XVIVO

Liver Assist™

Clinical evidence summary

Contents

The following document summarizes key clinical research using Liver Assist™, highlighting its role in improving patient outcomes, extending preservation time, and increasing utilization of donor livers in a cost-effective way. For a comprehensive list of published clinical reports on Liver Assist™*, see List of publications.

* to the best of our knowledge and until 2025.04.

ALT - Alanine Transaminase | CCI - Comprehensive Complication Index® | CI - Confidence Interval | CIT - Cold Ischemic Time | COR - Controlled Oxygenated Rewarming | DBD - Donation after Brain Death | DC - Death Censored | DCD - Donation after Circulatory Death | DHOPE - Dual Hypothermic Oxygenated Perfusion | DRI - Donor Risk Index | EAD - Early Allograft Dysfunction | ECD - Extended Criteria Donor | FMN - Flavin Mononucleotide | HAT - Hepatic Artery Thrombosis | HCC - Hepatocellular Carcinoma | HMP - Hypothermic Machine Perfusion | HOPE - Hypothermic Oxygenated Perfusion | ICU - Intensive Care Unit | IPTW - Inverse Probability of Treatment Weighting | IQR - Interquartile Range | IRI - Ischemia-Reperfusion Injury | LT - Liver Transplant | MEAF - Model For Early Allograft Function | NAS - Non-anastomotic Biliary Strictures | NMP - Normothermic Machine Perfusion | NRP - Normothermic Regional Perfusion | OPR - Organ Perfusion and Resuscitation | OR - Odds Ratio | PNF - Primary Non Function | PRO - Prolonged | PRS - Post Reperfusion Syndrome | RBC - Red Blood Cells | RCT - Randomized Controlled Trial | RR - Risk Ratio | SCS - Static Cold Storage | Tx - Transplantation | UW-MPS - University of Wisconsin – Machine Perfusion Solution.

Liver Assist™

Unlock the power of flexibility

Liver Assist is a pressure controlled ex-vivo perfusion system for donor livers. With customizable settings, it offers the flexibility to choose from various protocols, including DHOPE, HOPE, COR, and NMP.*

Liver Assist™ at a glance

- O_2 Oxygenated
- Temperature controlled 12°C - 37°C
- Full cooling mode: <12°C
- 24h Up to 24H cold perfusion to support logistics
- Pressure controlled pulsatile (60 bpm) and continuous perfusion
- Functional viability assessment
- Remote monitoring ready (selected regions only)

*Not available in all markets. Please contact XVIVO for more information regarding availability in your specific region.
CAUTION - Investigational device. Limited by Federal (or United States) law to investigational use.

Machine perfusion in liver transplantation

During the vital period that starts at the time of circulatory arrest and extends to the point of transplantation, donor organs are exposed to a number of challenges, such as ischemic injury whilst the organ remains in the donor, progressive deterioration of the organ during conventional organ preservation, and ischemic-reperfusion injury (IRI) during reperfusion in the recipient. To address these challenges, improved preservation methods are required.

A recent meta-analysis published in the Cochrane Database of Systematic Reviews[1], evaluating the effects of machine perfusion in liver transplantation, demonstrated that compared to SCS, HMP (HOPE or DHOPE) improves graft survival by 55% (p=0.02), reduces the rate of serious adverse events by 55% in ECD-DBD liver transplantation (p=0.03), and reduces the incidence of biliary complications by 69% in DCD liver transplantation (p=0.03). While NMP was associated with improved organ utilization compared to SCS, NMP did not provide the same clinical benefits as HMP. Out of the seven RCTs included in the review, four were performed using Liver Assist™ [2].

Outcome	HMP Relative Effect (95% CI)	HMP GRADE*	NMP Relative Effect (95% CI)	NMP GRADE*
Early Allograft Dysfunction	OR 0.35 (0.23 to 0.53)	●●●●	OR 0.4 (0.22 to 0.74)	●●●○
Ischemic biliary complications**	OR 0.31 (0.11 to 0.92)	●●●●	OR 0.78 (0.27 to 2.27)	●○○○
Graft Survival	HR 0.45 (0.23 to 0.87)	●●●●	HR 1.2 (0.44 to 3.29)	●○○○
Patient Survival	HR 0.91 (0.42 to 1.98)	●●○○	HR 1.08 (0.31 to 3.8)	●○○○

*Certainty of the evidence, **in DCD

1. Tingle, S.J., et al., Machine perfusion in liver transplantation. Cochrane Database Syst Rev, 2023. 9(9): p. Cd014685.
2. Czigany et al 2021; van Rijn et al 2021; Schlegel et al 2023; Ghinolfi et al 2019.

Example of common protocols in clinical practice:

HOPE/DHOPE

During hypothermic machine perfusion (≤12°C), the graft is perfused with a cold, dedicated solution for efficient internal cooling of the organ, a continuous supply of oxygen and nutrients and removal of waste products, resulting in an optimal preservation.

NMP

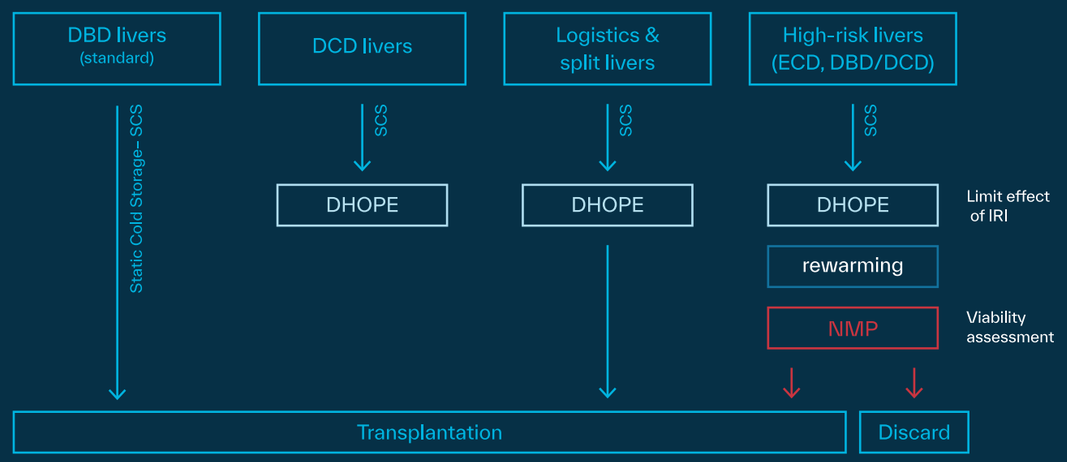
Normothermic machine perfusion (35°C-38°C) aims to provide a near-physiologic environment for a potential liver graft, maintaining it in a fully functional metabolic state Since the liver is 'active' during perfusion, it is possible to assess the viability of the donated liver prior to transplantation into recipient.

DHOPE-COR-NMP

Sequential use of DHOPE and NMP is believed to combine the benefits of both perfusion protocols by reducing the detrimental effect of ischemia-reperfusion injury (IRI) and allowing for viability testing of the liver graft prior to transplantation into recipient.

APPLICATION OF LIVER ASSIST™ AND SUPPORTED CLINICAL PROTOCOLS

For instance, University Medical Centre Groningen, has established a framework based on clinical data to guide the precise application of these protocols.



Schematic overview of liver perfusion protocols used at UMCG. Image adapted from van Leeuwen OB, Porte RJ. Ex situ machine preservation of donor livers for transplantation: HOPE for all?. Br J Surg. 2021;108(10)

Improved outcomes

Hypothermic oxygenated machine perfusion (HMP) involves perfusing a donor liver with an oxygenated acellular machine perfusion solution at temperatures of 12°C or below.

HMP can be performed through dual perfusion (DHOPE), where both the portal vein and hepatic artery are perfused simultaneously. The hepatic artery is known to be vital for oxygenating the delicate bile ducts, and dual perfusion ensures flow through both major vessels. Alternatively, HMP can be carried out solely through portal vein perfusion, often referred to as HOPE, removing the need for hepatic artery cannulation. HOPE / DHOPE mitigates ischemia-reperfusion injury by restoring mitochondrial function, decreasing accumulated metabolites, and replenishing cellular energy levels before transplantation[1]. Liver Assist supports both HOPE and DHOPE.

DHOPE in DCD

Hypothermic machine perfusion in liver transplantation – A randomized trial.

van Rijn R, Schurink IJ, de Vries Y, van den Berg AP, Cortes Cerisuelo M, Darwish Murad S, Erdmann JI, Gilbo N, de Haas RJ, Heaton N, van Hoek B, Huurman VAL, Jochmans I, van Leeuwen OB, de Meijer VE, Monbaliu D, Polak WG, Slangen JJG, Troisi RI, Vanlander A, de Jonge J, Porte RJ.

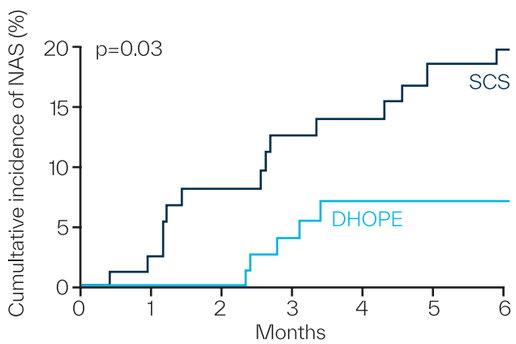
N Engl J Med | 2021 | doi: 10.1056/NEJMoa2031532

This multicentre, randomized controlled trial (RCT), published in the New England Journal of Medicine, studied the effect of dual hypothermic oxygenated perfusion (DHOPE) on the incidence of non-anastomotic biliary strictures (NAS) following transplantation of livers donated after circulatory death (DCD).

Patients were randomly assigned (1:1 ratio) to receive a liver preserved either with static cold storage (SCS; n=78) alone, or with SCS followed by a period of DHOPE (n=78) using Liver Assist prior to transplantation.

