Date: 01.05.2026
NCT: not yet assigned

Impact of delta MELD on recipient outcomes after orthotopic liver transplantation in adults with high MELD

Principal Investigators:

Markus Selzner, MD
Multi-Organ Transplant Program, University Health Network/University of Toronto
585 University Ave.
Toronto, ON M5G 2N2
(416) 340-5242, markus.selzner@uhn.ca

Research Personnel:

Pollmann, Nicola, MD, Research Fellow
Multi-Organ Transplant Program, University Health Network/University of Toronto
585 University Ave. NCSB 11C-G08
Toronto, ON M5G 2N2
Nicola.sariyepollmann@uhn.ca

Abdullah Mosabbir, Research Analyst
Multi-Organ Transplant Program, University Health Network
585 University Ave, 9-MaRS
Toronto, ON M5G 2N2
abdullah.mosabbir@uhn.ca

Peregrina Peralta, Research Coordinator
Multi-Organ Transplant Program, University Health Network
585 University Ave, 9-MaRS-9027S
Toronto, ON M5G 2N2
peregrina.peralta@uhn.ca0

1. SYNOPSIS

Study Title	Elucidating major impact factors for high MELD recipient outcomes after orthotopic liver transplantation in adults.
Trial Design	Retrospective cohort study.
Trial Participants	High MELD patients receiving a liver transplant.
Planned Sample Size and Trial Duration	Eligible patients that received a liver graft within the last 15 years.
Trial duration	Up to 15 years Follow up.
Data Collection Period	January 01, 2010 to December 31, 2025
Primary Objective	To identify main risk factors for long term survival of high Sodium medical Model for End-Stage Liver Disease (NaMELD) patients and long-term graft survival after liver transplantation, with the aim prevent and treat pivotal factors prior to transplantation.
Secondary Objectives	To confirm the risk factors for other long and short-term complication in high NaMELD patients. To investigate the combination of risk factors and NaMELD graduation over time.
Primary Endpoint	Patient survival after liver transplantation.
Secondary Endpoints	Assessment of biochemical parameters of liver function in the recipient during the initial postoperative phase and during the Follow up. ICU stay. Reasons for graft loss, death and retransplantation.

2. BACKGROUND AND RATIONALE:

2.1 Liver Transplantation and Model for End-Stage Liver Disease

Liver transplantation (LT) represents an important curative option for end stage liver disease such as decompensated cirrhosis, which remains a major challenge for today's health care system. The Model for End-Stage Liver Disease (MELD) is a worldwide-established scoring system for the evaluation of the severity of liver disease in allocation processes. However, the interpretation of MELD in clinical practice, particularly with regard to prioritizing potential liver transplant recipients, has revealed some hazards. These include the adaptation of MELD based on patient's characteristics, e.g. the presence of hepatocellular carcinoma, kidney failure and cardiovascular disease (Freeman et al. 2002). In addition, the remaining paucity of organ donors contributes to a rising number of transplantations of high MELD recipients. This leads to the risk of impaired outcomes, especially considering the interaction of additional donor and recipient risk factors, such as extended cold preservation, kidney function and warm ischemia (Schlegel et al. 2017). For a certain patient cohort living donation might represent a feasible approach as reported previously for high MELD patients (Selzner et al. 2010).
Overall, the interaction of donor and recipient characteristics on the outcomes after LT in high MELD patients remains a scarcely investigated field. Therefore, the identification of factors influencing patient's outcomes after orthotopic liver transplantation becomes increasingly important, especially in high MELD recipients.

2.2 Aim of the Study

We will create a comprehensive database to address several questions regarding the selection and outcome of liver transplantation in high NaMeld recipients:

1. Is the change of NaMeld score (delta Meld) prior to liver transplantation predictive for post-transplant outcome?
2. What are the characteristics of futile liver transplants in high NaMeld patients (high NaMeld recipients that do well vs early death)
3. Is exceeding the NaMeld threshold of 30 predictive of poor outcome?
4. Do all NaMeld factors are of equal importance for the prediction of futile outcome in high Meld recipients?

2.3 Study-Plan

This study is a retrospective single centre cohort study in order to investigate the impact of high NaMELD on long term outcomes after liver transplantation. For this purpose, a comprehensive data analysis will be performed.

3. OBJECTIVES

3.1 Primary Objectives

Long-term patient survival of high NaMELD recipients after liver transplantation.

3.2 Secondary Objectives

To assess clinical and laboratory parameters during hospital stay and within and up to 15 years Follow up.

4. Primary and Secondary Endpoints/Outcome Measures

- **Primary Endpoints**
- Patient survival

4.1 Secondary Endpoints

- Biochemical assessment of liver and organ function including laboratory parameters during the Follow up (Day 7, 3 months, 6months, yearly).
- Meaning for health care related parameters including ICU stay.
- Reasons for graft loss, death, and re-transplantation.

