

# Clinical Outcomes of Abdominal Normothermic Regional Perfusion versus Sequential Hypo- and Normothermic Machine Perfusion: a Single Center Comparison.

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## Introduction

To address the donor shortage, extended criteria donors after circulatory death (ECD-DCD), are increasingly used. However, ECD-DCD livers bear higher risk of primary non-function and biliary complications. Two main perfusion techniques exist to assess liver function: in-situ abdominal normothermic regional perfusion (aNRP), and ex-situ normothermic machine perfusion, in our center combined with dual hypothermic oxygenated perfusion and controlled oxygenated rewarming (DHOPE-COR-NMP). This study presents a single center comparison of DHOPE-COR-NMP and aNRP of clinical outcomes of ECD-DCD livers.

### Main objectives

- Evaluate the death-censored graft survival and patient survival.
- Analyze post-transplant (biliary) complications.

## Methods

This retrospective, single-center study, included DCD livers that required viability assessment and were thus classified as ECD-DCD grafts. Cases were included between October 2018 for aNRP and from August 2021 for DHOPE-COR-NMP and ended in December 2023 for all groups. Start dates correspond to the initiation of the respective perfusion technique at our center, while the end date was selected to ensure a minimum follow-up period of one year to include all major post-transplant biliary complications

aNRP was performed for DCD donors aged over 50 years during procurement weeks assigned to the Erasmus Medical Center (EMC) or Leiden University Medical Center (LUMC) within the Dutch-Western procurement region. DHOPE-COR-NMP was performed for all Dutch DCD donors above the age of 61 years and older, provided they had not already undergone aNRP. Additional indications for viability assessment other than donor age were elevated lab values, functional warm ischemia time (fWIT) exceeding 30 minutes, macroscopic concerns regarding graft quality or organ donation after euthanasia as of June 1, 2023.

Viability assessment criteria of both perfusion strategies are displayed below.

|                                               | DHOPE-COR-NMP<br>(at 2.5 hours of NMP) | aNRP<br>(up to 2 hours of aNRP)                           |
|-----------------------------------------------|----------------------------------------|-----------------------------------------------------------|
| Hepatocyte criteria                           |                                        |                                                           |
| ALT                                           | -                                      | Stable and ≤400 U/L                                       |
| Lactate                                       | ≤ 2.0 mmol/L at end of perfusion       | Decreases with ≥ 1 mmol/L/hour                            |
| Bile production                               | ≥4mL in last hour                      |                                                           |
| Cholangiocyte criteria (Δ = bile – perfusate) |                                        |                                                           |
| Bile glucose                                  | Δ glucose ≤ 5 mmol/L                   | <1.1 mmol/L<br>OR 3 mmol/L and bicarbonate and pH reached |
| Bile bicarboate                               | Δ HCO <sub>3</sub> <sup>-</sup> ≥ 5    |                                                           |
| Bile pH                                       | pH ≥ 7.45                              | -                                                         |
|                                               | Δ pH ≥ 0,1                             |                                                           |

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
- Over **74%** utilization rate of otherwise discarded grafts
- No cases of primary non-function
- No differences in biliary complications
- Post-Tx biliary interventions occurred more frequently in DHOPE-COR-NMP vs. aNRP