The study demonstrates that end-ischemic DHOPE reduces the risk of developing NAS by 64% (RR 0.36, p=0.03) and leads to significant reductions in early allograft dysfunction (EAD; RR 0.61) and post-reperfusion syndrome (PRS; RR 0.43) compared to SCS alone.

> "The cumulative number of treatments for non-anastomotic biliary strictures was lower by a factor of almost 4 after machine perfusion, as compared with control."
>
> Van Rijn et al., 2021



1. van Leeuwen et al (2025) 'Back-to-base' combined hypothermic and normothermic machine perfusion of human donor livers.

DHOPE in ECD/DBD

Outcome of liver transplantation with grafts from brain-dead donors treated with dual hypothermic oxygenated machine perfusion, with particular reference to elderly donors.

Patrono D, Cussa D, Sciannameo V, Montanari E, Panconesi R, Berchialla P, Lepore M, Gambella A, Rizza G, Catalano G, Mirabella S, Tandoi F, Lupo F, Balagna R, Salizzoni M, Romagnoli R.

Am J Transplant | 2022 | doi: 10.1111/ajt.16996

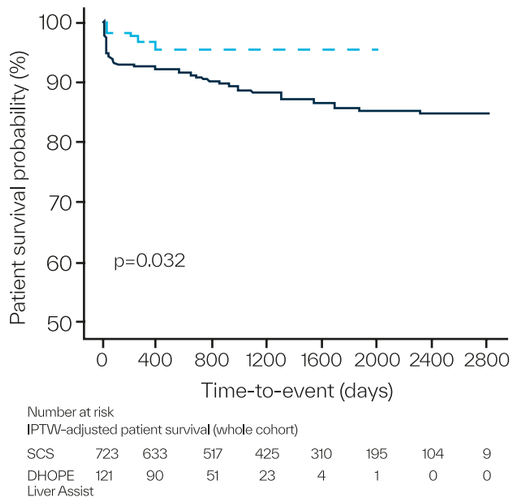
In this single-center, retrospective cohort study, the effect of end-ischemic DHOPE on extended criteria DBD-grafts (ECD-DBD) was assessed.

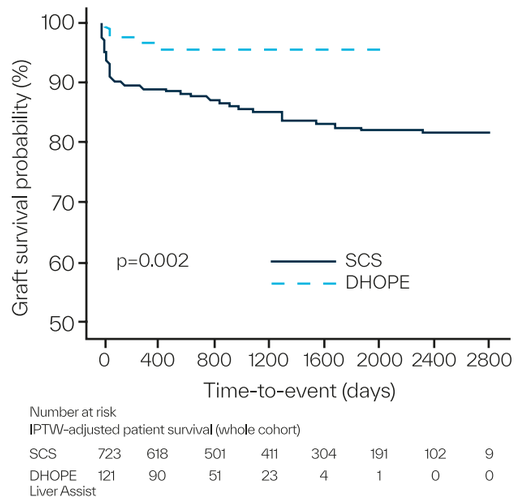
Inverse probability of treatment weighting (IPTW) was used to overcome selection bias and allow comparison of outcomes in DHOPE-treated grafts (n=121) with grafts preserved by SCS (n=723).

The study demonstrated that end-ischemic DHOPE using Liver Assist™ was associated with a significant reduction of early allograft failure (OR 0.24, p=0.024), fewer severe post-operative complications (Clavien-Dindo grade ≥III; OR 0.57, p=0.046) and lower cumulative morbidity at discharge (CCI®: –7.20 points, p=0.003). DHOPE was also associated with improved patient and graft survival (p=0.032; p=0.002).

The authors conclude that these findings prompt a wider adoption of this preservation technique in clinical practice, especially when grafts from elderly donors are used.

> "/.../ a simple intervention applied at the end of cold preservation improves graft survival and post-transplant course."
>
> Patrono et al., 2022





1. Van Rijn et al (2021) Hypothermic Machine Perfusion in Liver Transplantation – A Randomized Trial.

DHOPE in DBD

Routine end-ischemic hypothermic machine perfusion in liver transplantation from donors after brain death: results of 2-year follow-up of a randomized controlled trial.

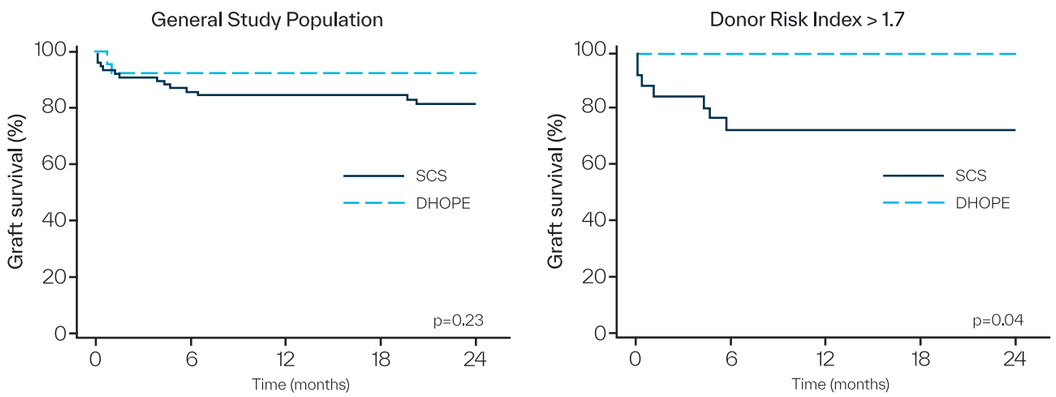
Morawski M, Zhylko A, Rykowski P, Krasnodębski M, Hołówko W, Lewandowski Z, Mielczarek-Puta M, Struga M, Szczepankiewicz B, Górnicka B, Krawczyk M and Grąt M.

Int J Surg | 2024 | doi: 10.1097/js9.0000000000001919

In the initial report of this randomized controlled trial (RCT), Grat et al (2023)[1] presented the early effects (up to 90-days) of end-ischemic DHOPE in routine DBD liver transplantation.

Livers donated after brain death were allocated (3:1) to either static cold storage (SCS, n=78) or SCS followed by at least 2 hours of DHOPE using Liver Assist (n=26). While no statistically significant differences in early outcomes were seen following transplantation of low-risk DBD livers, DHOPE-treatment of higher risk DBD-livers (DRI>1.7) led to significantly better early graft function (MEAF score: 4.92 vs 6.31, p=0.037), lower overall morbidity (CCI®: 4.35 vs 22.60, p=0.05) and improved patient survival (100% vs 84.6%).

In this 2-year follow-up of the RCT, the beneficial effect of DHOPE treatment in the higher risk DBD group remained, with significant improvements in overall graft survival (100% vs. 73.1%; p=0.038) compared to untreated livers. When considering the entire study population, overall graft survival was 92.3% and 81.4% for DHOPE-treated and untreated livers, respectively, and while statistical significance was not reached (p=0.23), the difference in graft survival was clinically relevant. Furthermore, recipients of DHOPE-treated donor livers, irrespective of risk-profile, experienced fewer biliary complications (23.7% vs. 43.4%).



1. Grat et al (2023) Routine End-ischemic Hypothermic Oxygenated Machine Perfusion in Liver Transplantation from Donors After Brain Death: A Randomized Controlled Trial.

HOPE in DCD

First comparison of hypothermic oxygenated perfusion versus static cold storage of human donation after cardiac death liver transplants: An international-matched case analysis.

Dutkowski P, Polak WG, Muiesan P, Schlegel A, Verhoeven CJ, Scalera I, DeOliveira ML, Kron P, Clavien PA.

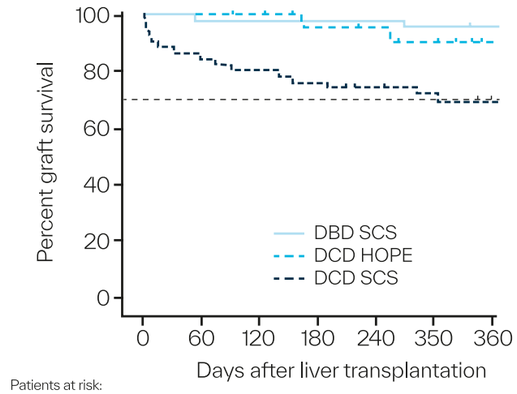
Ann Surg | 2015 | doi: 10.1097/sla.0000000000001473

Published in 2015, Dutkowski et al present the results of the first comparative study on the impact of Hypothermic Oxygenated Perfusion (HOPE) using Liver Assist* in DCD liver transplantation.

Twenty-five (n=25) HOPE-treated DCD livers were compared to a matched cohort of 50 DCD livers preserved with SCS.

The study shows that, compared to SCS, end-ischemic HOPE of DCD-livers improves early allograft function (EAD: 20% vs 44%, p=0.046), reduces graft injury in terms of intrahepatic cholangiopathy (0% vs 22%, p=0.015), biliary complications (20% vs 46%, p=0.042), and improves 1-year graft survival (90% vs 69%, p=0.035). In addition, HOPE-treated DCD livers achieved similar results as matched DBD livers (n=50) in all investigated endpoints.

The authors conclude that the study provides strong evidence that applying HOPE protects extended DCD livers from initial reperfusion injury leading to better graft function and the prevention of intrahepatic biliary complications.



> "HOPE may therefore offer optimization of liver grafts before implantation by a simple and practical perfusion technique with a high impact on enlarging the donor pool."
>
> Dutkowski et al., 2015

*The device used was ECOPS – an early version of Liver Assist.

HOPE in DBD

A multicenter randomized-controlled trial of hypothermic oxygenated perfusion (HOPE) for human liver grafts before transplantation.