4.2 Overall Description of Trial Participants

Adult patients (18 years or older) who received a liver transplantation in participating hospitals (Toronto General Hospital) and satisfy the inclusion and exclusion criteria outlined below are eligible to take part in this study.

4.2.1. Inclusion Criteria

- Patient registered for liver transplantation.
- Patients at least 18 years of age

4.2.2. Exclusion Criteria

- Patients undergo transplantation of organ(s) in addition to the liver.
- Patients who are enrolled in clinical trials of other unlicensed therapy.
- Patients younger than 18 years
- Patients for retransplant

5. Data Collection Procedure:

Data from January 01, 2010 to December 31, 2025 will be collected from hospital specific database. The collected data will be identified by unique study identifier only. Data will be stored for ten years after study completion in accordance with requirements of the corresponding ethic committees; publication or data source file stored will not contain any personal identifiers.

6. Data Analyses:

All statistical data will be generated by using JMP 13 (SAS Institute, Cary, NC), SPSS 22 statistical package (IBM, Chicago, IL, USA), or R (The R Foundation for Statistical Computing, Vienna, Austria). The main outcome measure will be the incidence of patient survival among different groups. Cumulative overall rejection-free rates will be calculated by Kaplan-Meier methods and differences between curves will be evaluated with the log-rank test and Bonferroni or Holm's correction. Continuous variable data will be analyzed nonparametrically using the Wilcoxon / Kruskal-Wallis' correction.

Categorical variables will be summarized as counts and proportions and compared by Chi squared test or Fisher's exact test as appropriate. These results will be represented as Odd's ratio or Hazard ratio with 95% confidence interval (CI). $P < 0.05$ will be considered statistically significant.

7. Ethical Consideration:

This protocol was approved by the local ethic committees of participating centers. No study activities will begin until approval is obtained. A waiver of informed consent is requested for this study since it meets the requirements for the common rule. Namely, it would be impractical to attempt to obtain consent for this study since many of these patients may now be deceased and/or lost to follow-up. Further, the exclusion of any patients would impact the quality of the study data. Finally, the study involves minimal risk to participants, as no change to patient care is taking place.

8. APPENDIX

8.1 Donor variables

Donor Variables	
Biographic Characteristics	Age
	Height
	Weight
	Gender
	Living Donation (1) / Heart beating donation (NDD) (2)/ Non heat beating donor (DCD)
	Cause of Death
	ICU stay

Laboratory values prior to LT and following LT	Sodium Level
	Bilirubin Level
	AST/ALT Level
	Creatinine Levels

8.2 Recipient Variables

Recipient Variables		
Overall Characteristics	Date of transplant Date of Death Date of Retransplant Date of last clinical visit	
Biographic Characteristics	Age at Transplant	
	Height	
	Weight	
	Gender	
	Etiology of liver Disease	
	Bilirubin; INR; Creatinine; Sodium at MELD Timepoints	
	Creatinine	D1-7
		3 months
		D90
		6months
		yearly
	eGFR	D1-D7
		3 months 6 months yearly
		D90
		6months
		12months
	INR	D7
		3 months
		D90
		6months
		Yearly
	AST	D1 – D7
		3 months
		6months
		yearly
	ALT	D1 – D7
		3 months
		6months
		yearly

	Bilirubin	D7
		3 months
		6months
		yearly
	Sodium	D7
		3 months
		6months
		Yearly
	Alkaline	D7
	phosphatase	3 months
		6months
		Yearly
	Graft Survival at 1, 3, 5, 10 yrs	
	Patient Survival at 1, 3, 5, 10 yrs	
	Post-transplant ICU Stay	
	Readmission within 30 days (1=yes; 0=no)	
	Retransplantation date	
	Cause of Graft Loss	
	Cause of Death	

9. Reference

Freeman, Richard B.; Wiesner, Russell H.; Harper, Ann; McDiarmid, Sue V.; Lake, Jack; Edwards, Erick et al. (2002): The new liver allocation system: moving toward evidence-based transplantation policy. In: Liver Transplantation 8 (9), S. 851–858. DOI: 10.1053/jlts.2002.35927.
Schlegel, A.; Linecker, M.; Kron, P.; Györi, G.; Oliveira, M. L. de; Müllhaupt, B. et al. (2017): Risk Assessment in High- and Low-MELD Liver Transplantation. In: American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons 17 (4), S. 1050–1063. DOI: 10.1111/ajt.14065.
Selzner, Markus; Kashfi, Arash; Cattral, Mark S.; Selzner, Nazia; McGilvray, Ian D.; Greig, Paul D. et al. (2010): Live donor liver transplantation in high MELD score recipients. In: Annals of surgery 251 (1), S. 153–157. DOI: 10.1097/SLA.0b013e3181bc9c6a.