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Survival Benefit: Optimal Balance of Sickness and Utility

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CUTTING EDGE OF TRANSPLANTATION

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BALANCING EQUITY AND UTILITY IN THE FACE OF AN ORGAN SHORTAGE

Disclosures

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Learning Objectives

- Examine metrics beyond short-term post-transplant survival as a means to define post-transplant success.
- Discuss recent publications exploring alternative measures of post-transplant survival

Personal story

- January 2017 received call from college roommate
- Frustrated was waiting >6 months for a transplant
- MELD score 33 (exceptions) in NYC
  - Frequent admissions for cholangitis
  - Terrible QOL
- Asked how someone could be waitlisted with higher priority
- Said likely people with MELD scores of 34, 35, … in NYC
- His response, “I am a 37 year-old father of a 1-year old. Doesn’t that matter?”
- My answer: “No, it’s all in the MELD score.”
- His question, “What if the donor is the same age as me, and there’s a 75 year-old with a score of 34, shouldn’t I have higher priority.”
- My answer: “You’re preaching to the choir.”

How should we define success after transplantation?

- Is preventing death on the waitlist enough?

Why do we have to debate this topic?

- 2019 OPTN/UNOS data:
  - 8,765 liver transplants
  - 1,168 waitlisted patients died
  - 1,186 waitlisted patients removed for being “too sick to transplant”
- 5 out of 6 patients who could benefit from a transplant (HCC or decompensated cirrhosis) never waitlisted[1,2]
- Transplant allocation (prioritization) must consider the principles of equality, priority to the worst off, and utility

1-Goldberg DS, French B, Sahota G, Wallace AE, Lewis JD, Halpern SD. American Journal of Transplantation 2016;16:2903-11; 2-Goldberg D, French B, Newcomb C, et al. 2016;14:1638-46.e2.

Background: Principles of organ allocation

- Equality: fair access to transplant for all patients
  - Considering factors such as gender, race/ethnicity, disease etiology
  - Waiting time has been used as an equality metric
    - First come-first served undermined by disparities in access to healthcare (e.g., kidney)
- Urgency-based priority: favoring the 'worst' off ('sickest-first')
  - Context of transplant → seeks to minimize waitlist mortality
- Utility: maximizing the benefit of transplant
  - Overall survival
  - Net survival benefit
    - Difference of expected pre- and post-transplant survival in years or quality-adjusted life-years

Organ Procurement and Transplantation Network Ethical Principles in the Allocation of Human Organs (https://optn.transplant.hrsa.gov/resources/ethics/ethical-principles-in-the-allocation-of-human-organs/.); Persad G, Wertheimer A, Emanuel EJ. Principles for allocation of scarce medical interventions. Lancet 2009;373:423-31)

Background: Who are the stakeholders

- Waitlisted patients
  - Don’t want patient to die
  - Want to live a long time
- Patient families
  - Want to see their loved one live
- Donors/donor families
  - Want a live to be saved
  - Want to see good outcome
- Broader population
  - Maximize utilization of a scarce resource

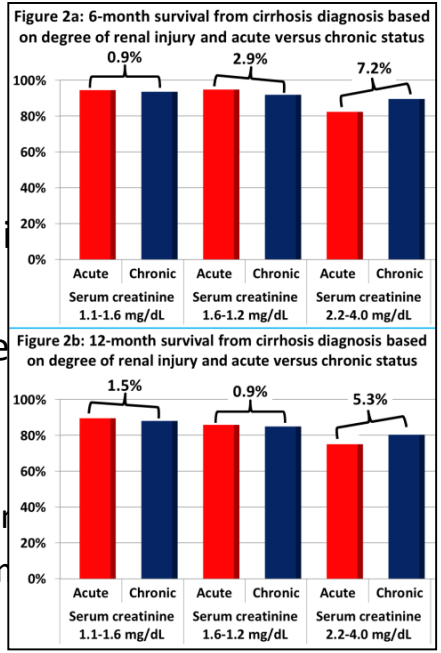
Empiric data on what the public wants

- "Public attitudes towards contemporary issues in liver allocation"[1]
- 2 independent surveys
  - 100 online respondents using conjoint analysis
  - 500 online respondents for nonconjoint survey
- Conjoint analysis → respondents valued both posttransplant survival and risk of waitlist mortality
- Comparison of relative weights
  - 18.5% felt that organ should always go to the patient with the higher posttransplant survival
  - 38% felt the organ should always go to the person with the higher waiting list mortality
  - 62% felt posttransplant survival should be considered in allocation decisions

