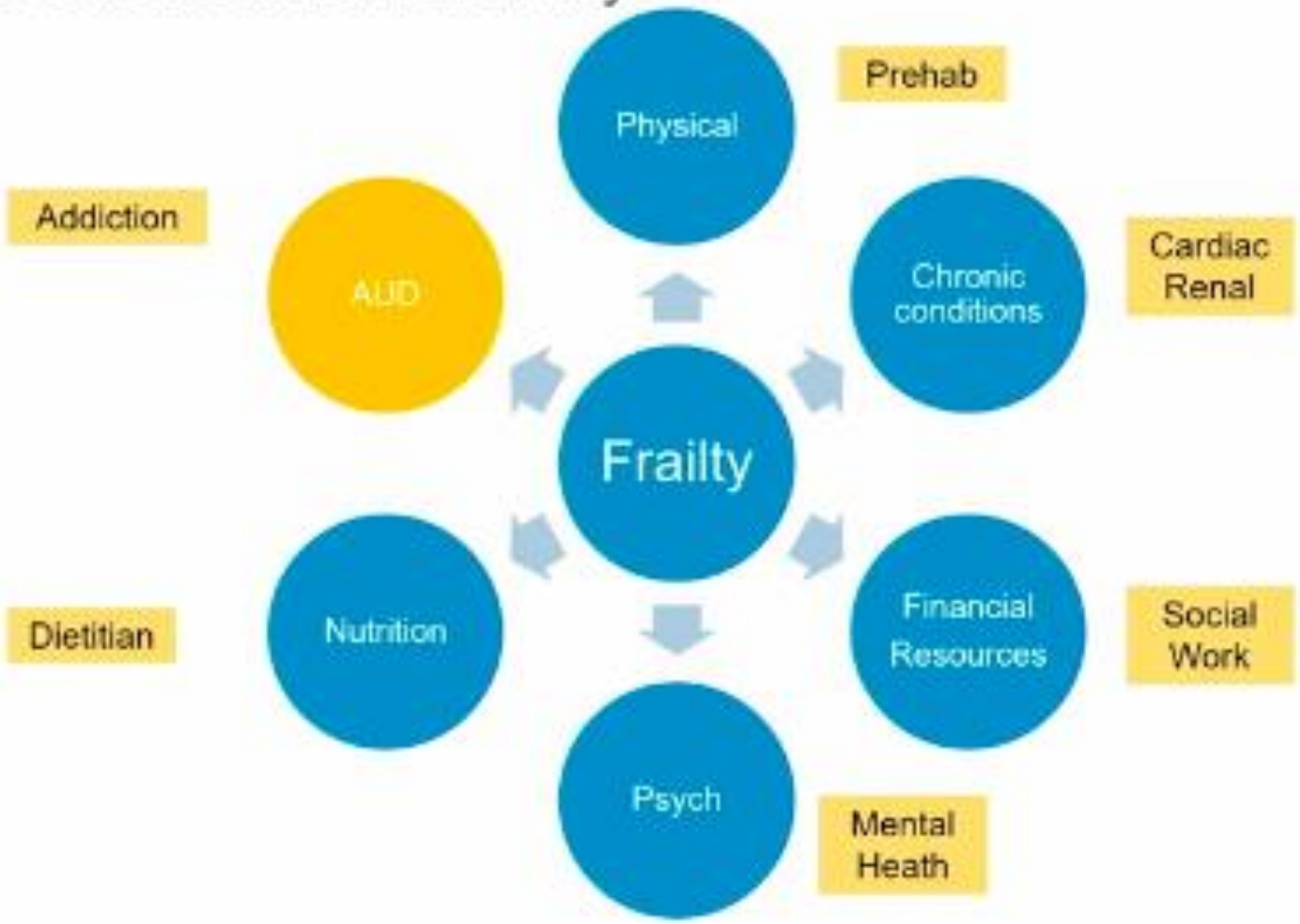
Structure

Biomarkers and biosensors

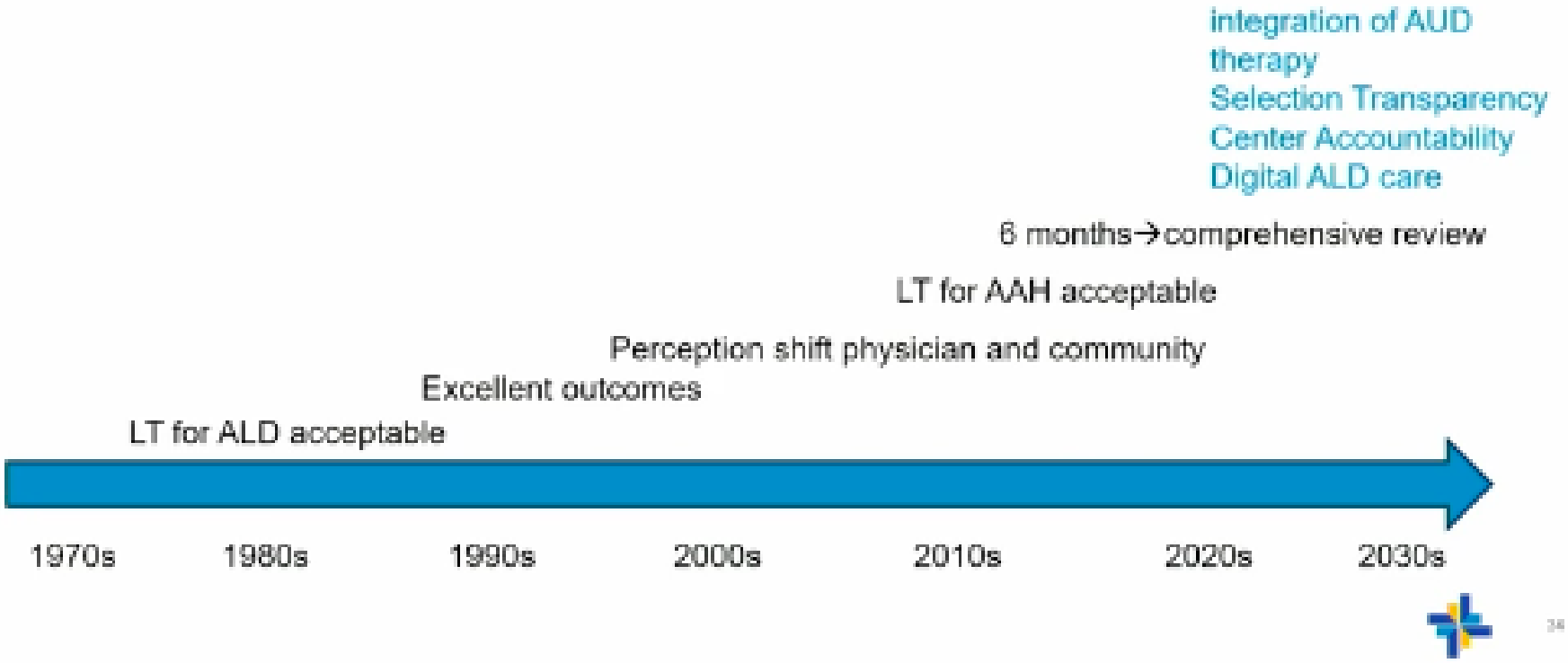
Integration of AUD care

(Re) defining success

AUD as an extension of frailty



A (nuanced) view of ALD and LT



November 12, 2023 09:00 am - 10:00 am EST

Transplant Surgery Plenary

Handouts:

SURGICAL BILIARY DIVERSION IS ASSOCIATED WITH AN INCREASED RISK OF LIVER TRANSPLANTATION OR DEATH IN ALAGILLE SYNDROME

VALIDATION OF THE R3-AFP MODEL FOR RISK PREDICTION OF HCC RECURRENCE AFTER LIVER TRANSPLANTATION IN THE SILVER CLINICAL TRIAL

IMPACT OF ACUTE KIDNEY INJURY RESPONSE ON SURVIVAL AND LIVER TRANSPLANT RATES IN HOSPITALIZED PATIENTS WITH CIRRHOSIS AWAITING LIVER TRANSPLANTATION: RESULTS FROM THE HRS-HARMONY CONSORTIUM

Live Stream

Location: Auditorium, Hynes Convention Center

Charlotte Laurent...
Massachusetts General Hospital an...

David W. Victor
Houston Methodist Hospital


Xing Li
Massachusetts General Hospital

Shannon M. Vandriel
The Hospital for Sick Children, The...

Session Evaluation | + Add to My Schedule | View More Details

Background

- AKI occurs in 22 – 47% of hospitalized patients with cirrhosis and is an independent predictor of mortality
- AKI response or recovery is associated with improved survival
- However, for patients on the waitlist for LT, how AKI response affects transplant rate and timing is less clear
- With the approval of terlipressin for the treatment of HRS-AKI, there are concerns raised about how its use may negatively affects the priority of patients on the LT waitlist
- Therefore, there is a need to establish a better baseline understanding of how AKI response impacts patients awaiting LT

Study Aim

- To assess the impact of AKI response to medical therapy on survival rate, liver transplantation rate and timing, as well as on metrics of healthcare resource utilization, for hospitalized patients with cirrhosis who are on the LT waitlist

Results

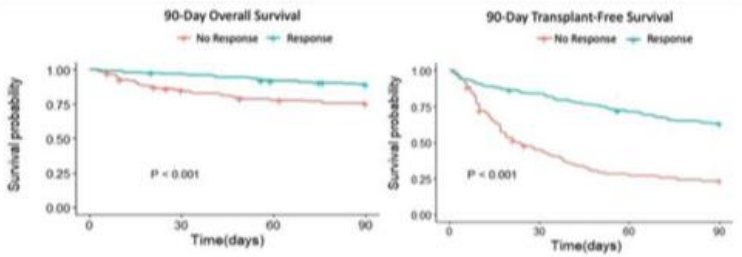
- 317 patients hospitalized with AKI and active on the LT waitlist
- 170 patients had AKI response (53.6%) versus 147 had no response (46.4%)
- Baseline demographics and clinical characteristics mostly similar between the two groups, with a few exceptions

Table 1. Demographics and Clinical Characteristics of the Study Population

	Response (n = 170)	No Response (n = 147)	
Age (y), median [IQR]	59 [51, 65]	59 [48.5, 65]	59
Sex, n (%)			
Male	107 (62.9)	83 (56.5)	19
Female	63 (37.1)	64 (43.5)	12
White race, n (%)	143 (84.1)	118 (80.3)	26
Hispanic race, n (%)	12 (7.1)	19 (12.9)	3
Etiology of cirrhosis, n (%)			
Alcohol	69 (40.6)	44 (29.9)	11
Hepatitis C	8 (4.7)	12 (8.2)	2
Multifactorial	18 (10.6)	13 (8.8)	3
NASH	48 (28.2)	44 (29.9)	9
Other	27 (15.9)	34 (23.1)	6
MELD-Na, median [IQR]	28 [23, 31]	31 [25, 35]	29
MELD-Na 9-23, n (%)	84 (49.4)	77 (52.4)	12
MELD-Na 19 – 24, n (%)	18 (10.6)	33 (22.4)	5
MELD-Na >= 18, n (%)	105 (61.8)	33 (58.2)	14
CLIF-C, median [IQR]	44.3 [39.4, 50.5]	51.1 [44.0, 57.1]	47.2
Medications RTA, n (%)			
Loop diuretic	133 (78.2)	97 (66.0)	23
Aldosterone antagonist	110 (65.1)	83 (56.5)	19
NSAID	11 (6.5)	3 (2.0)	1
Beta-blocker	68 (40.0)	44 (29.9)	11
Complications of cirrhosis, n (%)			
Ascites	159 (93.5)	132 (89.8)	29
Encephalopathy	110 (65.1)	103 (70.1)	21
GI bleeding	61 (35.9)	54 (36.7)	11
SBP	40 (23.5)	32 (21.8)	7
HCC	18 (10.6)	10 (6.8)	2
Type of AKI, n (%)			
Pre-renal	96 (56.5)	34 (23.1)	13
HRS-AKI	32 (18.8)	42 (28.6)	7
ATN	28 (16.5)	54 (36.7)	8
Other	7 (4.1)	2 (1.4)	1
Unable to classify	7 (4.1)	15 (10.2)	3

Results

- **Survival:** AKI responders had improved 90-day overall and transplant-free survival compared to non-responders, after adjusting for age, sex, race, etiology of cirrhosis, study site and MELD-Na score