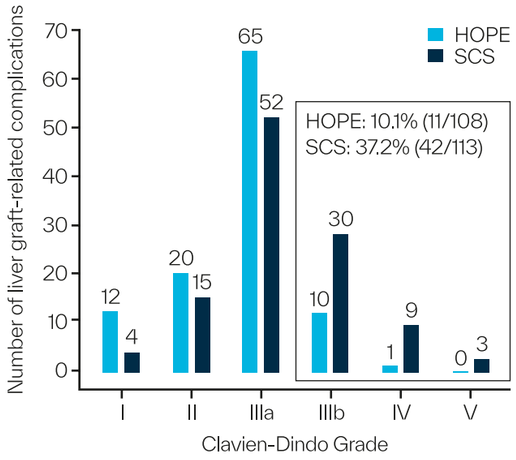
Schlegel A, Mueller M, Muller X, Eden J, Panconesi R, von Felten S, Steigmiller K, Sousa Da Silva RX, de Rougemont O, Mabrut JY, Lesurtel M, Cerisuelo MC, Heaton N, Allard MA, Adam R, Monbaliu D, Jochmans I, Haring MPD, Porte RJ, Parente A, Muiesan P, Kron P, Attia M, Kollmann D, Berlakovich G, Rogiers X, Petterson K, Kranich AL, Amberg S, Müllhaupt B, Clavien PA and Dutkowski P.

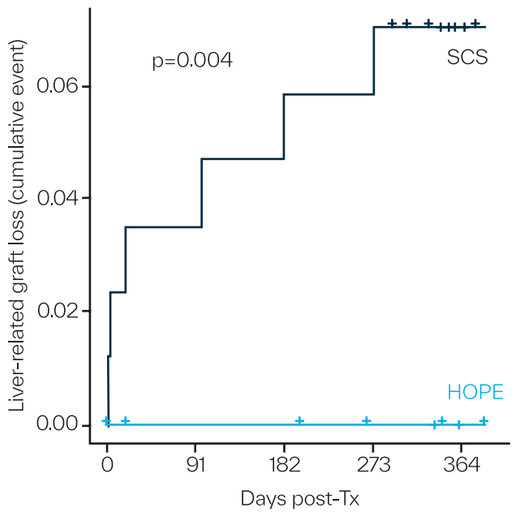
J Hepatol | 2023 | doi: 10.1016/j.jhep.2022.12.030

In this multicenter randomized controlled trial, studying the effect of hypothermic oxygenated perfusion (HOPE) on post-transplant morbidity, livers donated after brain death (DBD) were randomly assigned (1:1 ratio) to either SCS alone (n=85), or SCS followed by 1-2 hours of hypothermic oxygenated perfusion (HOPE, n=85) prior to transplantation.

The study shows that while the overall number of reported complications were similar between groups, recipients of HOPE-treated livers experienced a 41% reduction in severe (Clavien-Dindo≥IIIb) complications (6.6% vs 12.0%) overall, and a 74% reduction of liver graft-related severe complications (10.1% vs. 37.2%; p=0.016). Also, no graft failures due to liver-related complications occurred in the HOPE group, while 6 liver-related graft failures occurred in the control group (p=0.004).

> "As it is a simple and quick perfusion technique, it [HOPE] can be applied easily after organ transport during recipient hepatectomy."
>
> Schlegel et al., 2023





HOPE in ECD/DBD

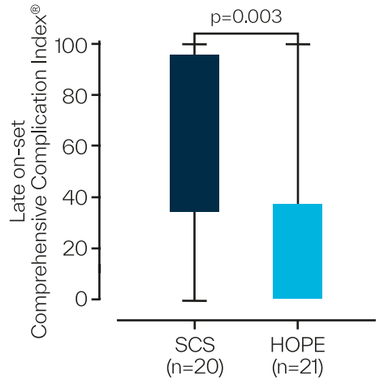
Improved outcome after hypothermic oxygenated machine perfusion in liver transplantation – Long-term follow-up of a multicenter randomized controlled trial.

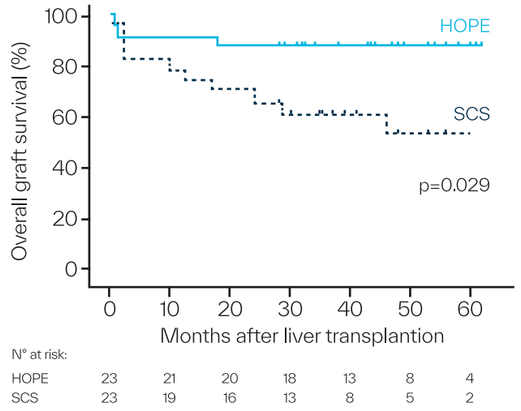
Czigany Z, Uluk D, Pavicevic S, Lurje I, Froněk J, Keller T, Strnad P, Jiang D, Gevers T, Koliogiannis D, Guba M, Tolba RH, Meister FA, Neumann UP, Kocik M, Kysela M, Sauer IM, Raschzok N, Schöning W, Popescu I, Tacke F, Pratschke J and Lurje G.

Hepatol Commun | 2024 | doi: 10.1097/HC9.0000000000000376

In this follow-up study of the multicenter 'HOPE ECD-DBD' randomized controlled trial[1], Czigany et al assessed the long-term effects of end-ischemic hypothermic oxygenated machine perfusion (HOPE) using Liver Assist in extended criteria donation after brain death (ECD-DBD) liver transplantation. With a median follow-up of 48 months, HOPE treatment resulted in significantly improved long-term graft survival (p=0.029), fewer late-onset[2] major complications (Clavien-Dindo grade ≥III: 43% vs 85%; p=0.009) and reduced morbidity (CCI®: 23 [IQR 0-37]) vs 46 [IQR 34-95], p=0.003) compared to SCS alone. Also, multvariate analysis revealed that HOPE treatment was the only variable with a significant and independent correlation with a reduced risk of developing late-onset major complications (Clavien-Dindo grade ≥III: OR 0.15; p=0.03).

This long-term follow-up demonstrates that the beneficial effects of HOPE extend beyond the early post-operative phase, with a sustained reduction of late-onset complications and superior long-term graft survival.





> "This trial provides first-time evidence that HOPE, in comparison to SCS, significantly improves long-term post-transplant outcomes in ECD LT."
>
> Czigany et al., 2024

73%
reduced risk of graft loss up to 5-years post Tx. (DBD livers)

1. Czigany et al (2021) Hypothermic Oxygenated Machine Perfusion Reduces Early Allograft Injury and Improves Post-transplant Outcomes in Extended Criteria Donation Liver Transplantation From Donation After Brain Death: Results From a Multicenter Randomized Controlled Trial (HOPE ECD-DBD)
2. Complications occurring later than 6 months after LT

LONG-TERM OUTCOMES

Long-term outcomes after hypothermic oxygenated machine perfusion and transplantation of 1,202 donor livers in a real-world setting (HOPE-REAL study)

Eden J, Brüggenwirth MA, Berlakovich G, /.../ Dutkowski P and de Meijer VE.

J Hepatol | 2024 | doi: 10.1097/LVT.0000000000000476

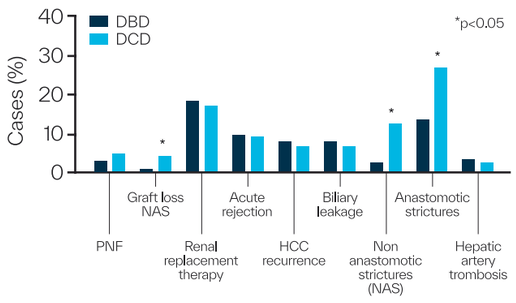
This international, multicenter, observational cohort study assessed long-term outcome after transplantation of (D)HOPE-treated donor livers based on real-world data.

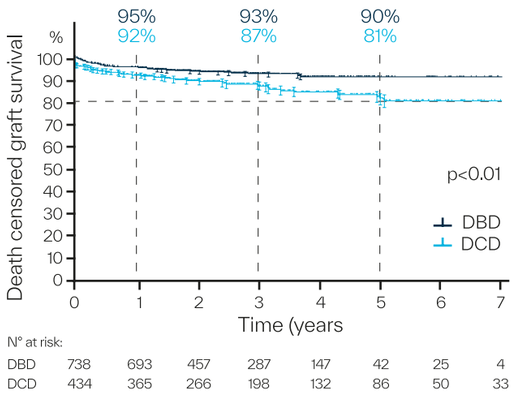
A total of 1202 (D)HOPE-treated and transplanted livers from 22 European centers were included in the study. The majority (83%; n=994) of grafts were perfused using Liver Assist, whereof 50% (n=502) were perfused using DHOPE, 36% (n=359) with HOPE, and 13% (n=133) with NRP+(D)HOPE.

> "HOPE-treatment has now reached IDEAL-D stage 4**, which further supports the implementation of HOPE in routine clinical practice."
>
> Eden et al., 2024

The primary outcome measure was death-censored graft survival up to 5 years, with rates at 1, 3, and 5 years of 94%, 90%, and 87%, respectively. Sub-analysis based on donor type revealed significantly better survival rates in DBD compared to DCD liver transplants, this was true for both death-censored graft survival (p=0.003) and overall graft survival (p <0.01). Patient survival at 1, 3, and 5 years were 91%, 86%, and 81%, respectively, with similar outcomes in DBD and DCD. Also, no significant differences were observed between DBD and DCD in the incidence of PNF, post-Tx renal replacement therapy, acute rejection, HCC recurrence, biliary leakage, or hepatic artery thrombosis. However, the cumulative incidence of NAS after 6, 12, and 24 months was 2.2%, 2.3%, and 2.5% for DBD grafts, and 8.0%, 10.0%, and 11.5% for DCD grafts, respectively (p <0.001).

This study provides valuable insights into the long-term outcomes of (D)HOPE in a real-world setting, further highlighting its effectiveness in improving graft survival and reducing the risk of post-transplantation complications.





**Refers to the final stage of the IDEAL framework for clinical evaluation of medical device i.e. monitoring long-term outcomes to establish effectiveness in an unbiased, real-world setting outside strictly controlled RCTs.