1-O'Dell HW, McMichael BJ, Lee S, Karp JL, VanHorn RL, Karp SJ; *American Journal of Transplantation* 2019; 19(4): 1212-1217

Failure of current sickest-first policy

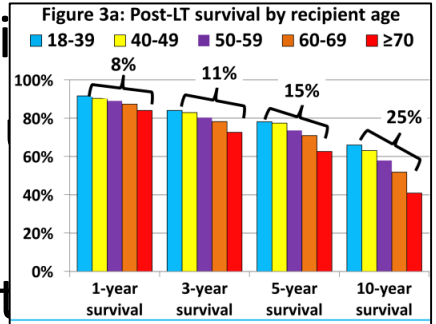
- Exception system
- Application of MELD score
  - Developed and validated to predict short-term liver-related mortality i
    "intrinsic renal disease."[1,2]
  - MELD points for kidney dysfunction only intended for the sickest patie
    kidney injury (AKI)
  - MELD formula does not distinguish between AKI and CKD
    - AKI in patients with cirrhosis dramatically increases the risk of short-term r
    - Elevated creatinine from CKD does not pose same risk of high short-term r
  - Creatinine vs eGFR in women

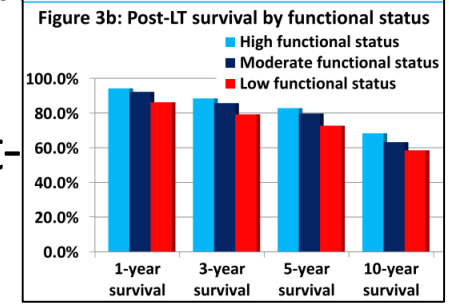


1-Kamath PS, Wiesner RH, Malinchoc M, et al. Hepatology 2001;33:464-70; 2-Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. Hepatology 2000;31:864-71.

Current failure to consider utility

- MELD score not developed to predict post-LT survi
- Higher MELD scores yield higher waitlist priority b lower post-LT survival
- Higher MELD is associated with more post-LT healt utilization (hospital days) and costs[1,2]
- AKI vs CKD in the MELD score: CKD increases post- by a factor of 2-5[3]





1-Bittermann T, Hubbard RA, Serper M, et al. AJT 2018;18:1197-205; 2-Serper M, Bittermann T, Rossi M, et al. AJT 2018;18:1187-96; 3-Allen AM, Kim WR, Therneau TM, Larson JJ, Heimbach JK, Rule AD. Journal of Hepatology 2014;61:286-92.