	HR unadjusted (95% CI)	p-value	HR adjusted (95% CI)	p-value
90-day mortality	0.42 (0.24, 0.74)	0.003	0.34 (0.18, 0.65)	0.001
90-day risk of death or transplant	0.30 (0.22, 0.41)	< 0.001	0.35 (0.25, 0.50)	< 0.001

Meeting

Results

- **Transplant status:** AKI responders underwent fewer transplants within the follow-up period and had a lower 90-day probability of transplant compared to non-responders
- LT tended to mostly occur after discharge for responders, compared to during the index admission for non-responders
- For patients transplanted after discharge, there was a trend toward longer time interval between discharge and LT for responders compared to non-responders

	Response (n = 170)	No Response (n = 147)	Overall (n = 317)	p-value
Transplant				
Transplanted, n (%)	78 (45.9)	90 (61.2)	168 (53.0)	0.01
Transplanted within admission, n (%)	16 (9.4)	56 (38.1)	72 (22.7)	< 0.001
Transplanted after discharge, n (%)	62 (36.5)	34 (23.1)	96 (30.3)	< 0.001
Days from discharge to LT, median [IQR]	103.0 [37.3, 253.3]	57.5 [11.5, 181.3]	79.5 [27.0, 243.3]	0.13

	HR unadjusted (95% CI)	p-value	HR adjusted (95% CI)	p-value
90-day probability of transplant	0.38 (0.26, 0.55)	< 0.001	0.55 (0.37, 0.84)	0.005

Results – Stratification by MELD-Na Categories

- For patients with MELD score ≥ 25, same finding of improved 90-day overall and transplant-free survival, and decreased transplant rate as we saw in the overall cohort

Table 4. Stratified Analysis on Survival and Transplant Outcomes by MELD-Na Categories

	Response (n = 170)	No Response (n = 147)	Overall (n = 317)	p-value
MELD-Na >= 25				
n (%)	114 (67.1)	112 (76.2)	226 (71.3)	
90-day overall survival, n (%)	103 (90.4)	84 (75)	187 (82.7)	0.002
90-day transplant-free survival, n (%)	62 (54.4)	19 (17.0)	81 (35.8)	< 0.001
Transplanted, n (%)	41 (36.0)	65 (58.0)	106 (46.9)	< 0.001
MELD-Na 19 - 24				
n (%)	35 (20.6)	22 (15.0)	57 (18.0)	
90-day overall survival, n (%)	30 (85.7)	18 (81.8)	48 (84.2)	0.72
90-day transplant-free survival, n (%)	27 (77.1)	10 (45.5)	37 (64.9)	0.02
Transplanted, n (%)	3 (8.6)	8 (36.4)	11 (19.3)	0.02
MELD-Na <=18				
n (%)	21 (12.3)	13 (8.8)	34 (10.7)	
90-day overall survival, n (%)	19 (90.5)	12 (92.3)	31 (91.2)	1
90-day transplant-free survival, n (%)	19 (90.5)	8 (61.5)	27 (79.4)	0.08
Transplanted, n (%)	0 (0.0)	4 (30.8)	4 (11.8)	0.02
All MELD-Na scores				
90-day overall survival, n (%)	152 (89.4)	112 (76.2)	264 (83.3)	0.003
90-day transplant-free survival, n (%)	108 (63.5)	37 (25.2)	145 (45.7)	< 0.001
Transplanted, n (%)	78 (45.9)	90 (61.2)	168 (53.0)	0.01

10-14, 20

Conclusion and Key Takeaways

- In patients with cirrhosis on the waitlist for LT who are hospitalized with AKI, AKI responders had better 90-day transplant-free survival and better 90-day overall survival than non-responders
- AKIs should be promptly recognized and treated with etiology-appropriate medical therapy
- AKI responders were less likely to undergo LT by 90 days, though 45% of AKI responders did eventually get transplanted
- Transplants for AKI responders were more likely to occur after discharge, while transplants for non-responders were more likely to occur during the index admission
- Close outpatient monitoring of patients is warranted even after AKI recovery
- AKI responders had shorter hospital and ICU stays, and less likely to require critical care utilization
- Prospective studies in the era of terlipressin use are needed

November 12, 2023 11:00 am - 12:30 pm EST

Liver Transplant Outcomes

Handouts:

PREDICTORS OF HOSPITAL-RELATED OUTCOMES OF COVID-19 INFECTION IN LIVER TRANSPLANT RECIPIENTS IN UNITED STATES: A NATIONWIDE INPATIENT STUDY

TRENDS IN UTILIZATION AND POST-TRANSPLANT OUTCOMES IN COVID-19 POSITIVE DECEASED DONOR LIVER TRANSPLANTATION

PHENOTYPIC CLUSTERING IDENTIFIES HIGH-RISK PROFILES FOR SARCOPENIA & 1-YEAR POST-TRANSPLANT MORTALITY IN PATIENTS WITH END-STAGE LIVER DISEASE

PREHABILITATION IN LIVER TRANSPLANT CANDIDATES IMPROVES FRAILTY METRICS LEADING TO IMPROVED SURVIVAL

EARLY GRAFT FAILURE AFTER LIVING DONOR LIVER TRANSPLANT

REAL-TIME MEASUREMENTS OF BIOMARKERS FOR GRAFT ASSESSMENT AND PATIENT MONITORING

Captured

Location: Ballroom A, Hynes Convention Center


Roy X Wang
University of Pennsylvania


Abdullah Sohail
The University of Iowa Hospitals an...


Florian Huwyler
University Hospital Zurich


Ahmad Anouti
University of Texas Southwestern...


Ameet Mandot


Fei-Pi Lin

Outcomes

Patient Characteristics	Liver Transplant with COVID-19 N(%)	Liver Transplant without COVID-19 N(%)	P Value
Mortality	309 (13.7%)	1155 (2.47%)	< 0.01
Mechanical Ventilation	314 (13.9%)	5552 (11.9%)	0.16
Intensive Care Unit	339 (15%)	5738 (12.3%)	0.06
Septic Shock	239 (10.6%)	3359 (7.2%)	< 0.01
Mean Length of Stay	8.96 days	8.17 days	0.12
Mean Hospitalization charge	$125,961	$177,058	0.12

COVID-19 infection is an independent predictor of mortality in LT recipients, with a 5-fold increase in mortality compared to LT patients without COVID-19.

This data (2020) predates the availability of COVID vaccines, and many LT recipients have since been vaccinated.

When LTX pts acquire infection, they should be treated promptly with the latest therapies to improve their clinical outcomes

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University of Texas Southwestern...

Ameet Mandot

Fei-Pi Lin

Background

- Demand for organs for transplant continues to exceed organ supply
- Organ supply and transplantation was significantly affected by the COVID-19 pandemic
- Potential use of COVID-19(+) donors

SPECIAL ARTICLE | HEPATOLOGY, VOL. 72, NO. 1, 2020

Clinical Best Practice Advice for Hepatology and Liver Transplant Providers During the COVID-19 Pandemic: AASLD Expert Panel Consensus Statement

Oren K. Fix,[1] Bilal Hameed,[2] Robert J. Fontana,[3] Ryan M. Kwok,[4] Brendan M. McGuire,[5] David C. Mulligan,[6] Daniel S. Pratt,[7] Mark W. Russo,[8] Michael L. Schilsky,[6] Elizabeth C. Verna,[9] Rohit Loomba,[10] David E. Cohen,[11] Jorge A. Bezerra,[12] K. Rajender Reddy,[13] and Raymond T. Chung[7]

Review JHEP|Reports

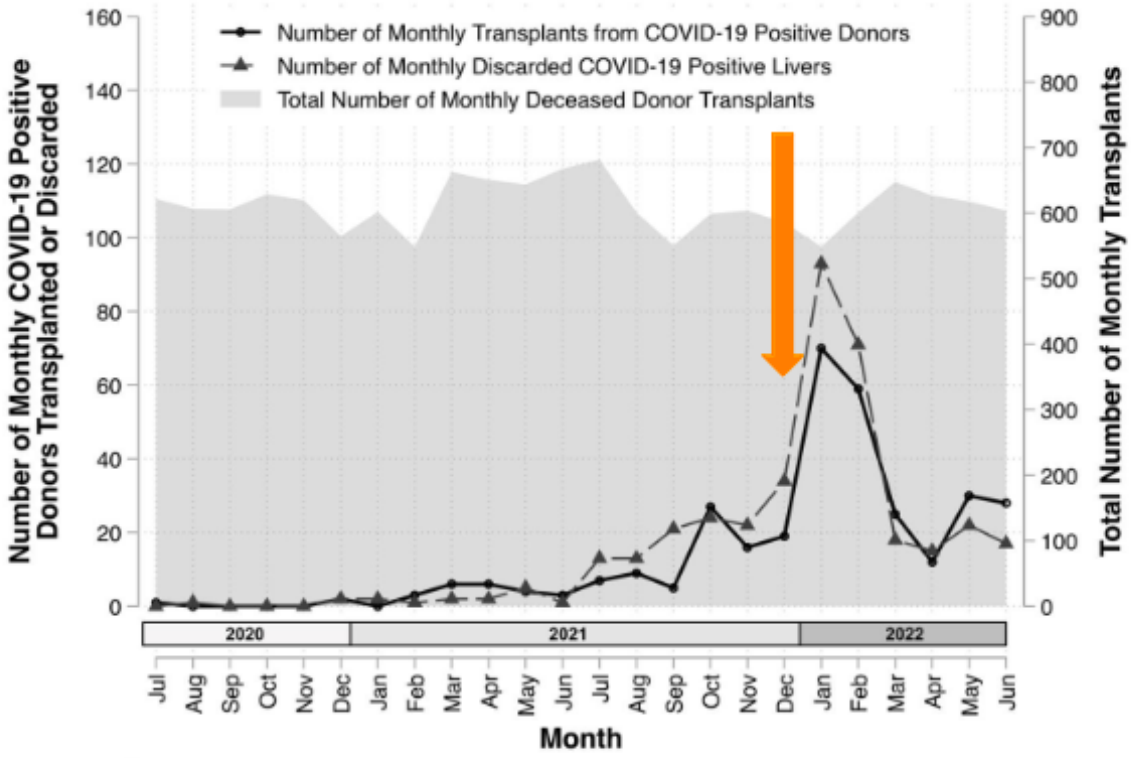
Impact of COVID-19 on the care of patients with liver disease: EASL-ESCMID position paper after 6 months of the pandemic

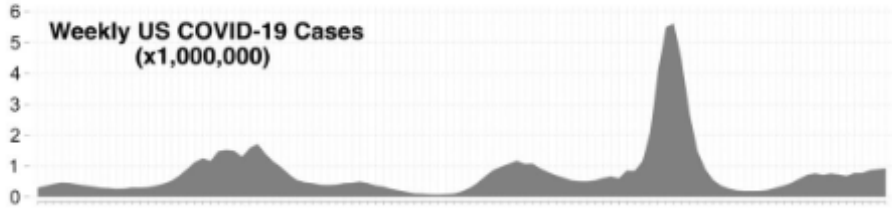
Tobias Boettler,[1,†] Thomas Marjot,[2,†] Philip N. Newsome,[3,4] Mario U. Mondelli,[5] Mojca Maticic,[6,7] Elisa Cordero,[8] Rajiv Jalan,[9] Richard Moreau,[10,11] Markus Cornberg,[12,13] Thomas Berg[14,*]

AASLD The Liver Meeting® Nov. 10-14, 2023

Wang RX, Abu-Gazala S, Mahmud N. *Liver Transpl*. 2023

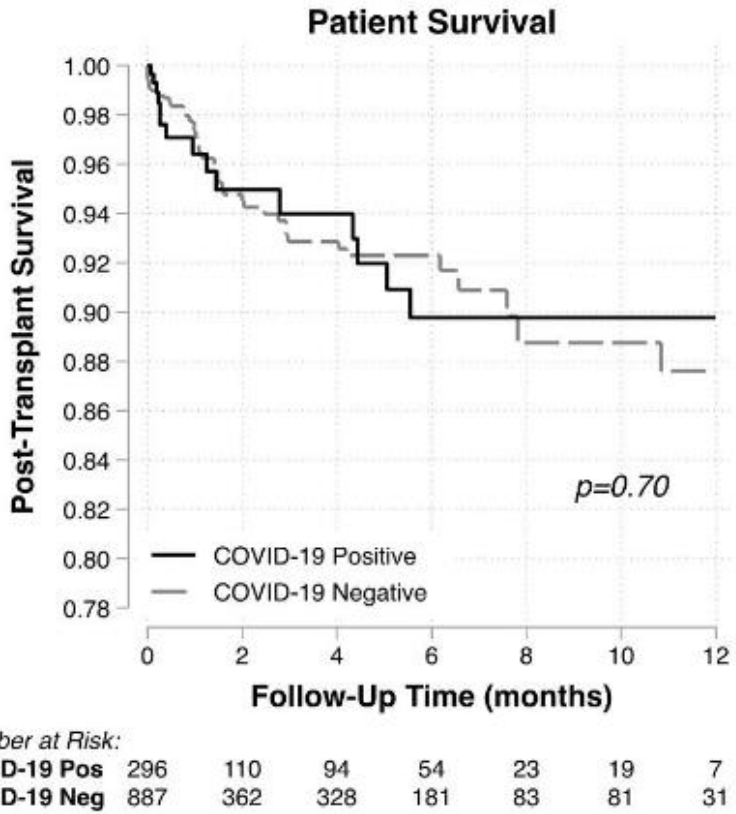
Utilization of COVID-19(+) livers over time