Extended preservation time

Liver transplant is a critical emergency procedure due to the limited time the donated liver can remain viable ex-vivo. DHOPE can safely extend the preservation time, offering more time for recipient selection and added flexibility in scheduling of transplant procedures. Liver Assist supports up to 24 hours of DHOPE.

PROLONGED DHOPE in DBD

Prolonged hypothermic machine perfusion enables daytime liver transplantation – an IDEAL stage 2 prospective clinical trial.

Brüggenwirth IMA, Lantinga VA, Lascaris B, Thorne AM, Meerdink M, de Kleine RHJ, Blokzijl H, van den Berg AP, Reyntjens KMEM, Lisman T, Porte RJ and de Meijer VE for the DHOPE-PRO Trial Investigators.

eClinicalMedicine | 2024 | doi: 10.1016/j.eclinm.2023.102411

This prospective first-in-human clinical trial aimed to evaluate the safety and feasibility of extended DHOPE to enable day-time scheduling of transplantation surgeries.

Based on the completion time of the donor procedure, 24 DBD livers were assigned to either standard DHOPE for 1-2 hours (n=12) or prolonged DHOPE for ≥4 hours (n=12).

No serious adverse device effects (SADEs) occurred during prolonged DHOPE, and perfusion parameters remained stable over time. With a median machine perfusion time of 9.3 hours (IQR 8.0-10.1), prolonged DHOPE using Liver Assist could safely extend the total graft preservation time for up to 20 hours while maintaining favorable outcomes.

All livers showed immediate graft function, there were no cases of NAS in either group, and both graft and patient survival were 100% at 1 year. Prolonged DHOPE did not increase serum markers of IRI, oxidative stress or endothelial injury, and liver biopsies showed only minimal signs of hepatocellular injury in either group.

The study demonstrates the safety and feasibility of DHOPE in prolonging the preservation time of donor livers to enable daytime transplantation. The authors suggest that prolonged preservation with DHOPE could help streamline transplantation logistics, transform liver transplantation into a semi-elective procedure, reduce organ discards due to logistical constraints, and contribute to a healthier work-life balance by minimizing nighttime surgeries.

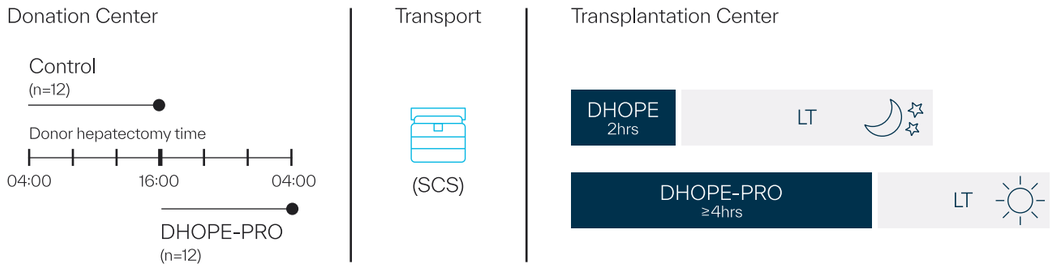


Image depicting study set-up. Adapted from source publication.

PROLONGED DHOPE in ECD/DBD + DCD

Are there any benefits of prolonged hypothermic oxygenated perfusion?: Results from a national retrospective study

De Carlis R, Lauterio A, Schlegel A, Gringeri E, Patrono D, Camagni S, Dondossola D, Pezzati D, Olivieri T, Pagano D, Bongini M, Montanelli P, Ravaioli M, Bernasconi D, Valsecchi MG, Baccarani U, Cescon M, Andorno E, Mazzaferro V, Gruttadauria S, Di Benedetto F, Ghinolfi D, Caccamo L, Pinelli D, Romagnoli R, Cillo U, De Carlis L and the Italian HOPE collaborator group.

Liver Transpl | 2024 | doi: 10.1097/LVT.0000000000000476

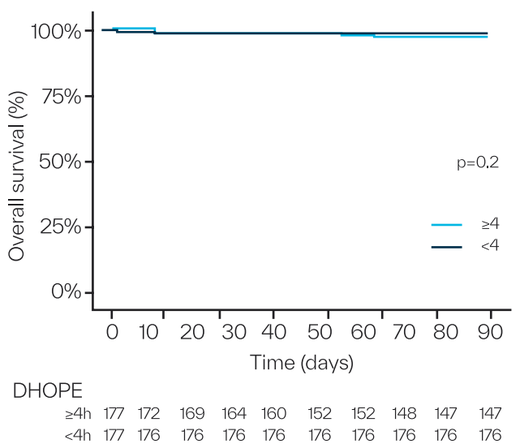
The ability to extend liver graft preservation times for improved transplant logistics is increasingly being applied in clinical practice through the use of DHOPE.

The aim of this retrospective study, including 12 Italian transplant centers, was to investigate the benefit of prolonged DHOPE in addition to improved logistics, and if prolonged preservation is equally suitable for livers of different risk profiles.

The outcomes of 177 liver transplants (DBD: n=124; DCD: n=53) preserved using prolonged DHOPE (≥4 hours) were compared to a matched control group of liver transplants preserved using 'short' DHOPE (<4 hours). Donor livers were generally of high-risk with a median DRI >2.5 in both groups.

Apart from a significantly lower incidence of post-transplant acute kidney injury (AKI) following prolonged DHOPE as compared to short DHOPE (30.5% vs. 44.6%, p=0.008), no significant differences in post-transplant outcomes were found between groups. Also, no differences in outcomes were observed when stratifying the prolonged DHOPE-liver transplants according to risk profiles.

Overall patient and graft survival at 90-days were similar between groups, with 98% and 92% for DHOPE ≥4h, and 99% and 96% for DHOPE <4h, respectively. The authors conclude that prolonged DHOPE improves transplant logistics, provides good results with high-risk grafts, and is associated with a lower risk of post-transplant acute kidney injury.



"The ability to extend the preservation window to up to 20 h using [DHOPE] has the potential to reshape the landscape of liver transplantation."

Brüggenwirth et al., 2024

Viability assessment

The ability to assess the quality and viability of a graft prior to transplantation is a valuable tool for improving the safe utilization of high-risk livers. Normothermic machine perfusion (NMP) involves perfusing the liver through both the portal vein and hepatic artery with a blood-based oxygenated solution at 37°C. This technique enables viability assessment under near physiological conditions. While it has been assumed that viability assessment is limited to NMP, recent studies show that perfusate analysis during HOPE/DHOPE offers a new and highly sought after tool to select individual grafts for transplantation. Liver Assist allows for viability assessment during both NMP and HOPE/DHOPE.

HOPE/DHOPE

Assessment of liver graft quality during hypothermic oxygenated perfusion: the first international validation study

Eden J, Thorne AM, Bodewes SB, Patrono D, Roggio D, Breuer E, Lonati C, Dondossola D, Panayotova G, Boteon APCS, Walsh D, Carvalho MF, Schurink IJ, Ansari F, Kollmann D, Germinario G, Rivas Garrido EA, Benitez J, Rebolledo R, Cescon M, Ravaioli M, Berlakovich GA, De Jonge J, Uluk D, Lurje I, Lurje G, Boteon YL, Guarrera JV, Romagnoli R, Galkin A, Meierhofer D, Porte RJ, Clavien PA, Schlegel A, de Meijer VE and Dutkowski P.

J Hepatol | 2024 | doi: 10.1016/j.jhep.2024.08.030

This is the first international, multicenter study validating the use of perfusate FMN-levels as a liver graft quality assessment tool during HOPE. Previous studies have shown that flavin mononucleotide (FMN), a biomarker of mitochondrial injury, can be assessed through perfusate analyses during HOPE. In order to validate the use of this potential graft-assessment tool, 473 perfusate samples from 10 independent, international transplant centers were collected and analyzed.

Results show that perfusate FMN values, measured during the first hour of HOPE or DHOPE, are predictive for graft loss, cholangiopathy and kidney failure after liver transplantation, and is superior to conventional scores derived from donor and recipient parameters in predicting graft loss. Also, as the release of mitochondrial FMN relates to the degree of inflammatory activation during HOPE, the authors were able to stratify liver grafts into different risk categories correlating to patient outcomes. These results are of high clinical relevance, as functional assessment of donor livers during HOPE offers a new and highly needed tool to select individual grafts for transplantation.

"/.../ assessment of livers during HOPE is possible by a relatively simple and rapid fluorometric measurement of perfusate, which is even feasible by real time monitoring."

Eden et al., 2024

NMP

Observations on the ex situ perfusion of livers for transplantation.