Current failure to consider utility

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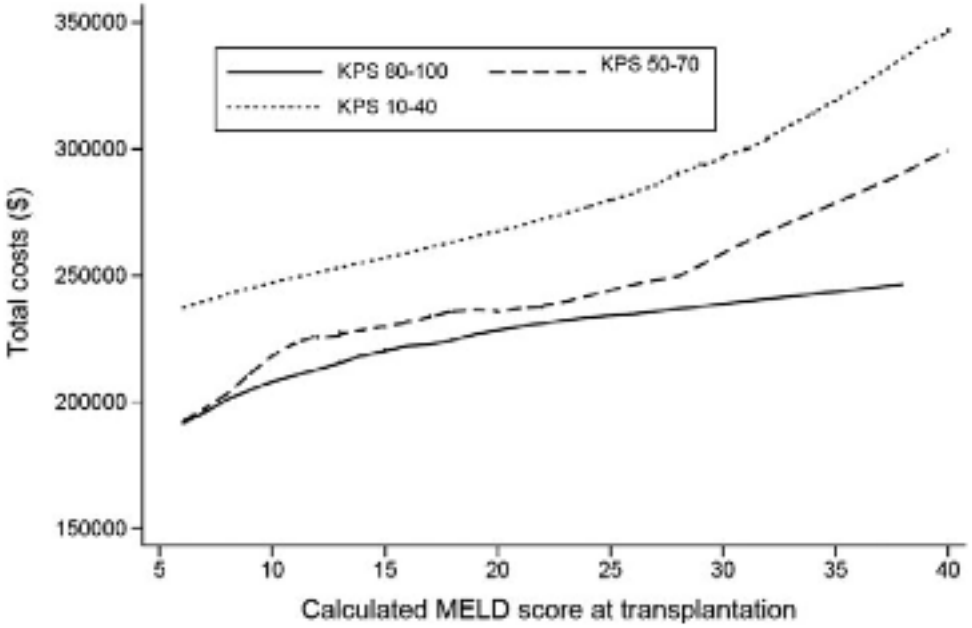

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re costs[2]

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What are the implications of focusing on "sickest first" for the individual patient

- HCC priority
  - Current allocation s
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- Gains in
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  - Time

Analysis Time (years)

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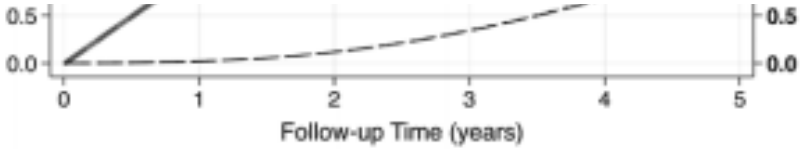
Estimated survival benefit of liver transplant vs resection or ablation (in y)

Follow-up timepoint	Full model		Immortal model[a]	
	LT vs resection	LT vs ablation	LT vs resection	LT vs ablation
1 y	0.02	0.02	0.02	0.02
2 y	0.11	0.12	0.12	0.11
3 y	0.34	0.34	0.34	0.32
4 y	0.68	0.69	0.67	0.63
5 y	1.13	1.14	1.10	1.04



Kanneganti M, Mahmud N, Kaplan DE, Taddei

What are the implications of focusing on "sickest first" for the broader population

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Table 1: Potential impact of changing HCC prioritization*

Prioritization system	Patient cohort	Number	Estimated 5-year post-LT survival	Aggregate post-LT life-years over 5 years
Current system (high HCC priority)	HCC with LT	1,857	74.4%	6,908
	Decompensated cirrhosis	5,138	76.7%	19,704
	Total			26,612 life-years Waitlist deaths†: 2,438
Alternative system (HCC patients not advantaged)	HCC with LT	929	74.4%	3,454
	HCC with RFA or resection	928	60%	2,786
	Decompensated cirrhosis	6,066	76.7%	23,265
	Total			29,504 life-years Waitlist deaths†: 1,510

Abbreviations: HCC=hepatocellular carcinoma; LT=liver transplant; RFA=radio frequency ablation
* Number of transplants based on 2017 data; 5-year survival for LT recipients in MELD era, excluding patients with HCV
† Waitlist deaths=Waitlist removals for death or becoming "too sick to transplant" in 2017

them

Why survival benefit is best-approach

- Balances urgency ("worst off") with utility
- Utility alone ignores the benefit
  - Compensated cirrhosis: 80% 10-year survival
  - Cirrhosis with ascites: 50% 2-year survival
- Hypothetical example
  - Patient 1: 40 year-old with compensated HCV cirrhosis with SVR
    - Mean predicted survival over 10-year period without transplant: 8 years
    - Mean predicted survival over 10-year period with transplant: 8 years
  - Patient 2: 60 year-old with decompensated PBC cirrhosis with ascites
    - Mean predicted survival over 10-year period without transplant : 2 years
    - Mean predicted survival over 10-year period with transplant: 7 years

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