AASLD The Liver Meeting® Nov. 10-14, 2023

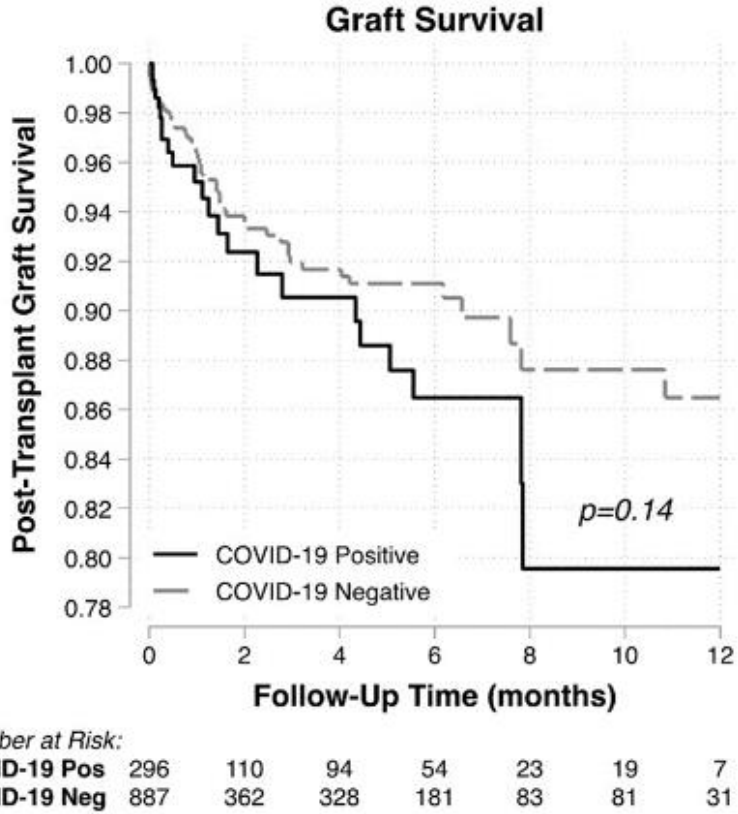
Post-transplant Outcomes



Number at Risk:

COVID-19 Pos	296	110	94	54	23	19	7
COVID-19 Neg	887	362	328	181	83	81	31

FGCR: subHR 1.11, 95% CI 0.61-2.00, p=0.74
***Retransplant as competing event**



Number at Risk:

COVID-19 Pos	296	110	94	54	23	19	7
COVID-19 Neg	887	362	328	181	83	81	31

Cox: HR 1.44, 95% CI 0.88-2.36, p=0.14

Discussion

- Utilization of COVID-19(+) livers has increased over time
- Transplanted COVID-19(+) livers came from younger donors and more often donors after brain death
- Regions with high median MELD score at transplant had higher utilization of COVID-19(+) livers
- No significant difference in 1-year post-TX pts or graft survival by donor COVID-19(+/-) status

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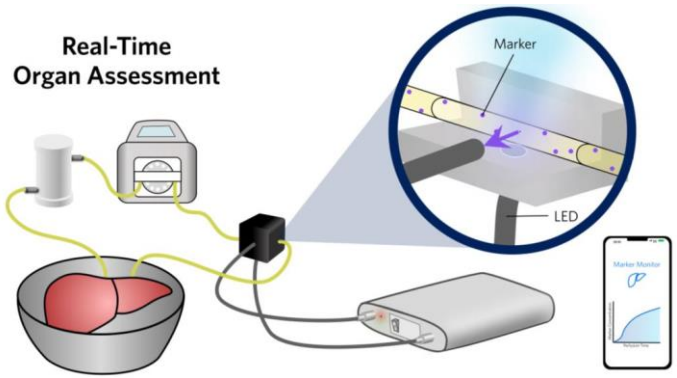
Ameet Mandot


Fei-Pi Lin

12.11.2023, TLM 2023
Boston

Real-Time Measurements of Biomarkers for Graft Assessment and Patient Monitoring

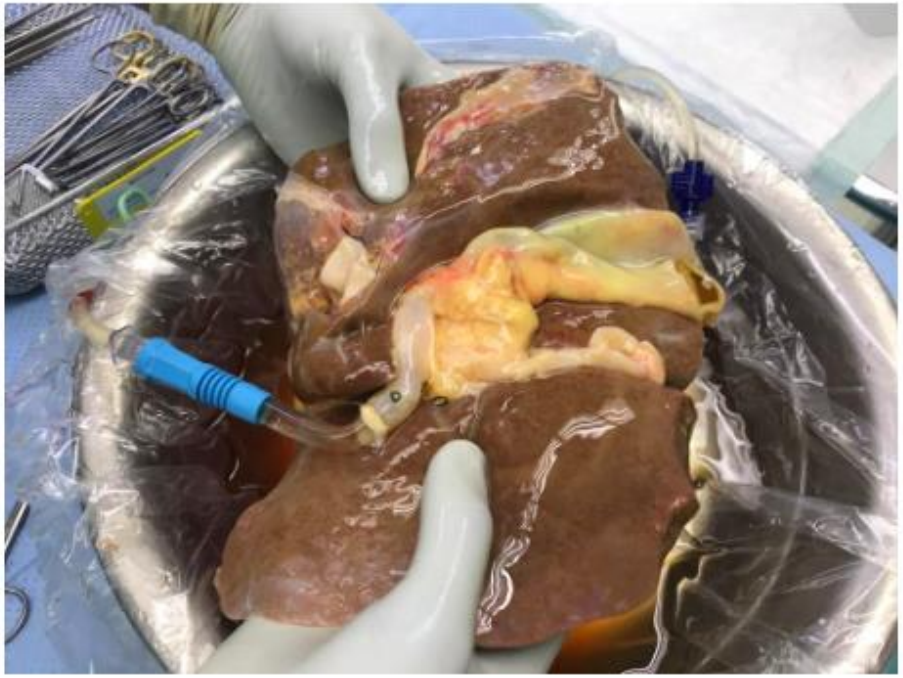
Florian Huwyler [1,2,3], *Janina Eden [2], Jonas Binz [1], Leslie Cunningham [1,2,3], Richard Sousa Da Silva [2,3], Max Hefti [3], Pierre-Alain Clavien [3], Philipp Dutkowski [2,3], Mark W. Tibbitt [1,3]*



Current Organ Assessment Strategy

- **Ischemic damage ??**
- Donor history
- Haptic evaluation
- Visual inspection
- Biopsy

→ Decision up to surgeon's "gut feeling" and experience



Hypothermic Oxygenated PErfusion (HOPE)

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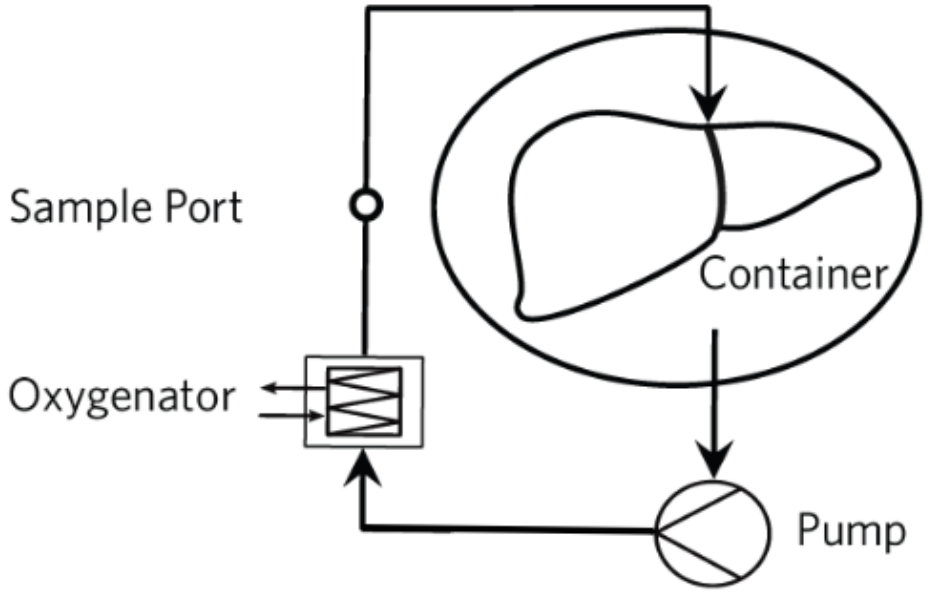
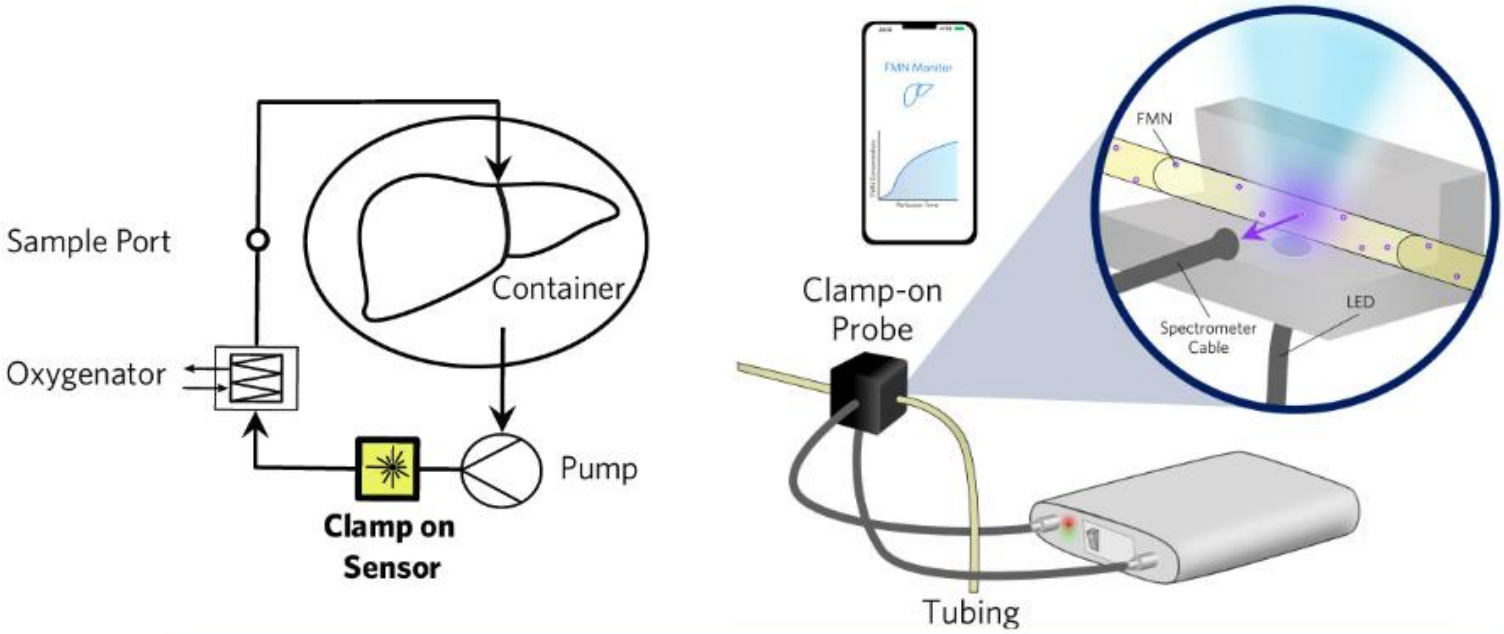


First re-oxygenation can happen ex-situ.