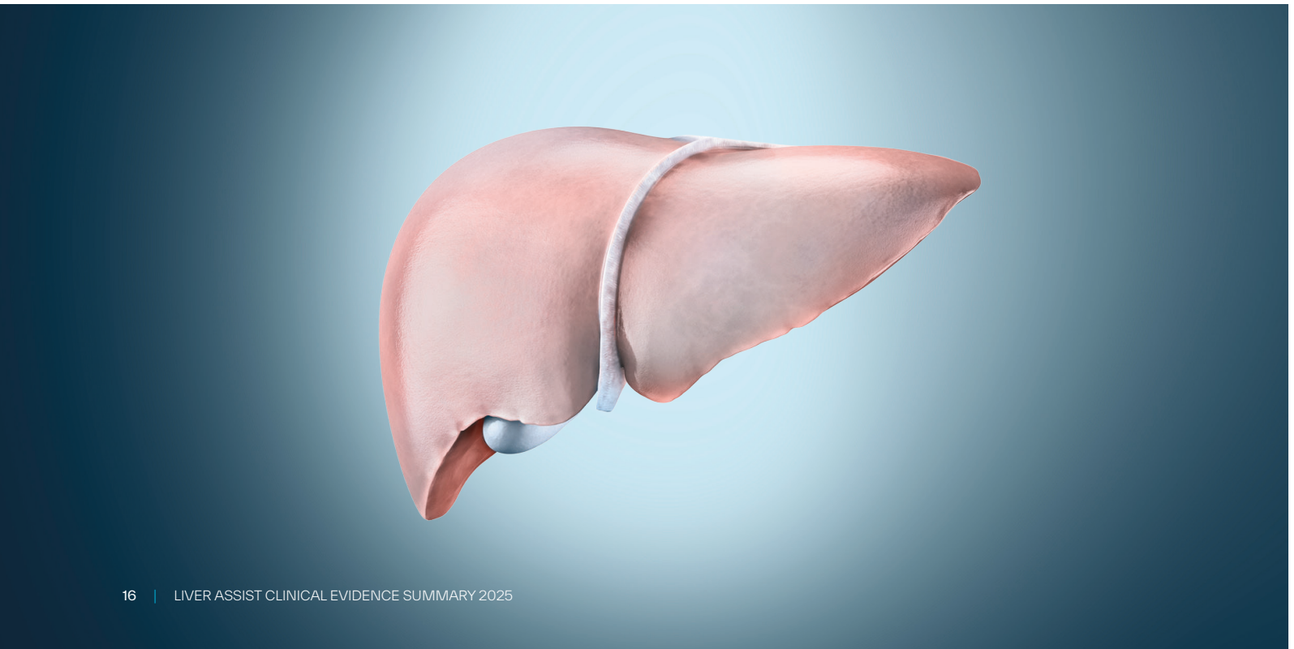
Watson CJ, Kosmoliaptsis V, Pley C, Randle L, Fear C, Crick K, Gimson AE, Allison M, Upponi S, Brais R, Jochmans I, Butler AJ.

Am J Transplant | 2018 | doi: 10.1111/ajt.14687

In this observational study, the biochemistry and perfusion characteristics of forty-seven (n=47) high-risk and initially rejected livers were studied using normothermic machine perfusion (NMP), resulting in 22 transplantations. By using readily available measurements that could be analyzed during NMP using the Liver Assist, the authors identified specific variables associated with successful transplantation.

They found that by using a combination of transaminase release, glucose metabolism, lactate clearance, and maintenance of acid-base balance, the viability of a donor liver can be assessed prior to transplantation, and that evaluation of bile pH may offer a valuable insight into bile duct integrity and the risk of post-transplant ischemic cholangiopathy.

> “Liver viability during normothermic perfusion can be assessed using a combination of transaminase release, glucose metabolism, lactate clearance, and maintenance of acid-base balance.”
>
> Watson et al., 2018



Increased utilization

One of the more advanced protocols used with Liver Assist is DHOPE-COR-NMP. Published in ‘Nature Protocols[1] it allows for safe transplantation of high-risk, initially rejected donor livers by combining the reconditioning effects of DHOPE with pre-Tx viability assessment during NMP. With more than 200 DHOPE–COR–NMP procedures performed, a utilization rate of ~70%, and outcomes comparable to benchmark studies*, the application of this protocol could help increase utilization of high-risk donor livers[1]. Thanks to the flexibility of Liver Assist, the device can operate the DHOPE-COR-NMP protocol.

DHOPE – COR - NMP

Sequential hypothermic and normothermic machine perfusion enables safe transplantation of high-risk donor livers.

van Leeuwen OB, Bodewes SB, Lantinga VA, Haring MPD, Thorne AM, Brüggenwirth IMA, van den Berg AP, de Boer MT, de Kleine RHJ, Lascaris B, Nijsten MWN, Reyntjens KMEM, de Meijer VE, Porte RJ.

Am J Transplant | 2022 | doi: 10.1111/ajt.17022

In this perspective, observational study, the effect of sequential hypothermic and normothermic machine perfusion was assessed. Briefly, after SCS, Fifty-four (n=54) initially discarded, high-risk (median DRI: 2.84) donor livers were placed on the Liver Assist™ for 1 hour of ‘resuscitation’ using DHOPE. After DHOPE, the temperature of the perfusion solution** was gradually increased (+1°C/2min) until reaching 37°C, whereby hepatobiliary viability was assessed during the initial 2.5h of NMP. After DHOPE-NMP, 34 livers (63%) met the predefined viability criteria and were subsequently transplanted.

With a 1-year patient and graft survival of 100% and 94%, respectively, no incidence of primary non function (PNF) or hepatic artery thrombosis (HAT) and only one patient (3%) developing non-anastomotic biliary strictures (NAS), this study demonstrates that seqential use of DHOPE and NMP using Liver Assist™ enables safe selection of initially rejected high-risk livers with excellent results, providing an effective tool to increase the number of suitable donor organs for transplantation.

> “/.../ [DHOPE-NMP] provides an effective tool to increase the number of suitable donor organs for transplantation.”
>
> van Leeuwen et al., 2022

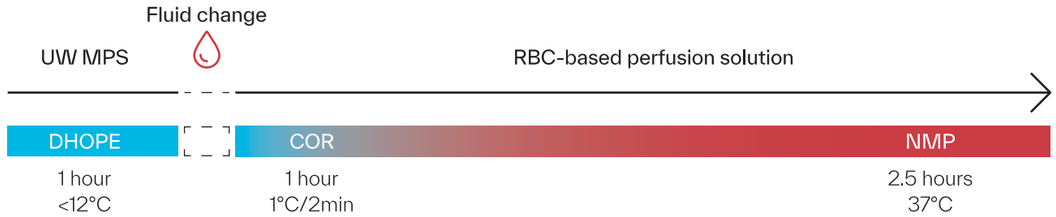


Image adapted from source publication.

*for livers that met the viability criteria **For details regarding exact protocol and perfusion solutions used, see van Leeuwen et al 2022.
1. van Leeuwen et al (2025) 'Back-to-base' combined hypothermic and normothermic machine perfusion of human donor livers.

HOPE + DHOPE-COR-NMP

Reducing cold ischemia time by donor liver “back-table” preparation under continuous oxygenated machine perfusion of the portal vein.

Lantinga V A, Buis CI, Porte RJ, de Meijer VE, van Leeuwen OB.

Clin Transplanti | 2022 | doi: 10.1111/ctr.14762

Back-table preparation of a donor liver prior to machine perfusion can be time-consuming and thus add to the overall cold ischemic time (CIT). In this prospective, observational cohort study, the authors assessed if CIT could be reduced by performing part of the back-table procedure under continuous, single-sided perfusion through the port vein (HOPE).

A total of ten (n=10) initially rejected livers were included in the study, and compared to sixty (n=60) regular back-table DHOPE-NMP livers. With a utilization rate of 90%, the study shows that CIT can be reduced by at least 1 hour if a donor liver is prepared ‘on the pump’ (median CIT: 214 vs 279, p<0.01).

The authors state that based on these results, they have now introduced back-table preparation under continuous HOPE as standard of care.

> “/.../ performing the back-table preparation under continuous HOPE has been introduced as standard of care in our transplant center.”
>
> Lantinga et al., 2022

Cost-effectiveness

HOPE/DHOPE has become recognized as a safe and effective method for reducing ischemia-related complications and extending the life of the transplanted graft. However, a comprehensive understanding of its cost-effectiveness is crucial for widespread clinical implementation. By reducing complications and associated costs, HOPE/DHOPE provides the added benefit of combining clinical efficacy and cost-effectiveness[1].

DHOPE in ECD/DBD

Hypothermic oxygenated perfusion improves extended criteria donor liver graft function and reduces duration of hospitalization without extra cost: the PERfusion et preservation hypothermique oxygénée study

Rayar M, Beaurepaire JM, Bajeux E, Hamonic S, Renard T, Locher C, Desfourneaux V, Merdrignac A, Bergeat D, Lakehal M, Sulpice L, Houssel-Debry P, Jezequel C, Camus C, Bardou-Jacquet E and Meunier B.

Liver Transpl | 2021 | doi: 10.1002/lt.25955

This prospective, single-center study (PERPHO study) evaluated the efficacy and economic impact of HOPE in extended criteria donation after brain death (ECD-DBD) liver transplantation.

Twenty-five (n=25) HOPE-treated ECD-DBD were compared (1:3 ratio) to a propensity score matched cohort preserved using only SCS. Compared to the control, HOPE reduced the incidence of EAD (28% vs. 42%; p=0.22) and led to fewer severe post-operative complications (Clavien-Dindo >III: 24% vs 45%; p=0.07), albeit, without significance. HOPE significantly reduced the median ICU stay (3 vs. 5 days; p=0.01) and total hospital stay (15 vs. 20 days; p=0.01).

For the economic assessment the following aspects were considered: the total additional cost for HOPE (estimated at €5298 per patient[2]), the average cost of a hospital stay per group, and the average hospital income per group. Due to the improved outcomes and reduction in hospital stay, the costs of the HOPE procedure were balanced out. Also, the total per-patient costs appeared to be somewhat lower for the HOPE group (€3023 vs. €4059; p=n.s.).

Consequently, the overall cost-revenue balance remains similar between the HOPE and control groups, making HOPE an economically viable option for improving clinical outcomes in liver transplantation with ECD grafts.

> “The additional cost of the procedure was compensated by better outcomes.”
>
> Rayar et al., 2021

1. Endo et al (2024) Cost-effectiveness of Dual Hypothermic Oxygenated Machine Perfusion versus Static Cold Storage in DCD Liver Transplantation.
2. incl. Device-costs (amortization etc.), cost of perfusion kits, machine perfusion solution, and maintenance.

DHOPE in DCD

Cost-effectiveness of Dual Hypothermic Oxygenated Machine Perfusion versus Static Cold Storage in DCD Liver Transplantation

Endo C, van Rijn R, Huurman V, Schurink I, van den Berg A, Murad SD, van Hoek B, de Meijer VE, de Jonge J, van der Hilst CS and Porte RJ.

Transplantation | 2024 | doi: 10.1097/TP.0000000000005232.

