

Sequential Hypo- and Normothermic Perfused Extended Criteria Livers: Two-center Results of 205 Cases

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Introduction

With the current organ shortage, liver machine perfusion is increasingly used to test and select extended criteria donor (ECD)-livers to counter decreasing quality of available organs. Combining sequential oxygenated hypothermic and normothermic machine perfusion, linked by one hour of controlled oxygenated rewarming (DHOPE-COR-NMP) can be used to resuscitate donor livers and subsequently perform previously validated hepatobiliary viability assessment. This procedure is routinely performed in The Netherlands for a couple of years for livers that previously would have been discarded. With this two-center study, we aim to demonstrate the recipient outcomes of a large cohort of high-risk ECD-livers perfused with the DHOPE-COR-NMP protocol.

Main objectives

- Evaluate the death-censored graft survival and patient survival.
- Analyze post-transplant complications, such as post-transplant cholangiopathy.

Methods

In this two-center, retrospective study, we collected data from liver grafts that required viability assessment prior to transplantation and underwent sequential hypothermic and normothermic machine perfusion linked with controlled oxygenated rewarming (DHOPE-COR-NMP). Inclusions ended on the 31st of October 2024, safeguarding a minimum follow-up of 6 months.

Viability assessment was performed for ECD-livers that would otherwise not have been transplanted. ECD-livers are defined as all DCD liver grafts above the age of 60, functional warm ischemia time exceeding 30 minutes (fWIT), concerns of viability upon macroscopy, or organ donation after euthanasia (DCD-V) as of the 1st of June 2023.

Viability assessment criteria after 2.5 hours of NMP are as follows:

- Hepatocyte
 - Perfusate lactate ≤ 2 mmol/L
 - Perfusate pH between 7.35 and 7.45
 - Bile production ≥ 10 mL, of which 4 mL in last 60 min
- Cholangiocyte (delta = bile – perfusate)
 - Bile pH ≥ 7.45
 - Delta pH ≥ 0.1
 - Delta bicarbonate ≥ 5.0 mmol/L
 - Delta glucose ≤ 5.0 mmol/L

The main objective of this study is to assess graft survival at one-year post-transplantation, excluding deaths with a functioning graft from the analysis. Patients who died with a functioning graft will be censored in this analysis.

Additional outcomes include overall patient survival one year after transplantation and the acceptance rate, defined as the proportion of livers transplanted after perfusion has been initiated. This study also examines the cumulative incidence of biliary complications following transplantation, including post-transplant cholangiopathy and anastomotic biliary strictures (AS).

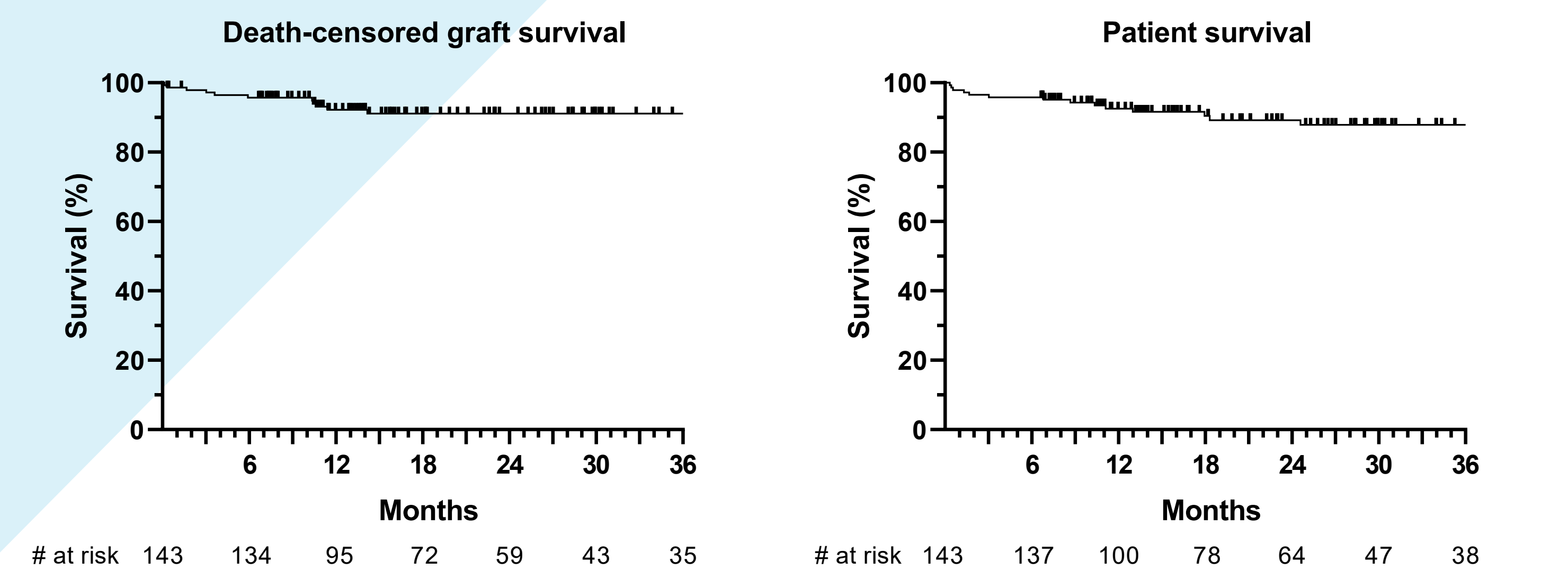
Conclusion

- High-risk ECD(DCD) grafts, safe transplantation, excellent outcomes
- 70% utilization rate of otherwise discarded grafts
- No cases of primary non-function
- 1-year cumulative incidence of post-transplant cholangiopathy of 5%
- 1-year death censored graft survival of 92%