Lower risk of non-anastomotic biliary strictures and severe post-transplant complications

Solution – A Portable Spectrofluorometric Device



Simple device allows non-invasive convenient real-time measurement

Future of Real-Time Sensors in Clinics

The same approach works also for non-fluorescent molecules and real-time data can be even set to smartphones

Advances in Liver Transplant for Children and Adults

Captured

Liver disorders are undergoing rapid changes in diagnostics and management, with novel investigative approaches and modifications to liver allocation systems. This session will bring state-of-the-art basic, translational, and clinical abstracts and updates to the attendees of TLM 2023, spanning both pediatric and adult practice.

Handouts:

SIMULTANEOUS LIVER TRANSPLANT AND SLEEVE GASTRECTOMY IS A SAFE SURGICAL OPTION THAT IMPROVES METABOLIC SYNDROME AND REDUCES ALLOGRAFT STEATOSIS

SINGLE CELL TRANSCRIPTIONAL T CELL DYNAMICS OF PEDIATRIC LIVER TRANSPLANT REJECTION

CENTER-SPECIFIC DATA FROM THE INTERNATIONAL MULTICENTER PEDIATRIC PORTAL HYPERTENSION REGISTRY (IMPPHR) – INITIAL ANALYSES OF 23 INTERNATIONAL SITES

ANONYMOUS LIVING LIVER DONATION IMPROVES ACCESS FOR MEDICALLY UNDERSERVED CHILDREN IN NEED OF LIVER TRANSPLANTATION: THE CANADIAN EXPERIENCE

IMMUNE SYSTEM IN THE LIVER OF POST-TRANSPLANT ALLOIMMUNE HEPATITIS AND AUTOIMMUNE HEPATITIS PATIENTS TIPPED IN FAVOR OF NON-SUPPRESSIVE MECHANISMS

FAVOURABLE OUTCOMES OF PEDIATRIC LIVER TRANSPLANTATION FOR PRIMARY LIVER TUMORS- RETROSPECTIVE ANALYSIS OF A LARGE CANADIAN COHORT

Location: Room 312, Hynes Convention Center

MAYO CLINIC

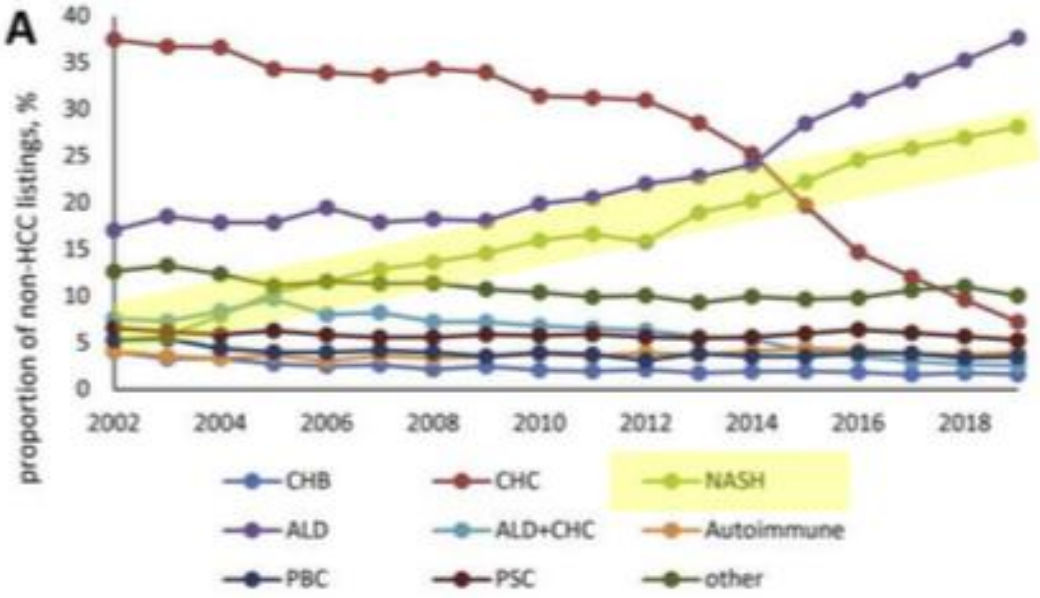
SIMULTANEOUS LIVER TRANSPLANT AND SLEEVE GASTRECTOMY IS A SAFE SURGICAL OPTION THAT IMPROVES METABOLIC SYNDROME AND REDUCES ALLOGRAFT STEATOSIS

Ellen Larson MD
Mayo Clinic General Surgery Resident

AASLD
November 12, 2023

THE RISE OF METABOLIC SYNDROME

- Metabolic syndrome:
  - Obesity
  - Diabetes
  - Hyperlipidemia
  - Hypertension
- 41.1% of candidates have BMI ≥ 30, and 17.3% had BMI ≥ 35 kg/m^2
- Metabolic associated steatohepatitis (MASH) is one of the fastest growing, now 2nd most common indication for transplant listing
- MS or its components may independently increase post-transplant morbidity/mortality



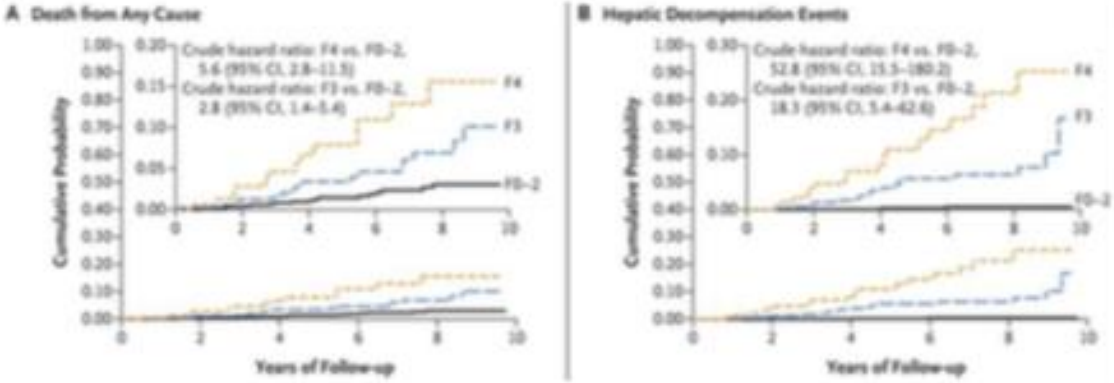
Younossi et al. Clin Gastroenterology and Hepatology, Vol 19, i3, 2021, Pp 580-589

Kwong et al. *OPTN/SRTR 2021 Annual Data Report: Liver.* Am J Transplant. 2023 Feb

FIBROSIS FROM MASLD IS MORBID… AND RECURRENT

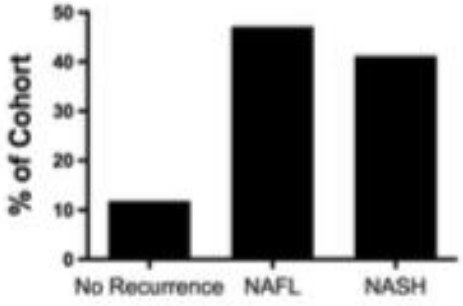
- **Fibrosis** is predictive of death from any cause and death from hepatic decompensation

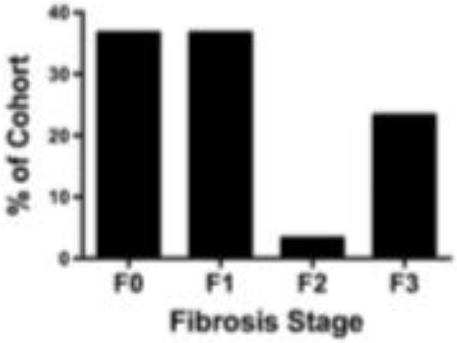
Sanyal et al. NEJM 2021;258:1559-69



- Up to 90% of patients transplanted for MASH have **recurrent** MASLD fibrosis

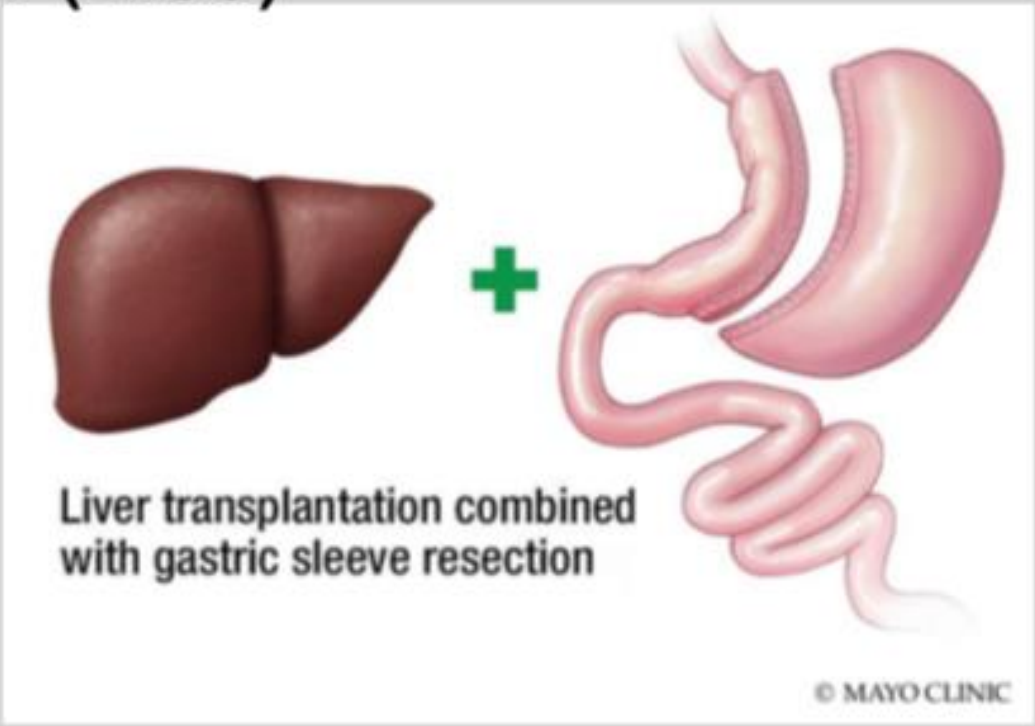
Bhati et al. Transplantation; 101(8):p 1867-1874, August 2017



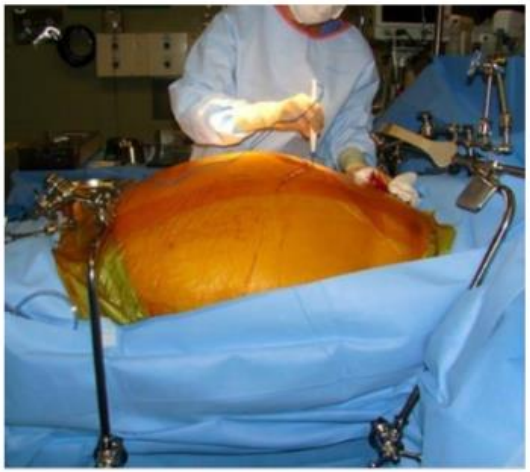


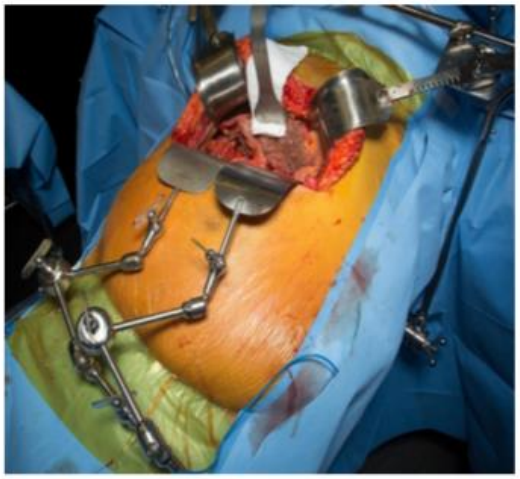
SIMULTANEOUS LIVER TRANSPLANT AND SLEEVE GASTRECTOMY (LTSG)

- Offered at Mayo Clinic since 2009
  - All patients with BMI>35 are enrolled in non-invasive weight loss protocol
  - Those who are unsuccessful are offered combined LT+SG
- SG performed by bariatric-trained surgeon