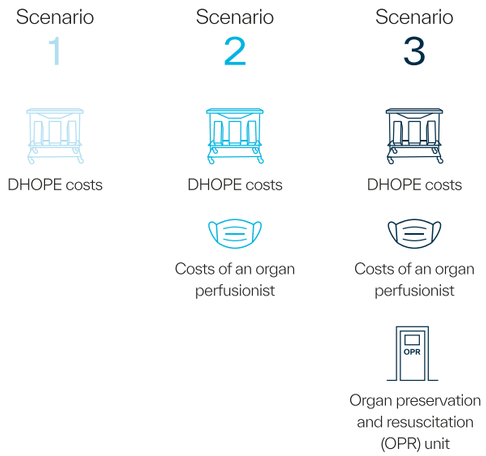
Based on the DHOPE-DCD multicenter RCT[1], Endo et al performed an economic evaluation of DHOPE using Liver Assist vs. SCS in DCD liver transplantation.

The economic assessment included the full spectrum of costs associated with the transplant procedure, such as initial hospital stay, readmissions, and outpatient treatments up to 1 year posttransplant. Costs for organ acquisition, static cold preservation, and physician fees were excluded as they were considered equal between the groups.

In order to facilitate translation of the data to different local situations, the costs of machine perfusion were analyzed using 3 different scenarios:

1. Machine perfusion costs[2] only (perfusion device, disposables, and diagnostics used during machine perfusion);
2. machine perfusion costs + the cost of a fulltime organ perfusionist per center;
3. machine perfusion costs + the cost of a fulltime organ perfusionist + the cost of a dedicated organ preservation and resuscitation (OPR) unit.

> "The mean reduction per patient in transplant-related costs in the [DHOPE] group, compared with the SCS group was € 25 832."
>
> Endo et al., 2024

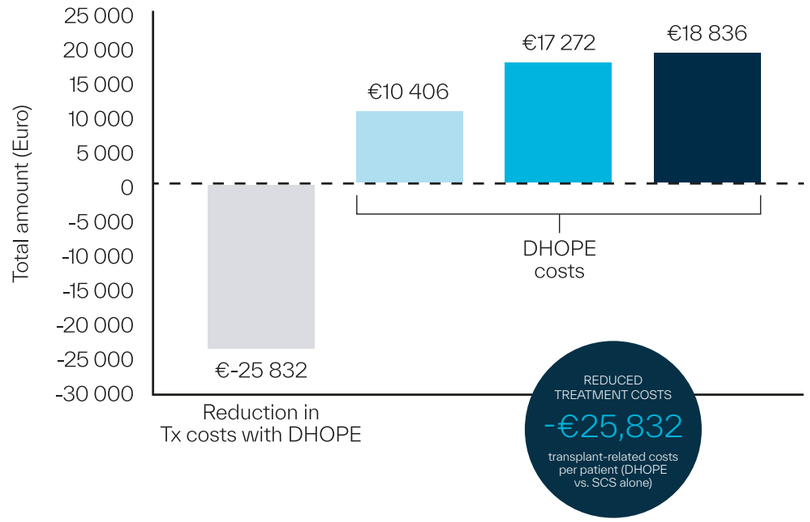


1. Van Rijn et al (2021) Hypothermic Machine Perfusion in Liver Transplantation – A Randomized Trial
2. The machine perfusion consumable costs were calculated on the basis of the actual market price (outside the clinical trial) used in the Netherlands in 2019.

The use of DHOPE consistently reduced the cost per patient in every category compared with SCS alone, with an overall cost reduction of 12.2%. The most significant reduction occurred in intensive care costs (28.4%), followed by nonsurgical interventions (24.3%). The mean reduction per patient in transplant-related costs in the machine perfusion group, compared with the SCS group was €25 832, which was higher than the costs for machine perfusion in all 3 cost scenarios.

The minimal number of procedures needed for cost-effectiveness was calculated for each scenario. When only considering the costs of machine perfusion (scenario 1), DHOPE was cost-effective already after the first perfusion procedure, while for scenario 2 and 3, the numbers of perfusion procedures needed for cost-effectiveness were 25 and 30 per year, respectively.

Mean reduction in transplant-related vs. the cost for DHOPE (per patient)



> "Most importantly, our data were not estimated but based on actual medical treatments, and our comprehensive economic evaluation, combining clinical efficacy and cost-effectiveness, contributes to the growing body of literature supporting the adoption of DHOPE in liver transplantation protocols."
>
> Endo et al., 2024

HOPE in ECD/DBD

Hypothermic oxygenated machine perfusion reduces early allograft injury and improves post-transplant outcomes in extended criteria donation liver transplantation from donation after brain death: results from a multicenter randomized controlled trial (HOPE ECD-DBD)

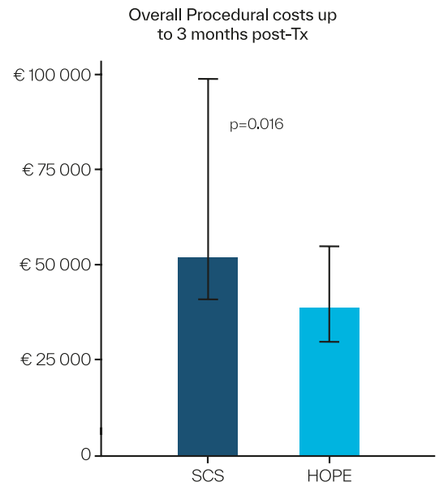
Czigany Z, Pratschke J, Froněk J, Guba M, Schöning W, Raptis DA, Andrassy J, Kramer M, Strnad P, Tolba RH, Liu W, Keller T, Miller H, Pavicevic S, Uluk D, Kocik M, Lurje I, Trautwein C, Mehrabi A, Popescu I, Vondran FWR, Ju C, Tacke F, Neumann UP and Lurje G.

Ann Surg | 2021 | doi:10.1097/sla.0000000000005110

This international, multicentre randomized controlled trial (RCT) studied the effects of HOPE in extended criteria liver grafts donated after brain death (ECD-DBD).

Forty-six (n=46) patients were randomly assigned to receive a liver preserved with either SCS alone, or SCS followed by a short period (median: 2h 15min) of HOPE prior to transplantation. Compared to SCS, end-ischemic HOPE using Liver Assist significantly reduced signs of early allograft injury, as demonstrated by a 47% decrease in serum peak ALT within the first 7 days post-transplant (primary endpoint). In addition, recipients of HOPE-treated livers presented with fewer major postoperative complications (Clavien-Dindo grade ≥ III: 44% vs 78%; p=0.036), had a lower overall morbidity (CCI® score: 32 vs 52; p=0.021), and spent less time in the ICU (5 vs. vs 8 days; p=0.045) and hospital (20 vs. 36 days; p=0.002).

In line with these findings, HOPE-treatment resulted in a 25% decrease in treatment costs over the first 3 months following transplantation compared to SCS (median €39 000 vs. €52 000; p=0.016)[1]. When considering the on average €5000 running costs per HOPE procedure, the overall cost reduction per patient was still considerable with approximately €8000.



> "/.../ the overall procedural costs after transplanting patients with HOPE was €13,000 lower compared to the SCS group."
>
> Czigany et al., 2021

1. Cost estimation analysis was based on 90-day CCI scores, as per: Staiger et al (2018) The Comprehensive Complication Index (CCI®) is a Novel Cost Assessment Tool for Surgical Procedures.

List of publications

SYSTEMATIC REVIEWS AND META-ANALYSES

Boteon YL, et al. *Impact of machine perfusion of the liver on post-transplant biliary complications: A systematic review*. World J Transplant. 2018;8(6):220-31.*

De Simone P, et al. *Hospital-Based Health Technology Assessment of Machine Perfusion Systems for Human Liver Transplantation*. Transpl Int. 2022;35:10405.*

Faleiro MD, et al. *Oncologic Outcomes of Interventions to Decrease Allograft Ischemia-Reperfusion Injury within Patients Undergoing Liver Transplantation for Hepatocellular Carcinoma: A Systematic Review*. Curr Oncol. 2024;31(6):2895-906.*

Feng GY, et al. *Benefits of Hypothermic Oxygenated Perfusion Versus Static Cold Storage in Liver Transplant: A Comprehensive Systematic Review and Meta-analysis*. J Clin Exp Hepatol. 2024;14(3):101337.*

Garzali IU, et al. *Early outcome of machine perfusion vs static cold storage of liver graft: A systemic review and meta-analysis of randomized controlled trials*. Hepatol Forum. 2024;5(4):211-6.*

Ghinolfi D, et al. *Machine Perfusions in Liver Transplantation: The Evidence-Based Position Paper of the Italian Society of Organ and Tissue Transplantation*. Liver Transpl. 2020;26(10):1298-315.*

Jaber F, et al. *Machine perfusion strategies in Liver Transplantation: A systematic review, pairwise, and network meta-analysis of randomized controlled trials*. Liver Transpl. 2025;31(5):596-615.*

Jia J, et al. *A Systematic Review and Meta-Analysis of Machine Perfusion vs. Static Cold Storage of Liver Allografts on Liver Transplantation Outcomes: The Future Direction of Graft Preservation*. Frontiers in Medicine. 2020;7:135.*

Jiang X, et al. *Optimizing Livers for Transplantation Using Machine Perfusion versus Cold Storage in Large Animal Studies and Human Studies: A Systematic Review and Meta-Analysis*. Biomed Res Int. 2018;2018:9180757.*

Lai Q, et al. *Use of machine perfusion in livers showing steatosis prior to transplantation: a systematic review*. Updates Surg. 2020;72(3):595-604.*

Liang A, et al. *Effects of machine perfusion strategies on different donor types in liver transplantation: a systematic review and meta-analysis*. Int J Surg. 2023;109(11):3617-30.*

Liew B, et al. *Liver transplant outcomes after ex vivo machine perfusion: a meta-analysis*. Br J Surg. 2021;108(12):1409-16.*

Michelotto J, et al. *Ex vivo machine perfusion: current applications and future directions in liver transplantation*. Langenbecks Arch Surg. 2021;406(1):39-54.*