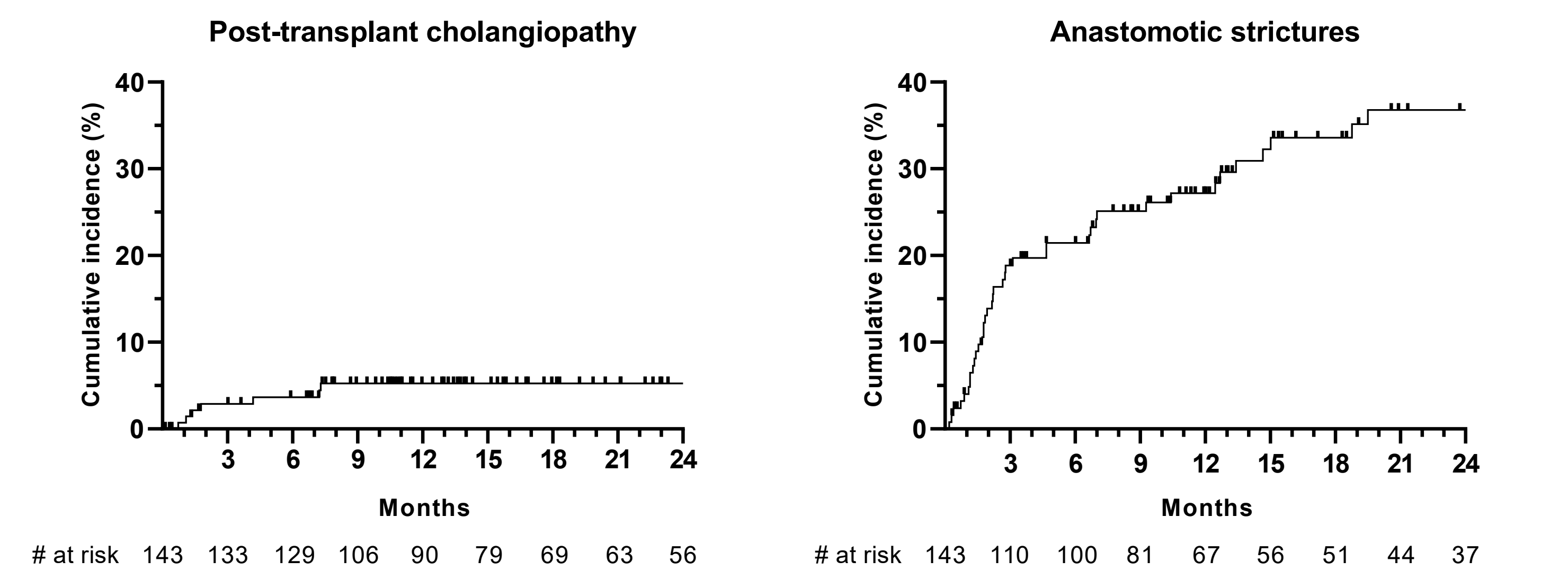
Results

Between March 2019 and October 2024, 205 ECD-livers were perfused through the previously described DHOPE-COR-NMP protocol. Of these livers, 143 resulted in transplantation (utilization rate 70%) with a median follow-up of 625 days. Most transplanted livers were DCD grafts (96%), with a median age of 65 (IQR 59-71) and a median ET-DRI of 2.60 (IQR: 2.25-2.85). In our transplanted group, 63 livers had a donor WIT of 30 to 60 minutes, and 20 livers a donor WIT of 60 up to 120 minutes. The main indications for transplantation in our cohort were hepatocellular carcinoma (HCC), alcohol related liver disease (ALD) and metabolic dysfunction-associated steatohepatitis (MASH), with a median age of 59 (IQR 51-56). Median MELD-score prior to transplantation was 16 (IQR 10-22).

Death-censored graft survival at 1- and 2-years post transplant was 92% and 91%, respectively. For patient survival, this was 92% and 91%. Both Kaplan-Meier survival curves are displayed below.



Cumulative incidences of post-transplant cholangiopathy and AS at 1-year were 5% and 27%, respectively, and are displayed below. Post-transplant cholangiopathy did not occur after 9 months in our cohort.



Post-transplant, recipients had a median hospital stay of 14 days (IQR 10-20). A Clavien-Dindo score of 3 and above was present in 80 patients (56%). The EASE-score, indicating the risk of early allograft failure after liver transplantation in the first 90 days post transplant had a median of -2.69 (IQR -3.31 - -1.68). This value is similar to low-risk, mainly DBD grafts.

The following post-transplant complications are displayed as a number and percentage of the total cohort:

- Primary non-function: 0
- Retransplantation: 8 (5.6%)
- Portal vein thrombosis: 3 (2.1%)
- Hepatic artery thrombosis: 5 (3.5%)

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