INTRA-OP



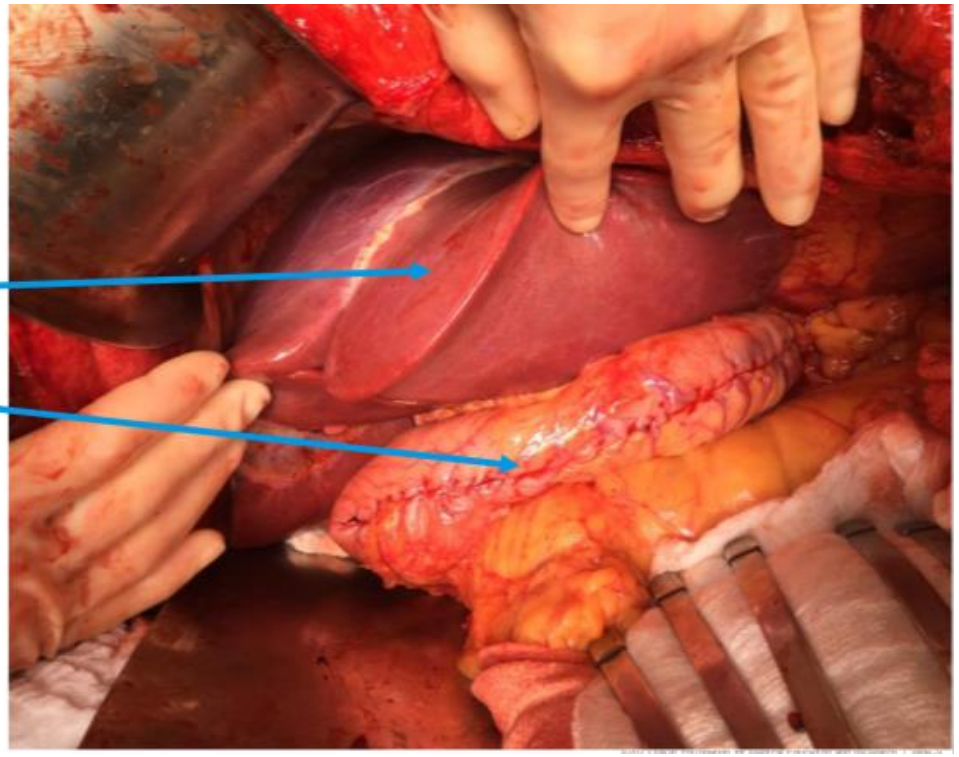


Subcostal exposure

INTRAOP

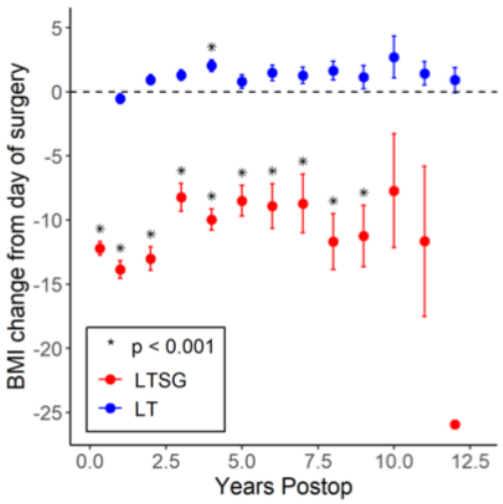
Liver allograft

Stomach suture line



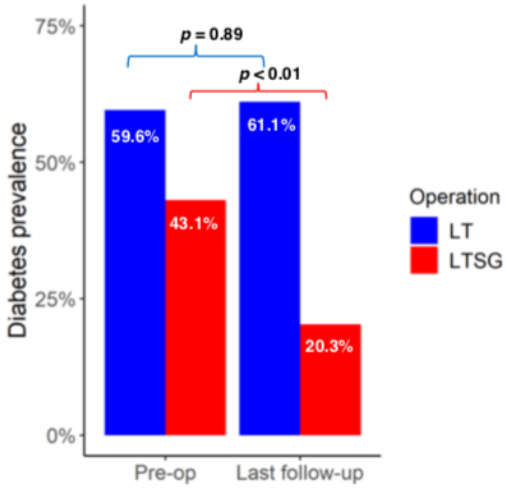
RESULTS: SUSTAINED WEIGHT LOSS AFTER LTSG

- No significant trend in weight after LT
- LTSG causes significant weight loss that persists for > 9 years



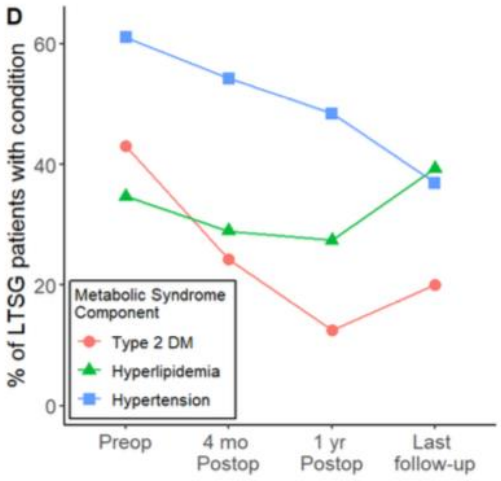
RESULTS: RESOLUTION OF METABOLIC SYNDROME AFTER LTSG

- LT patients have no significant change in the prevalence of diabetes after transplant
- LTSG patients have a significant decrease



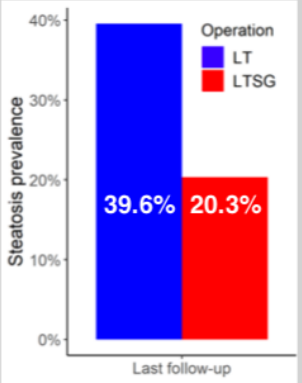
RESULTS: RESOLUTION OF METABOLIC SYNDROME AFTER LTSG

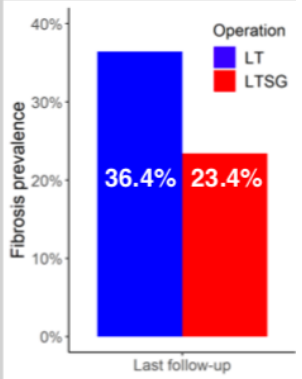
- Diabetes decreases significantly, from 43% to 20%
- Hyperlipidemia decreases during the first year but is unchanged in the long term
- Hypertension decreases significantly, from 59% to 37%



RESULTS: DECREASED RECURRENCE OF HEPATIC STEATOSIS AND FIBROSIS

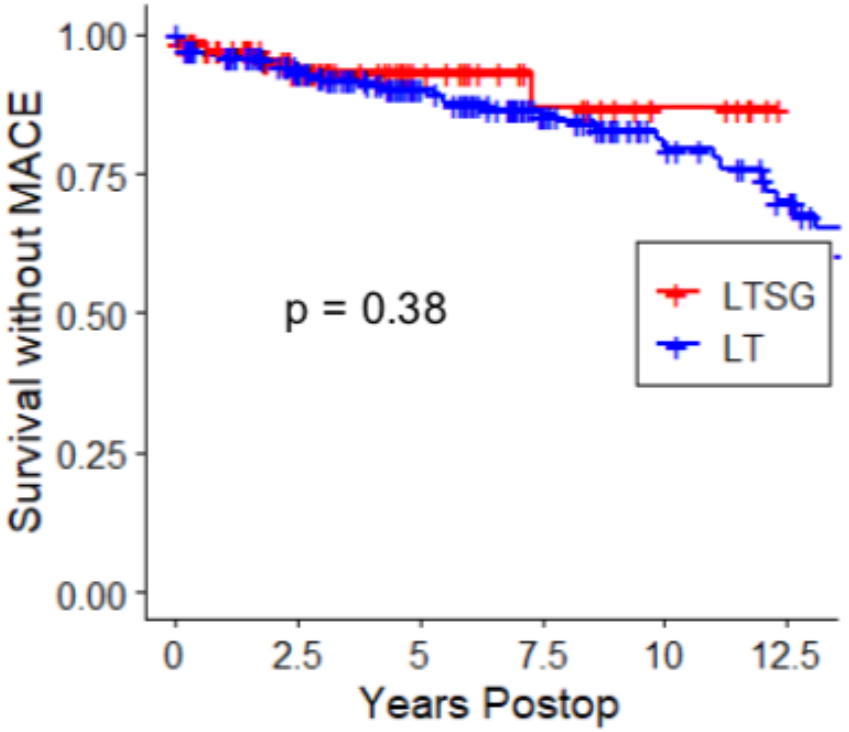
Steatosis	Fibrosis
• Annual ultrasound to assess post-op steatosis	• Intermittent post-op magnetic resonance elastography
• $p = 0.015$ (significant)	• $p = 0.16$ (not significant)





RESULTS: SURVIVAL EQUIVALENCY FOR LTSG AND LT

- No difference in overall survival between LT and LTSG patients
- No difference in allograft survival between LT and LTSG patients
- No difference in incidence of major adverse cardiac events (MACE) between LT and LTSG patients
  - MACE: nonfatal MI, nonfatal stroke, or cardiovascular cause of death

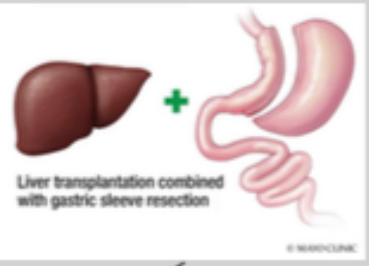


SLEEVE COMPLICATIONS: STAPLE LINE LEAK: • 1 patient

REFLUX: 16 Pts • Diabetes • Male gender • Pre-op GERD

CONCLUSIONS

LTSG is a safe procedure in both short and long term. It is associated with sustained weight loss, improvement in metabolic syndrome, and decreased recurrence of MASLD.



4 months
- DM2 and HTN improve
- Men with GERD & DM2 at risk for severe reflux

1 year
- DM2 and HTN improve

Postop
No increase in all-cause mortality, graft failure, or MACE events

9 years
Persistent decrease in BMI

Last follow up
decreased prevalence of steatosis, fibrosis, DM2, HTN

Liver Transplantation for Severe Acute on Chronic Liver Failure: Results of a Prospective National Programme of Waitlist Prioritization.

W Bernal [1], R Taylor [2], A Chauhan[3], MJ Armstrong[3], MED Allison[4], T Pirani [1], J Moore[5], L Burke[5], [6]S Masson, [6]D Cressy, [7]BJ Hogan, [7]R Westbrook, [7]R Jalan, [8]KJ Simpson, [3]J Isaac, [7]D Thorburn.

[1] Kings College Hospital, London, [2] NHS Blood and Transplant, [3]Queen Elizabeth Hospital, Birmingham, [4]Addenbrookes Hospital, Cambridge, [5] St James University Hospital, Leeds, [6]Freeman Hospital, Newcastle, [7] Royal Free Hospital, London, [8]Edinburgh Royal Infirmary, Edinburgh.
United Kingdom.

Late breaking

Background: ACLF: EASL-CLIF Classification.

EASL-CLIF Organ Failure Score

Organ System	1 Point	2 Points	3 Points
Liver	Bilirubin <6 mg/dl	Bilirubin 6.0–11.9 mg/dl	Bilirubin ≥12 mg/dl
Kidney	Creatinine <1.5 mg/dl Creatinine 1.5–1.9 mg/dl	Creatinine 2.0–3.4 mg/dl	Creatinine ≥3.5 mg/dl or RRT
Brain (West Haven criteria)	Grade 0	Grade 1–2	Grade 3–4
Coagulation	INR <2.0	INR 2.0–2.4	INR ≥2.5
Circulation	MAP ≥70 mm Hg	MAP <70 mm Hg	Vasopressor requirement
Respiration	Pao_2/Fio_2 >300 Spo_2/Fio_2 >357	Pao_2/Fio_2 201–300 Spo_2/Fio_2 215–357	Pao_2/Fio_2 ≤200 Spo_2/Fio_2 ≤214

Arroyo V et al NEJM 2020;382:2137-2145

Moreau et al Gastroenterology 2013 144: 1426-13

ACLF-1

Renal or cerebral failure alone or renal dysfunction with other organ failure.

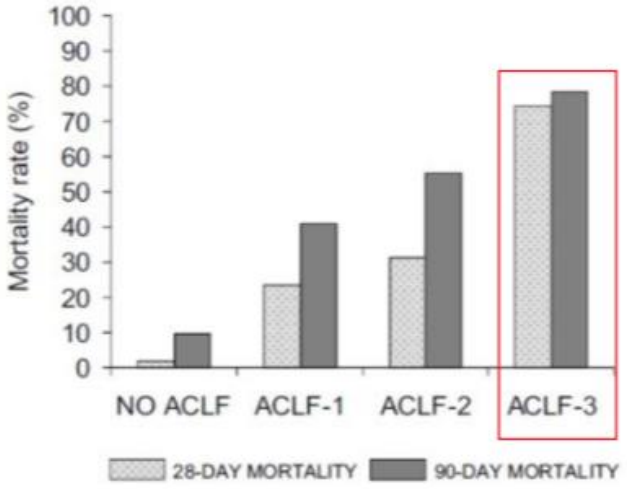
ACLF-2

Two Organ Failures.