Mugaanyi J, et al. *A Meta-Analysis and Systematic Review of Normothermic and Hypothermic Machine Perfusion in Liver Transplantation*. Journal of Clinical Medicine. 2023;12(1):235.*

Parente A, et al. *Current evidence on the beneficial HOPE-effect based on systematic reviews and meta-analyses in liver transplantation*. J Hepatol. 2023;80(3):e116-e9.*

Parente A, et al. *Machine perfusion techniques for liver transplantation - A meta-analysis of the first seven randomized controlled trials*. J Hepatol. 2023;79(5):1201-13.*

Ramírez-Del Val A, et al. *Does machine perfusion improve immediate and short-term outcomes by enhancing graft function and recipient recovery after liver transplantation? - A systematic review of the literature, meta-analysis and expert panel recommendations*. Clin Transplant. 2022:e14638.*

Risbey CWG, et al. *Hypothermic Oxygenated machine PErfusion for high-risk liver grafts for transplantation: A systematic review and meta-analysis*. Artificial Organs. 2024;48(10):1085-99.*

Risbey CWG, et al. *Normothermic Ex Vivo Machine Perfusion for Liver Transplantation: A Systematic Review of Progress in Humans*. J Clin Med. 2023;12(11).*

Tang G, et al. *Hypothermic oxygenated perfusion in liver transplantation: a meta-analysis of randomized controlled trials and matched studies*. International Journal of Surgery. 2024;110(1):464-77.*

Tingle SJ, et al. *Machine perfusion in liver transplantation*. Cochrane Database Syst Rev. 2023;9(9):CD014685.*

Xie X, et al. *Hypothermic oxygenated perfusion in human liver transplantation: meta-analysis of randomized clinical trials*. Br J Surg. 2023;111(1):znad403.*

Yang X, et al. *Effectiveness of machine perfusion in liver transplantation: A meta-analysis of randomized controlled trials*. Journal of Liver Transplantation. 2023;12:100176.*

Zhang Y, et al. *Hypothermic machine perfusion reduces the incidences of early allograft dysfunction and biliary complications and improves 1-year graft survival after human liver transplantation: A meta-analysis*. Medicine (Baltimore). 2019;98(23):e16033.*

*Includes other devices in addition to Liver Assist

CLINICAL INVESTIGATIONS

Aspord C, et al. *Hypothermic Oxygenated Machine Perfusion and Static Cold Storage Drive Distinct Immunomodulation During Liver Transplantation: A Pilot Study*. Transplantation. 2025;109(4):658-70.

Blondeel J, et al. *Dynamic Preservation of Do nation After Circulatory Death Liver Grafts From Donors Aged 60 y and Older*. Transplantation. 2024;109(5):844-52.

Brüggenwirth IMA, et al. *Prolonged hypothermic machine perfusion enables daytime liver transplantation - an IDEAL stage 2 prospective clinical trial*. EClinicalMedicine. 2024;68:102411.*

Brüggenwirth IMA, et al. *Prolonged preservation by hypothermic machine perfusion facilitates logistics in liver transplantation: A European observational cohort study*. Am J Transplant. 2022;22(7):1842-51.

Burlage LC, et al. *Opposite acute potassium and sodium shifts during transplantation of hypothermic machine perfused donor livers*. Am J Transplant. 2019;19(4):1061-71.*

Cillo U, et al. *Full-left/Full-right Liver Splitting With Middle Hepatic Vein and Caval Partition During Dual Hypothermic Oxygenated Machine Perfusion*. Transplantation. 2024;108(6):1417-21.*

Czigany Z, et al. *Hypothermic Oxygenated Machine Perfusion Reduces Early Allograft Injury and Improves Post-transplant Outcomes in Extended Criteria Donation Liver Transplantation From Donation After Brain Death: Results From a Multicenter Randomized Controlled Trial (HOPE ECD-DBD)*. Ann Surg. 2021;274(5):705-12.

Czigany Z, et al. *Improved outcomes after hypothermic oxygenated machine perfusion in liver transplantation–Long-term follow-up of a multicenter randomized controlled trial*. Hepatology Communications. 2024;8(2):e0376.

De Carlis R, et al. *Are there any benefits of prolonged hypothermic oxygenated perfusion?: Results from a national retrospective study*. Liver Transpl. 2024;31(1):70-84.

De Carlis R, et al. *How to Preserve Liver Grafts From Circulatory Death With Long Warm Ischemia? A Retrospective Italian Cohort Study With Normothermic Regional Perfusion and Hypothermic Oxygenated Perfusion*. Transplantation. 2021;105(11):2385-96.*

De Carlis R, et al. *Hypothermic Machine Perfusion of Liver Grafts Can Safely Extend Cold Ischemia for Up to 20 Hours in Cases of Necessity*. Transplantation. 2017;101(7):e223-e4.

De Carlis R, et al. *Successful donation after cardiac death liver transplants with prolonged warm ischemia time using normothermic regional perfusion*. Liver Transpl. 2017;23(2): 166-73.*

de Jong IEM, et al. *Restoration of Bile Duct Injury of Donor Livers During Ex Situ Normothermic Machine Perfusion*. Transplantation. 2023;107(6):e161-e72.

De Simone P, et al. *First-in-human liver transplantation from a centenarian deceased donor after brain death*. Am J Transplant. 2023;24(2):304-7.

de Vries Y, et al. *Pretransplant sequential hypo- and normothermic machine perfusion of suboptimal livers donated after circulatory death using a hemoglobin-based oxygen carrier perfusion solution*. Am J Transplant. 2019;19(4):1202-11.

Dingfelder J, et al. *Validation of mitochondrial FMN as a predictor for early allograft dysfunction and patient survival measured during hypothermic oxygenated perfusion*. Liver Transpl. 2025;31(4):476-88.

Dondossola D, et al. *Preliminary Experience With Hypothermic Oxygenated Machine Perfusion in an Italian Liver Transplant Center*. Transplant Proc. 2019;51(1):111-6.

Dondossola D, et al. *The Role of Ex Situ Hypothermic Oxygenated Machine Perfusion and Cold Preservation Time in Extended Criteria Donation After Circulatory Death and Donation After Brain Death*. Liver Transpl. 2021;27(8):1130-43.*

Dutkowski P, et al. *First Comparison of Hypothermic Oxygenated PErfusion Versus Static Cold Storage of Human Donation After Cardiac Death Liver Transplants: An International-matched Case Analysis*. Ann Surg. 2015;262(5):764-70.

Dutkowski P, et al. *HOPE for human liver grafts obtained from donors after cardiac death*. J Hepatol. 2014;60(4):765-72.

Eden J, et al. *Assessment of liver graft quality during hypothermic oxygenated perfusion: the first international validation study*. J Hepatol. 2024;82(3):523-34.*

Eden J, et al. *Long-term outcomes after hypothermic oxygenated machine perfusion and transplantation of 1,202 donor livers in a real-world setting (HOPE-REAL study)*. J Hepatol. 2024;82(1):97-106.*

Eden J, et al. *Screening for mitochondrial function before use-routine liver assessment during hypothermic oxygenated perfusion impacts liver utilization*. eBioMedicine. 2023;98:104857.*

Elgosbi M, et al. *Hypothermic oxygenated machine perfusion influences the immunogenicity of donor livers in humans*. Liver Transpl. 2024;31(3):311-22.

Endo C, et al. *Cost-effectiveness of Dual Hypothermic Oxygenated Machine Perfusion Versus Static Cold Storage in DCD Liver Transplantation*. Transplantation. 2024;109(2):e101-e8.

Endo C, et al. *The Risk of Microbial Transmission in Recipients of Donor Livers That Underwent Hypothermic or Normothermic Machine Perfusion*. Transplant Direct. 2024;10(7):e1664.

Gaurav R, et al. *Liver Transplantation Outcomes From Controlled Circulatory Death Donors: SCS vs in situ NRP vs ex situ NMP*. Ann Surg. 2022;275(6):1156-64.*

Ghinolfi D, et al. *Liver transplantation with uncontrolled versus controlled DCD donors using normothermic regional perfusion and ex-situ machine perfusion*. Liver Transpl. 2023;30(1):46-60.

Ghinolfi D, et al. *Pilot, Open, Randomized, Prospective Trial for Normothermic Machine Perfusion Evaluation in Liver Transplantation From Older Donors*. Liver Transpl. 2019;25(3):436-49.

Ghinolfi D, et al. *Sequential Use of Normothermic Regional and Ex Situ Machine Perfusion in Donation After Circulatory Death Liver Transplant*. Liver Transpl. 2021;27(3):385-402.*

Ghinolfi D, et al. *The role of sequential normothermic regional perfusion and end-ischemic normothermic machine perfusion in liver transplantation from very extended uncontrolled donation after cardiocirculatory death*. Artif Organs. 2023;47(2):432-40.*

Grat M, et al. *Routine End-ischemic Hypothermic Oxygenated Machine Perfusion in Liver Transplantation from Donors After Brain Death: A Randomized Controlled Trial*. Ann Surg. 2023.

Gruttadauria S, et al. *Liver transplantation after ex vivo normothermic machine preservation without recooling the graft: A clinical series from a single center*. Liver Transpl. 2025;Epub ahead of print.

Horné F, et al. *Hypothermic Oxygenated Machine Perfusion (HOPE) Prior to Liver Transplantation Mitigates Post-Reperfusion Syndrome and Perioperative Electrolyte Shifts*. J Clin Med. 2022;11(24).

Hoyer DP, et al. *Controlled Oxygenated Rewarming of Cold Stored Livers Prior to Transplantation: First Clinical Application of a New Concept*. Transplantation. 2016;100(1):147-52.

Hoyer DP, et al. *Long-term Outcomes After Controlled Oxygenated Rewarming of Human Livers Before Transplantation*. Transplant Direct. 2020;6(4):e542.

Koch DT, et al. *Mono-HOPE Versus Dual-HOPE in Liver Transplantation: A Propensity Score-Matched Evaluation of Early Graft Outcome*. Transplant International. 2025;38:13891.