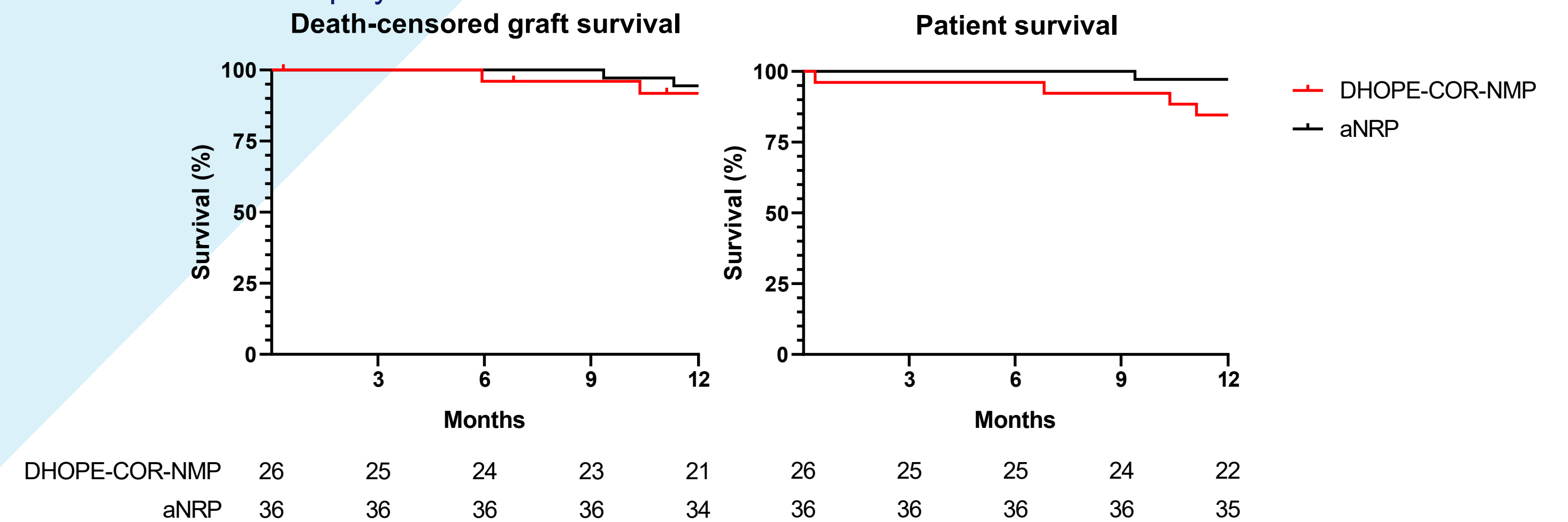
## Results

A total of 83 liver grafts were included, of which 35 were subjected to DHOPE-COR-NMP and 48 underwent aNRP. The indication for hepatobiliary viability assessment during MP prior to LT was DCD aged older than 61 years in 82.9% for DHOPE-COR-NMP and 87.5% in aNRP. The acceptance rates were 26 out of 35 (74%) for DHOPE-COR-NMP and 36 out of 48 (75%) for aNRP grafts (p=0.941).