ACLF-3

Three or More Organ Failures.

Background: ACLF-3: high mortality, little improvement over time.



Supplementary Figure 2. Mortality rate at 28 days and 90 days according to the grade of ACLF.

Moreau et al Gastroenterology 2013 144: 1426-13

No survival benefit:

- **Extra-Corporeal Devices:**

Prometheus

Gastroenterology 2012 42(4)782-9

MARS

Hepatology 2013 57:1153-62

ELAD

Liver Transplantation 2018 24;380-393

- **Novel Medical Therapies**

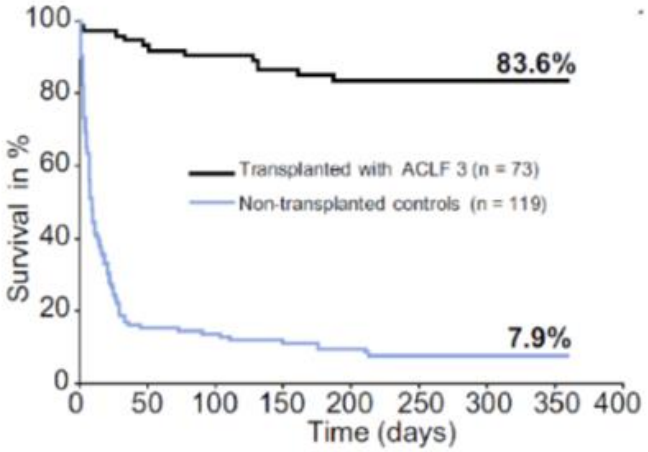
G-CSF

J Hep 2021 75: 1346-1354

- **Liver Transplantation?**

Background: Liver Transplantation (LT) for ACLF-3.

3 French centres 2004-2014



Artu et al J Hepatol 2017;67(4)708-15

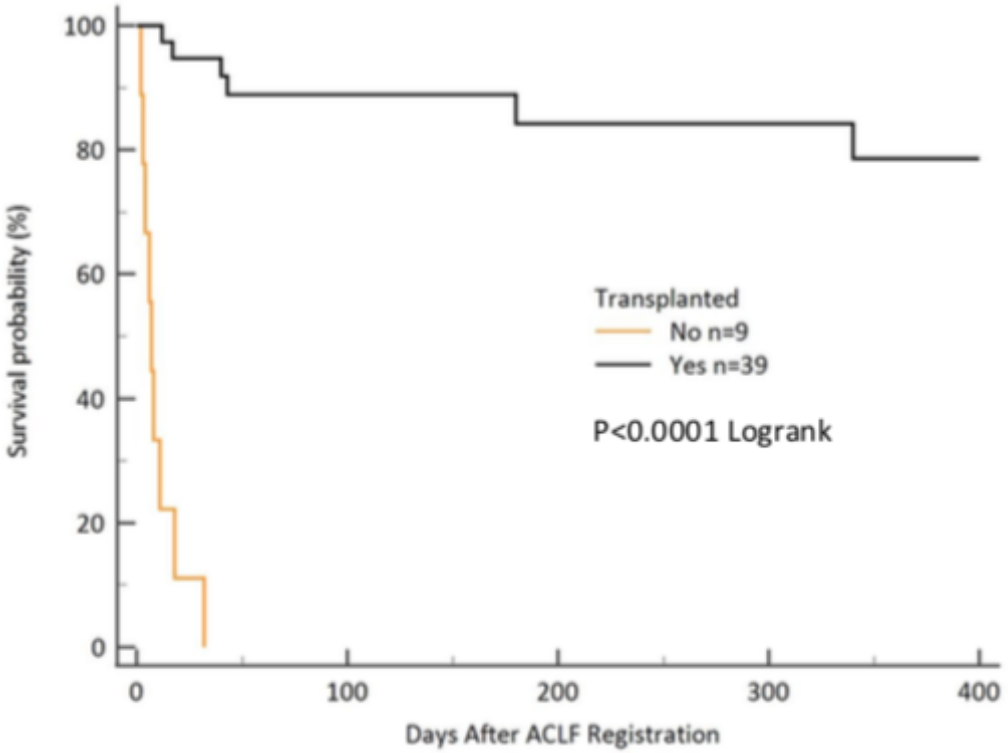
Concerns:

- **Unacceptably high mortality.**
  J Hepatol 2023 78 1118-23
- **Difficulty in case selection.**
  Gastro 2019 156(5):1381-91
- **Narrow time window.**
  J Hepatol 2022 77 S1-S118
- **High resource use.**
  Clin Gastro Hep 2022 22 S1542-3565
- **No prospective data.**

Background: UK Prioritised Liver Transplantation for ACLF.

- **United Kingdom Liver Advisory Group NHS Blood and Transplant**
  - Standard UK Transplant allocation models underestimate ACLF mortality.
  - Sought to confirm and replicate international retrospective findings.
- **National Pilot Programme of Prioritised Liver Transplantation for ACLF**
  - Prioritised 'ACLF tier' above standard offering.
  - Selected recipients, deceased brain-dead donor grafts.
  - 50 tier registrations and review.
  - Pre- and post-transplant management at centres discretion.
  - Endorsed by all 7 UK Transplant Centres.
  - Initiated in May 2021.
  - Results of Programme Evaluation: Process and Survival.

Results: Patient Survival after ACLF Tier Registration.



Non-Transplanted
n=9 (19%)
100% mortality
Median survival 7 (4-15) days.

Transplanted
n=39 (81%)
Median follow-up 171 days
85% survival
1 year survival 78%

Length of ICU Stay 14 (7-28) days
Length of Hospital Stay 35 (25-55) days

Conclusions: First Prospective National Series of prioritised LT for severe ACLF

Waitlist deaths:

- Prioritisation tier - transplantation at median 3 days after registration.
- Waitlist mortality approximately 20%
- longer wait-time, higher BMI, more severe multi-organ failure.

Transplant recipients:

• Optimal deceased donor grafts.

• Prolonged but not excessive hospitalisation. • 1 year survival approximately 80%.

• Most deaths in immediate post-LT stay.

Non-survivors of Transplantation:

• Longer wait-time, more severe multi-organ failure. • More often first presentations with ACLF.

Transplantation practical and effective for selected patients with ACLF.

• Currently no other such effective treatment options in this setting.

• Increased resource use and higher mortality than standard LT.

• Prioritisation required – very limited time window.

• ACLF tier to be operationalised in the UK.

Need for optimisation of process:

• Improved case selection:

• Multi-organ failure severity.

• Why worse outcomes in de novo presentations with ACLF.

Ultrashort GLE/PIB and Ezetimibe for HCV D+/R- Solid Organ Transplant: "Toronto Protocol"

Background: G/P and ezetimibe (E) given 1d pre and 7d post-SOT prevented chronic HCV in a clinical trial of 30 D+/R- organ recipients.

Aim: Report extended follow-up of clinical trial (n=30) and outcomes of standard of care (n=59) cohorts

Methods: Primary endpoint: establishment of chronic HCV

Results:

- **SOC cohort:** all but 5 kidney recipients completed full treatment before hospital discharge; none had HCV RNA breakthrough
- **Total cohort**: No virologic breakthrough, HCV complications, or retreatment

Conclusions: Ultrashort G/P + E protocol for HCV D+/R- prevents chronic HCV infection, is well-tolerated, and is feasible.

Recipients

Variables	Recipients (n=59)
Age (years)	59 (23-80)
Male	35 (59%)
Organ Received	
Lung	14 (24%)
Heart	6 (10%)
Kidney	33 (56%)
Pancreas	0 (0%)
Kidney-Pancreas	3 (5%)

Learning from implementation

1. **Specified Protocol**
   - Notification of all NAT+ donors to:
     - Surgeon
     - House-staff
     - Transplant team
     - Hepatology
   - Order sets for medications & HCV RNA/NAT testing post-op
   - Pre- and post-transplant infographics emailed to all involved staff
   - Follow-up visit with hepatology 3m post-transplant
2. **Missed/late NAT/HCV RNA testing** (n=19 (32%))
3. **Regular (monthly) audit** of all charts

Aleyadeh W, et al. Abstract 56

November 11, 2023 04:00 pm - 05:00 pm EST

Current Trends in Liver Transplants

Handouts:

234: ESTIMATING GFR IN PATIENTS WITH DECOMPENSATED CIRRHOSIS AWAITING TRANSPLANT: UPDATED GRAIL WITHOUT RACE PERFORMS BETTER THAN CKD EPI 2021

Common indication for liver transplantation among candidates with hepatocellular carcinoma in the United States

Predictors of Renal Recovery and Survival Outcomes in Liver Transplant Recipients Meeting SLK Eligibility Criteria

Location: Grand Ballroom, Sheraton Boston Hotel

Current Trends in Liver Transplants

Trinidad Serrano
HCU Lozano Blesa

Zobair M. Younossi
Inova Health System


Richie Manikat
Stanford University Medical Center


Sumeet Asrani
Baylor University Medical Center

Introduction of race neutral equations

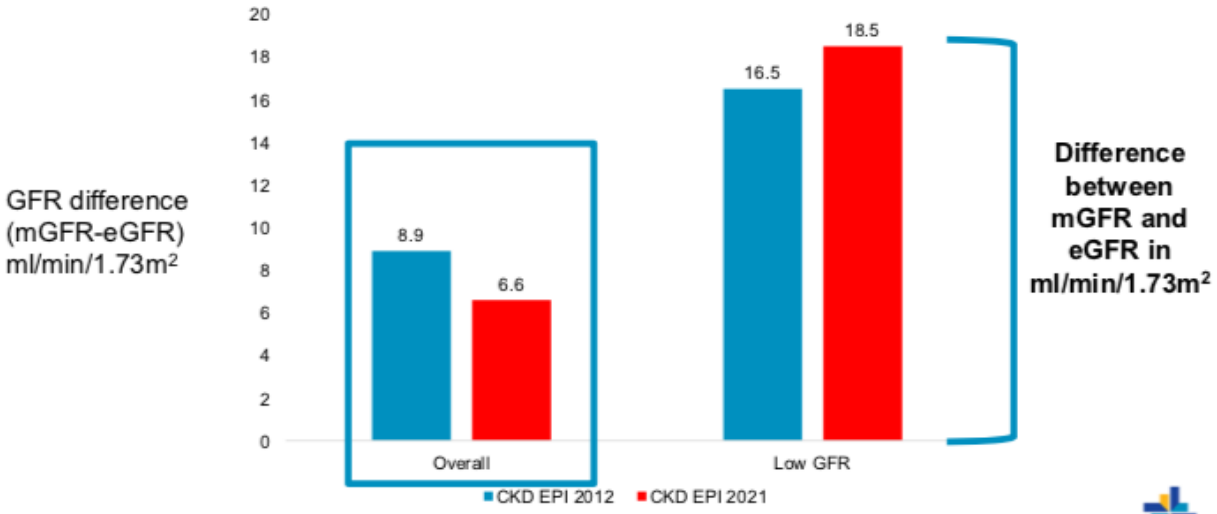
Accurate assessment of kidney function important in cirrhosis

New race neutral equations introduced and rapidly implemented across the US (CKD-EPI 2021)

Performance in cirrhosis patients unclear + not developed in cirrhosis

Pathophysiology of kidney dysfunction multifactorial in cirrhosis and may not be captured well by CKD equations