Lantinga VA, et al. *Reducing cold ischemia time by donor liver "back-table" preparation under continuous oxygenated machine perfusion of the portal vein*. Clin Transplant. 2022;36(8):e14762.

Lau NS, et al. *Long-term normothermic perfusion of human livers for longer than 12 days*. Artif Organs. 2022;46(12):2504-10.

Magistri P, et al. *Sequential Hypothermic and Normothermic Machine Perfusion of Extended Criteria Donors in Liver Transplantation: A Single-Center Preliminary Experience*. Artificial Organs. 2025;49(4):705-15.*

Maroni L, et al. *Normothermic with or without hypothermic oxygenated perfusion for DCD before liver transplantation: European multicentric experience*. Clin Transplant. 2021;35(11):e14448.*

Mergental H, et al. *Transplantation of Declined Liver Allografts Following Normothermic Ex-Situ Evaluation*. Am J Transplant. 2016;16(11):3235-45.

Minor T, et al. *Controlled oxygenated rewarming as novel end-ischemic therapy for cold stored liver grafts. A randomized controlled trial*. Clin Transl Sci. 2022;15(12):2918-27.

Morales Santana DA, et al. *Successful Transplantation of a Liver from a Donor with HELLP Syndrome Undergoing Hypothermic Oxygenated Machine Perfusion (HOPE) Prior to Implantation*. Am J Case Rep. 2023;24:e938131.

Morawski M, et al. *Routine end-ischemic hypothermic machine perfusion in liver transplantation from donors after brain death: results of 2-year follow-up of a randomized controlled trial*. Int J Surg. 2024;110(11):7003-10.

Mueller M, et al. *Hypothermic Oxygenated Liver Perfusion (HOPE) Prevents Tumor Recurrence in Liver Transplantation From Donation After Circulatory Death*. Ann Surg. 2020;272(5):759-65.

Muller X, et al. *Hypothermic Oxygenated Perfusion Versus Normothermic Regional Perfusion in Liver Transplantation From Controlled Donation After Circulatory Death: First International Comparative Study*. Ann Surg. 2020;272(5):751-8.

Muller X, et al. *Novel Real-time Prediction of Liver Graft Function During Hypothermic Oxygenated Machine Perfusion Before Liver Transplantation*. Ann Surg. 2019;270(5):783-90.

Nicolăescu D, et al. *Hypothermic Oxygenated Machine Perfusion of Liver Grafts: Preliminary Experience in a Single Center. Chirurgia (Bucur)*. 2021;116(4):451-65.

Patrono D, et al. *Hypothermic Oxygenated Machine Perfusion for Liver Transplantation: An Initial Experience*. Exp Clin Transplant. 2018;16(2):172-6.

Patrono D, et al. *Hypothermic Oxygenated Machine Perfusion of Liver Grafts from Brain-Dead Donors*. Sci Rep. 2019;9(1):9337.

Patrono D, et al. *Normothermic Regional Perfusion and Hypothermic Oxygenated Machine Perfusion for Livers Donated After Controlled Circulatory Death With Prolonged Warm Ischemia Time: A Matched Comparison With Livers From Brain-Dead Donors*. Transpl Int. 2022;35:10390.*

Patrono D, et al. *Outcome of liver transplantation with grafts from brain-dead donors treated with dual hypothermic oxygenated machine perfusion, with particular reference to elderly donors*. Am J Transplant. 2022;22(5):1382-95.

Patrono D, et al. *Perfusate Analysis During Dual Hypothermic Oxygenated Machine Perfusion of Liver Grafts: Correlations With Donor Factors and Early Outcomes*. Transplantation. 2020;104(9):1929-42.

Patrono D, et al. *Viability assessment and transplantation of fatty liver grafts using end-ischemic normothermic machine perfusion*. Liver Transpl. 2022;29(5):508-20.

Pereyra D, et al. *Dual hypothermic oxygenated machine perfusion of the liver reduces post transplant biliary complications - a retrospective cohort study*. Int J Surg. 2024;110(12):7909-18.

Pueyo-Périz EM, et al. *Liver Resuscitation With Hypothermic Oxygenated Perfusion After Donation in Asystolic Type Iii With Regional Perfusion in Normothermia: A Case Report About First Experience in Spain*. Transplant Proc. 2022;54(9):2562-4.*

Rayar M, et al. *Hypothermic Oxygenated Perfusion Improves Extended Criteria Donor Liver Graft Function and Reduces Duration of Hospitalization Without Extra Cost: The PERPHO Study*. Liver Transpl. 2021;27(3):349-62.

Rigo F, et al. *Impact of Hypothermic Oxygenated Machine Perfusion on Hepatocellular Carcinoma Recurrence after Liver Transplantation*. J Pers Med. 2023;13(5).

Rossignol G, et al. *Full left/full right liver graft ex situ split during hypothermic oxygenated perfusion*. Pediatr Transplant. 2022;26(5):e14284.

Rossignol G, et al. *Liver transplantation of partial grafts after ex situ splitting during hypothermic oxygenated perfusion-The HOPE-Split pilot study*. Liver Transpl. 2022;28(10):1576-87.

Schlegel A, et al. *A multicenter randomized-controlled trial of hypothermic oxygenated perfusion (HOPE) for human liver grafts before transplantation*. J Hepatol. 2023;78(4):783-93.

Schlegel A, et al. *Outcomes of DCD liver transplantation using organs treated by hypothermic oxygenated perfusion before implantation*. J Hepatol. 2019;70(1):50-7.

Spada M, et al. *The New Horizon of Split-Liver Transplantation: Ex Situ Liver Splitting During Hypothermic Oxygenated Machine Perfusion*. Liver Transpl. 2020;26(10):1363-7.

Thorne AM, et al. *Bile proteome reveals biliary regeneration during normothermic preservation of human donor livers*. Nat Commun. 2023;14(1):7880.

Thorne AM, et al. *Ex Situ Dual Hypothermic Oxygenated Machine Perfusion for Human Split Liver Transplantation*. Transplant Direct. 2021;7(3):e666.

Torri F, et al. *Sequential Normothermic Regional Perfusion and End-ischemic Ex Situ Machine Perfusion Allow the Safe Use of Very Old DCD Donors in Liver Transplantation*. Transplantation. 2024;708(6):1394-402.*

van den Boom BP, et al. *The international normalised ratio to monitor coagulation factor production during normothermic machine perfusion of human donor livers*. Thromb Res. 2023;228:64-71.

van Leeuwen OB, et al. *Excellent long-term outcome after sequential hypothermic and normothermic machine perfusion challenges the importance of functional donor warm ischemia time in DCD liver transplantation*. J Hepatol. 2023;79(6):e244-e5.

van Leeuwen OB, et al. *Sequential Hypothermic and Normothermic Machine Perfusion Enables Safe Transplantation of High-risk Donor Livers*. Am J Transplant. 2022;22(6):1658-70.

van Leeuwen OB, et al. *Transplantation of High-risk Donor Livers After Ex Situ Resuscitation and Assessment Using Combined Hypo- and Normothermic Machine Perfusion: A Prospective Clinical Trial*. Ann Surg. 2019;270(5):906-14.

van Rijn R, et al. *Dual hypothermic oxygenated machine perfusion in liver transplants donated after circulatory death*. Br J Surg. 2017;104(7):907-17.

van Rijn R, et al. *Hypothermic Machine Perfusion in Liver Transplantation - A Randomized Trial*. N Engl J Med. 2021;384(15):1391-401.

van Rijn R, et al. *Hypothermic oxygenated machine perfusion reduces bile duct reperfusion injury after transplantation of donation after circulatory death livers*. Liver Transpl. 2018;24(5):655-64.

Viero G, et al. *Hypothermic oxygenated machine-perfusion fluid-related infection in a liver transplant recipient: First case report in the literature*. Transpl Infect Dis. 2023;25(3):e14056.

Watson CJ, et al. *26-hour Storage of a Declined Liver Before Successful Transplantation Using Ex Vivo Normothermic Perfusion*. Ann Surg. 2017;265(1):e1-e2.

Watson CJ, et al. *Preimplant Normothermic Liver Perfusion of a Suboptimal Liver Donated After Circulatory Death*. Am J Transplant. 2016;16(1):353-7.

Watson CJE, et al. *D-dimer Release From Livers During Ex Situ Normothermic Perfusion and After In Situ Normothermic Regional Perfusion: Evidence for Occult Fibrin Burden Associated With Adverse Transplant Outcomes and Cholangiopathy*. Transplantation. 2023;107(6):1311-21.

Watson CJE, et al. *Normothermic Perfusion in the Assessment and Preservation of Declined Livers Before Transplantation: Hyperoxia and Vasoplegia-Important Lessons From the First 12 Cases*. Transplantation. 2017;101(5):1084-98.

Watson CJE, et al. *Observations on the ex situ perfusion of livers for transplantation*. Am J Transplant. 2018;18(8):2005-20.

Werner MJM, et al. *First report of successful transplantation of a pediatric donor liver graft after hypothermic machine perfusion*. Pediatr Transplant. 2019;23(3):e13362.

Zhang Z, et al. *First Preliminary Experience with Preservation of Liver Grafts from Extended-Criteria Donors by Normothermic Machine Perfusion in Asia*. Ann Transplant. 2020;25:e921529.

*Includes other devices in addition to Liver Assist

Nobody should die waiting for a new organ

Founded in 1998, XVIVO is the only MedTech company dedicated to extending the life of all major organs – so transplant teams around the world can save more lives. Our solutions allow leading clinicians and researchers to push the boundaries of organ transplantation.

XVIVO is a global company headquartered in Gothenburg, Sweden.

For more information about the device and availability in your market, please visit www.xvivogroup.com

XVIVO BV
Bornholmstraat 84 | 9723 AZ Groningen | Netherlands
Tel +31 50 313 1905 | xvivogroup.com

MAR-24750 Clinical Summary - Liver Assist 02 2025.05

XVIVO