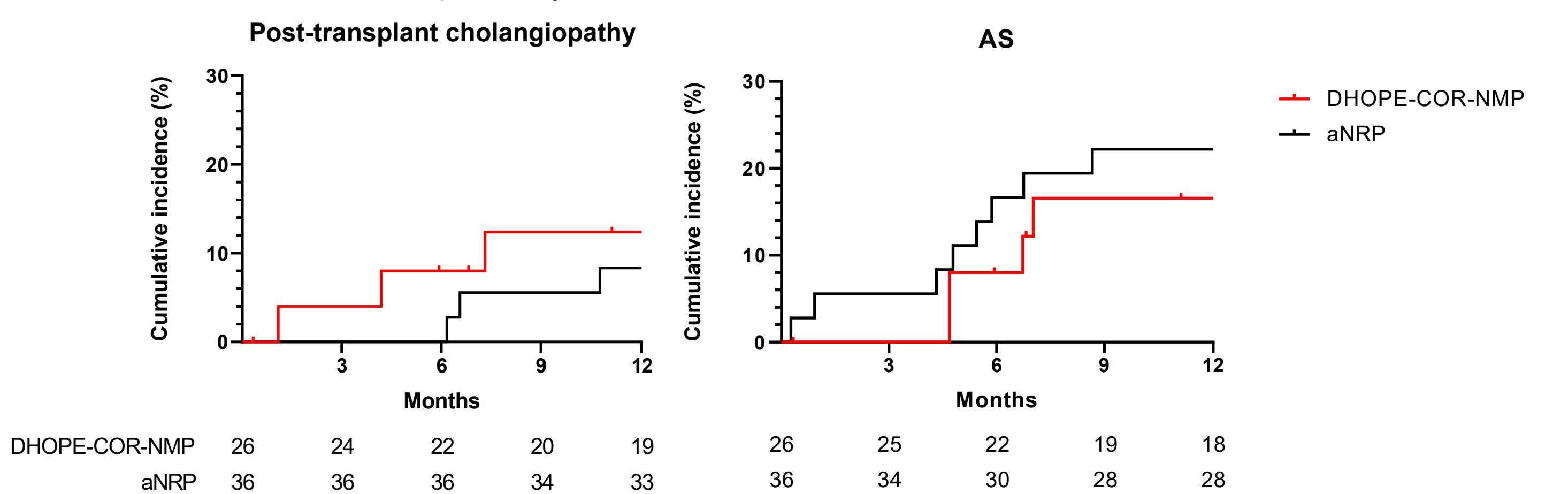
Donor characteristics were comparable in both study groups for transplanted livers (Table 1). The median Eurotransplant Donor Risk Index (ET-DRI) was higher in de DHOPE-COR-NMP group 2.8 [IQR: 2.4-3.0] in comparison to aNRP 2.5 [IQR: 2.2-2.6] (p=0.002). There were no significant differences in recipient age, sex, BMI, MELD score, or indication for liver transplantation between the groups. Functional donor warm ischemia time (fWIT) was shorter in DHOPE-COR-NMP (25 minutes [IQR: 20-27]) compared to aNRP (32 minutes [IQR: 25-38] (p < 0.001).

Recipient characteristics were similar, with a median MELD-score of 13 [IQR: 9-19] for DHOPE-COR-NMP and 14 [IQR: 9-17] for aNRP (p=0.932). Indications for transplantation were similar in both groups and consisted mainly of HCC and cirrhosis based on hepatitis. However, 4 recipients (15%) of the DHOPE-COR-NMP cohort were re-transplantations, whereas this indication was not present in the aNRP group.

Death-censored graft survival at 1-year post transplant was 92% for DHOPE-COR-NMP and 94% for aNRP (p=0.661). For patient survival, this was 85% and 97%, respectively (p=0.073) . Both Kaplan-Meier survival curves are displayed below.



Cumulative incidences of post-transplant cholangiopathy at one year were 12% for DHOPE-COR-NMP and 8% for aNRP (p=0.573). At one year, the cumulative incidence of AS for DHOPE-COR-NMP and aNRP was 17% and 22%, respectively.



Post-transplant, recipients had a similar hospital stay in both groups. No differences were present in all forms of biliary complications; however, biliary interventions (ERCP/PTC) were more frequent in the DHOPE-COR-NMP group compared to aNRP (65% vs. 31%, respectively (p=0.010))

More intra operative RBC transfusions occurred in the DHOPE-COR-NMP group with a median of 6 [IQR: 4-8] vs. 4 [IQR: 0-5] in aNRP (p=0.013). The EASE-score, indicating the risk of early allograft failure after liver transplantation in the first 90 days post transplant and incorporating the amount of blood transfusions, had a median of -2.3 [IQR -3.6- -1.3] for DHOPE-COR-NMP and -2.9 [IQR -3.8- -2.0] for aNRP (p=0.043).

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

|                           | DHOPE-COR-NMP | aNRP   | p-value |
|---------------------------|---------------|--------|---------|
| Primary non function      | 0             | 0      | -       |
| Portal vein thrombosis    | 0             | 0      | -       |
| Hepatic artery thrombosis | 0             | 0      | -       |
| Retransplantation         | 1 (4%)        | 1 (3%) | 1.000   |

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