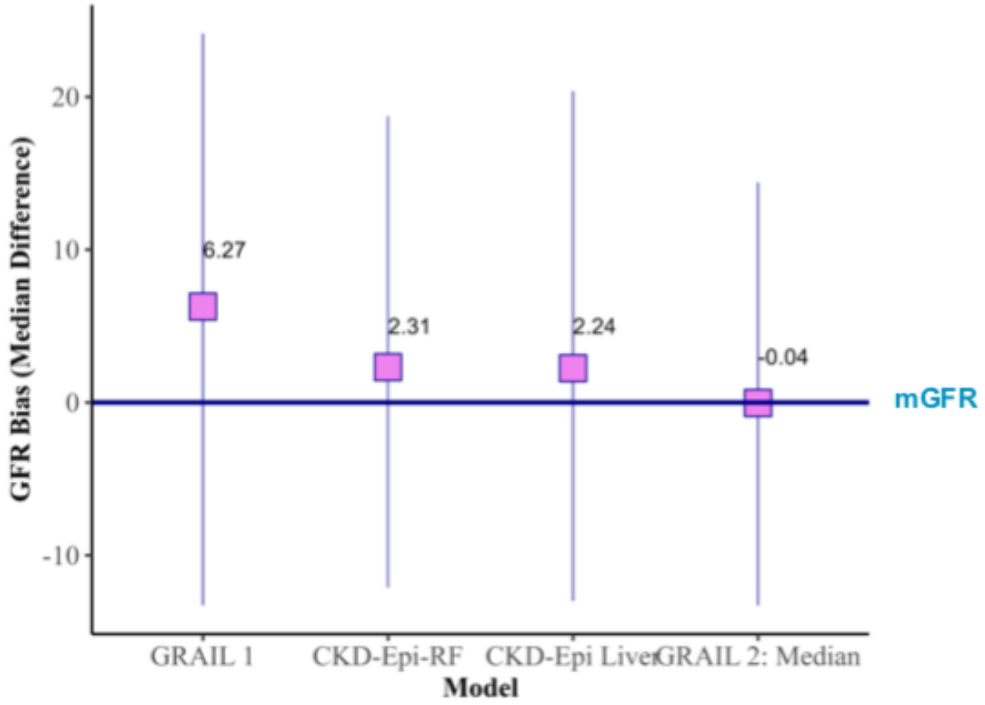
Performance of CKD EPI 2021 in cirrhosis



Liver-specific equations (GFR assessment in liver disease**, GRAIL**, Asrani et al. Hepatology 2019)

- better performance as compared to other GFR equations.
- GRAIL 2: The final components were: age, sex, albumin, creatinine, and BUN

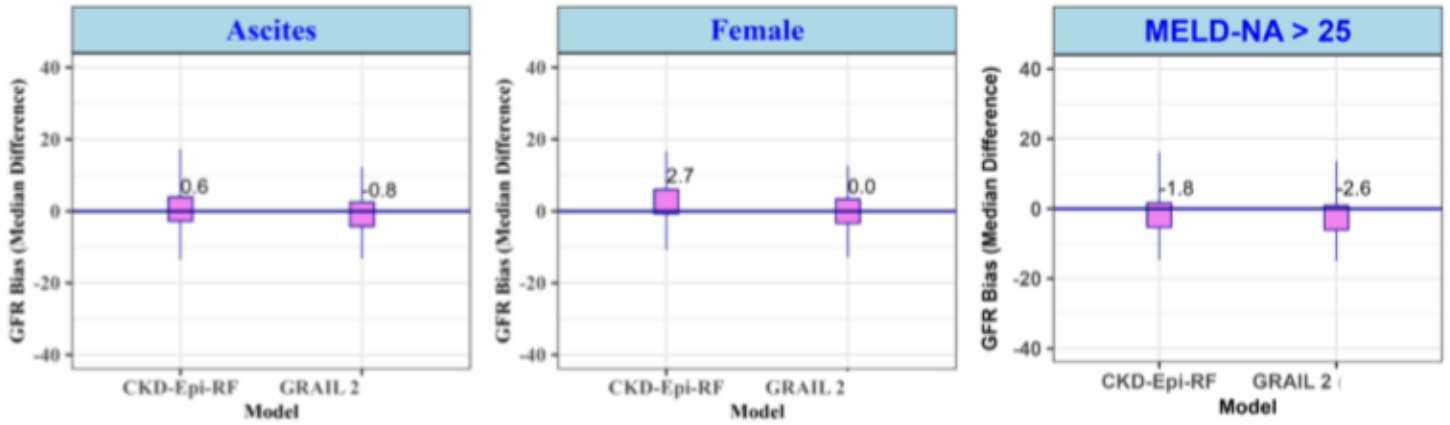
Overall Bias (difference between mGFR and eGFR)



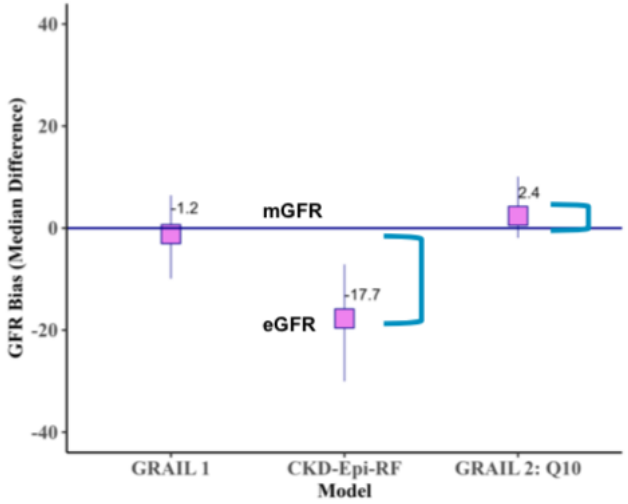
Updated GRAIL performs better than CKD-EPI 2021

	CCC (CI)	Bias (ml/min)	CKD agreement	P30%
CKD-EPI 2021	0.67 (0.64-0.69)	2.31	68%	74%
GRAIL 2.0	**0.79 (0.77-0.81)**	**-0.04**	**71%**	**77%**

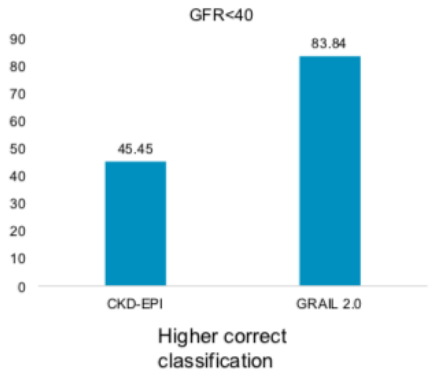
Performance across subgroups

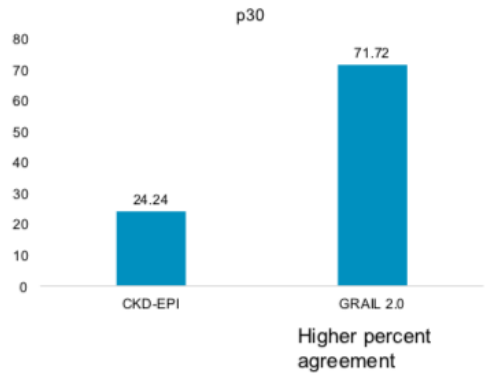


Bias lower in GFR<40 with GRAIL 2.0



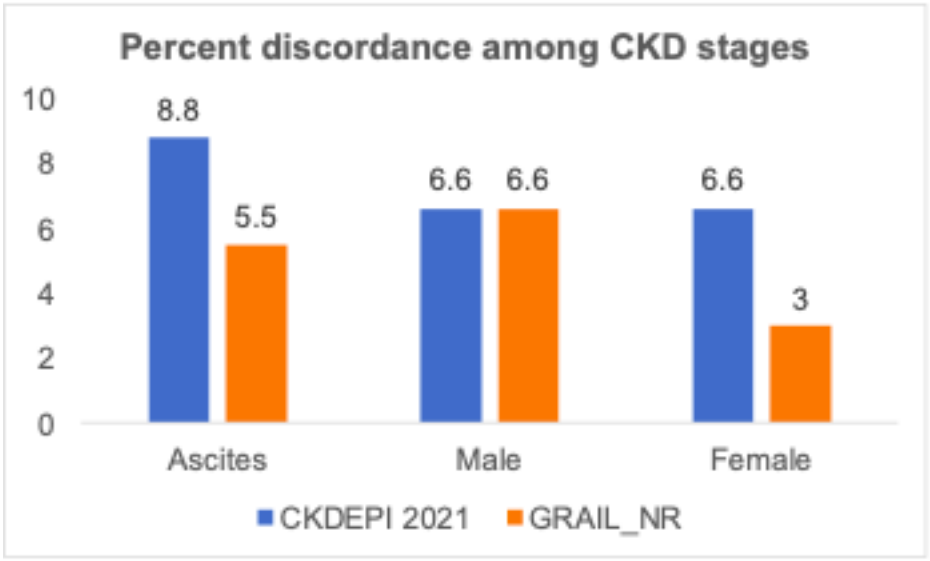
Low GFR

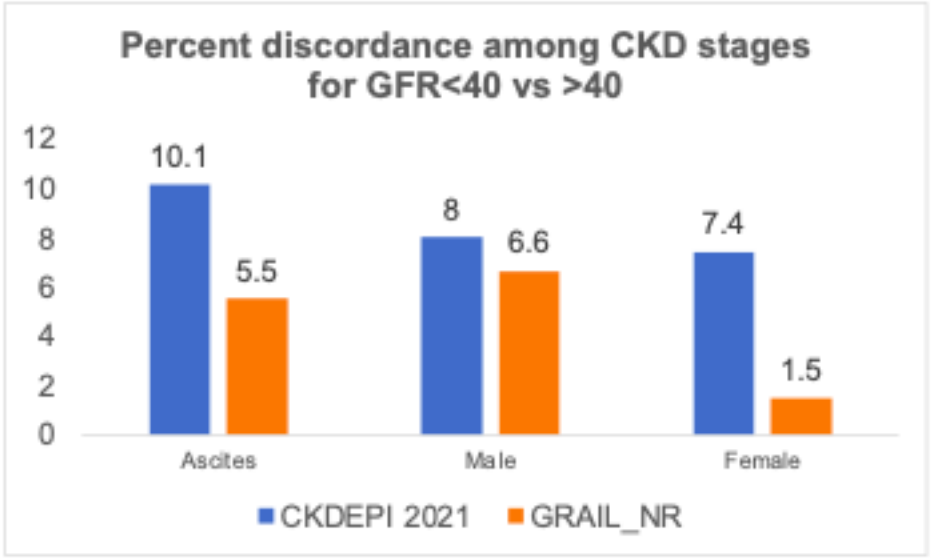




November 11, 2023 04:45 pm EST - November 11, 2023 05:00 pm EST

234: ESTIMATING GFR IN PATIENTS WITH DECOMPENSATED CIRRHOSIS AWAITING TRANSPLANT: UPDATED GRAIL WITHOUT RACE PERFORMS BETTER THAN CKD EPI 2021





Percent discordance between estimated CKD stage and actual CKD stage was lower with GRAIL_NR in patients with ascites and females. This was especially pronounced when limited to patients with GFR<40ml/min/1.73m^2

Summary

CKD-EPI 2021 has acceptable performance in patients with cirrhosis but has poor performance at low GFR

GRAIL 2.0 is a novel equation developed and validated in patients with cirrhosis that has better performance characteristics as compared to CKD-EPI 2021 especially at low GFR

GRAIL 2.0 may better capture kidney dysfunction in decompensated cirrhosis and predict future outcomes

Next steps: External validation and clinical application

November 12, 2023 09:00 am - 10:00 am EST

Transplant Surgery Plenary

Handouts:

SURGICAL BILIARY DIVERSION IS ASSOCIATED WITH AN INCREASED RISK OF LIVER TRANSPLANTATION OR DEATH IN ALAGILLE SYNDROME

VALIDATION OF THE R3-AFP MODEL FOR RISK PREDICTION OF HCC RECURRENCE AFTER LIVER TRANSPLANTATION IN THE SILVER CLINICAL TRIAL

IMPACT OF ACUTE KIDNEY INJURY RESPONSE ON SURVIVAL AND LIVER TRANSPLANT RATES IN HOSPITALIZED PATIENTS WITH CIRRHOSIS AWAITING LIVER TRANSPLANTATION: RESULTS FROM THE HRS-HARMONY CONSORTIUM

Live Stream

Location: Auditorium, Hynes Convention Center

Charlotte Laurent...
Massachusetts General Hospital an...

David W. Victor
Houston Methodist Hospital


Xing Li
Massachusetts General Hospital

Shannon M. Vandriel
The Hospital for Sick Children, The...

Session Evaluation | + Add to My Schedule | View More Details

Background

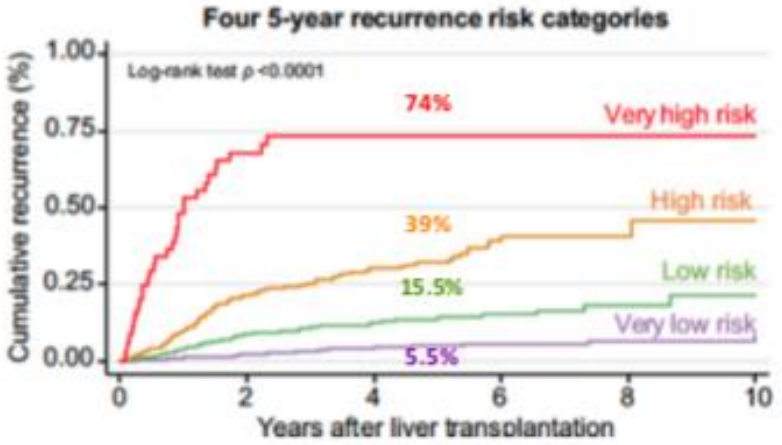
Research article JHEP Reports

R3-AFP score is a new composite tool to refine prediction of hepatocellular carcinoma recurrence after liver transplantation

Recurrence
Risk
Reassessment
- AFP

European derivation cohort (n=1359)
Latin American validation cohort (n=1085)
(clinicaltrials.gov NCT03775863)

R3-AFP variables	Score
<Number of nodules	
≥4 nodules	1
Size largest nodule	
≤3 cm	0
3-6 cm	1
>6 cm	5
Vascular invasion	
Yes	2
Nuclear grade >II	
Yes	1
Last pre-LT AFP value (ng/ml)	
<100	0
100-1,000	1
>1,000	2
Recurrence risk categories	
Very low = 0 points	
Low = 1 to 2 points	
High = 3 to 6 points	
Very high >6 points	



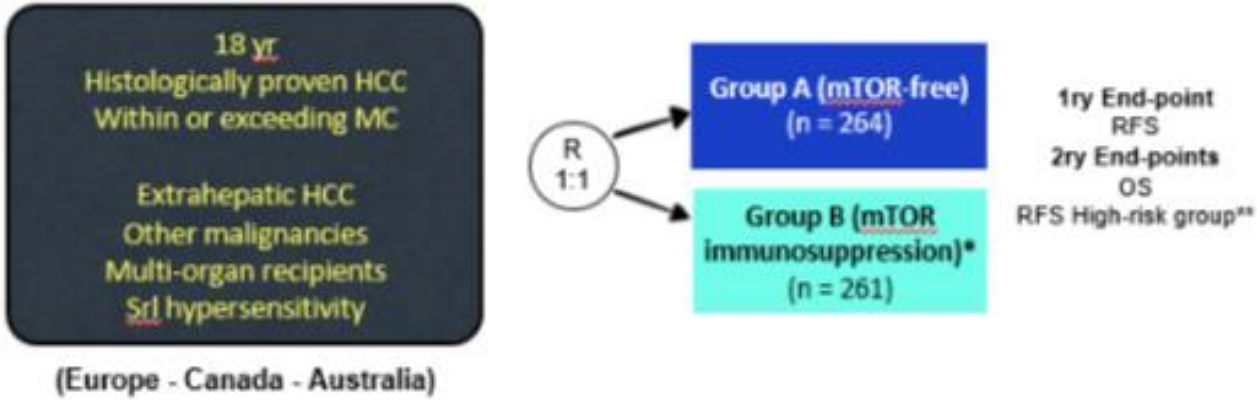
Wolber's c-index of 0.78 (95%CI=0,73-0,83)

AASLD The Liver Meeting® Nov. 10-14, 2023

Discrepencies between preLT imaging and explant features are observed in 20-30% of the cases

Silver study :

- International multicenter randomized trial
- Test the effectiveness of immunosuppression regimen with or without mTor inhibitor (sirolimus) in reducing the risk of recurrence in patients transplanted for HCC
- Primary endpoint (recurrence free survival): not statistically better in mTor inhibitor group at study end of the study



Geissler,EK et al, Transplantation 2016

The Liver

Validate the R3-AFP model in the ITT population from the prospective SilVER trial

November 12, 2023 09:00 am EST - November 12, 2023 09:15 am EST

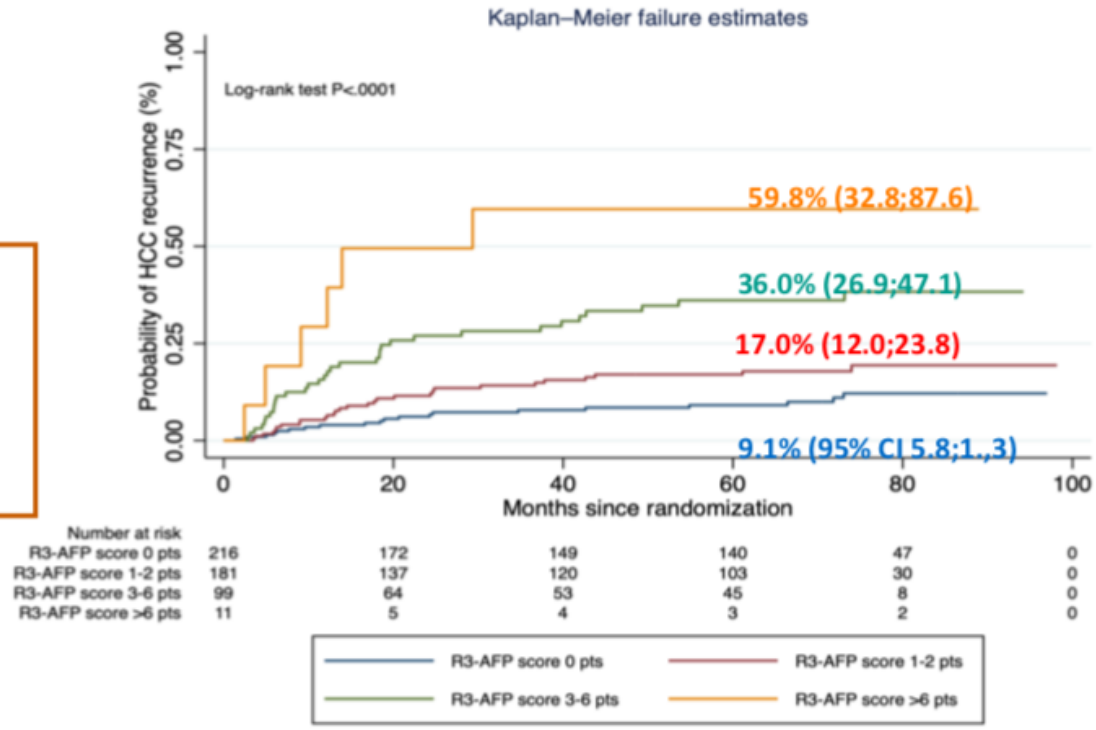
9: VALIDATION OF THE R3-AFP MODEL FOR RISK PREDICTION OF HCC RECURRENCE AFTER LIVER TRANSPLANTATION IN THE SILVER CLINICAL TRIAL

Results

R3-AFP correctly stratified HCC recurrence risk in 4 groups in the ITT population

Overall median follow-up 64 months.

5-year recurrence rate
19% (95% CI 15.3-22.6; n=88 recurrences).

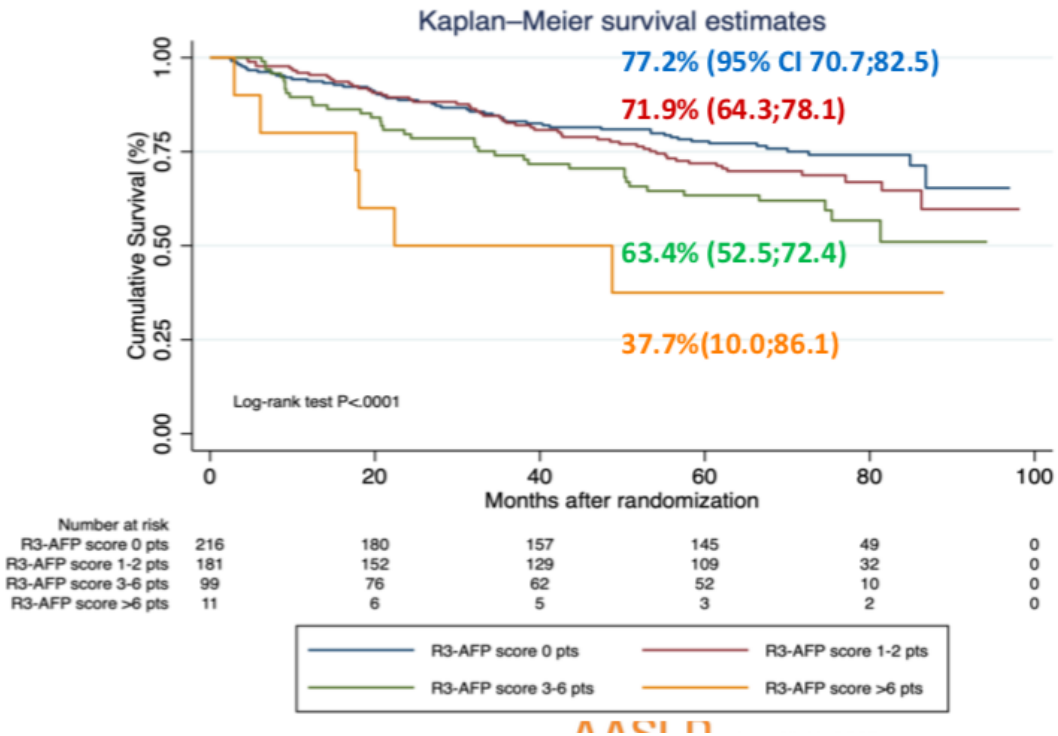


Results

R3-AFP identified 4 distinct survival groups

Overall median follow-up 64 months.

The 5-year survival rate
72% (95% CI 67.5-75.7)

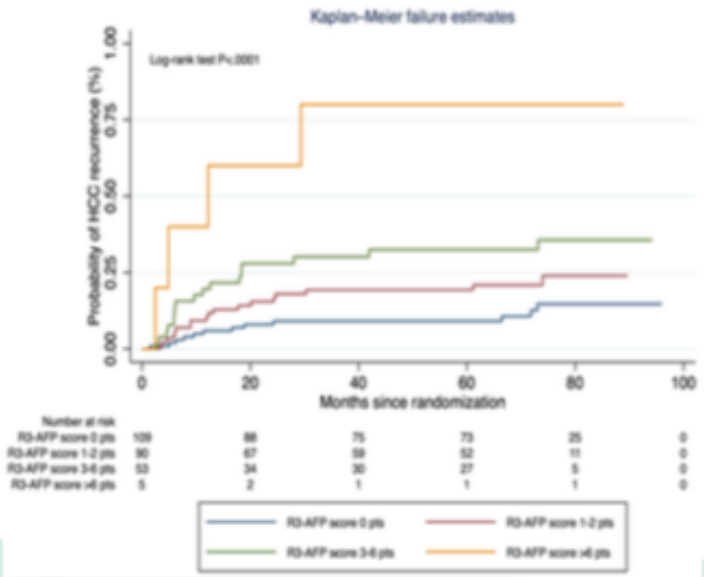


Results

5-year HCC cumulative recurrence in each R3-AFP strata

Group A without mTOR

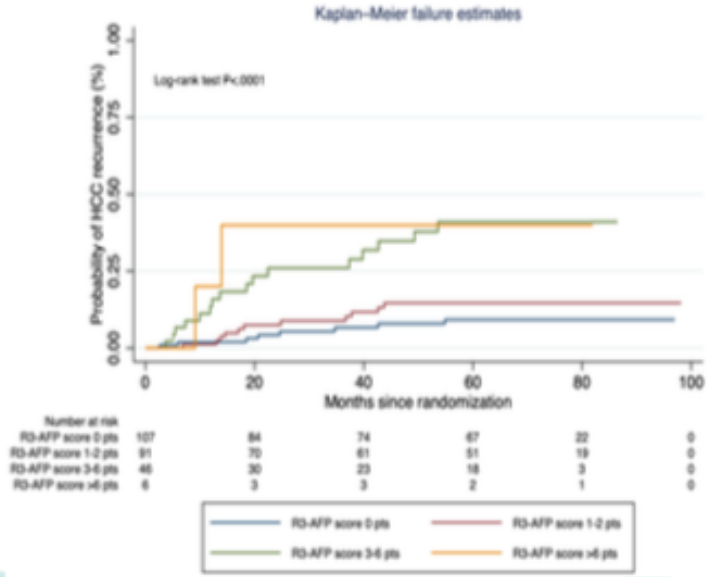
C-statistics 0.75 (CI 0.69-0.81)



Group B with mTOR

C-statistics 0.67 (0.59-0.75)

p=0.048



Conclusions

R3-AFP

- has been validated in the ITT population of the prospective SiLVER trial, showing good performance
- can be proposed to reassess the risk of recurrence after LT
- is a robust tool to test surveillance and immunosuppressive strategies post LT tailored to the individual risk of HCC recurrence