XVIVO

Kidney Assist Transport™

Clinical evidence summary

Contents

ATP – Adenosine triphosphate | CI – Confidence Interval | DBD - Donation after Brain Death | DCD – Donation after Circulatory Death | DGF - Delayed Graft Function | ECD – Extended Criteria Donor | eGFR: Estimated glomerular filtration rate | HMP – Hypothermic Machine Perfusion (non-oxygenated) | HOPE – Hypothermic Oxygenated Perfusion | HR – Hazard Ratio | IRI – Ischemia/reperfusion Injury | RCT – Randomized Controlled Trial | RR – Risk Ratio | SCS – Static Cold Storage | Tx - Transplant | ETC – Electron Transport Chain | ROS – Reactive Oxygen Species

Kidney Assist Transport™

Unlock the power of oxygen

XVIVO's Kidney Assist Transport is a portable device that allows hypothermic pulsatile perfusion of donor kidneys with an oxygenated solution for up to 24 hours.

Kidney Assist Transport™ at a glance

- O_2 Oxygenated
- Hypothermic perfusion
- 24h Up to 24 perfusion to support logistics
- Pressure-controlled pulsatile flow
- Remote monitoring ready (selected regions only)

*Not available in all markets. Please contact XVIVO for more information regarding availability in your specific region.

Machine perfusion in kidney transplantation

Over the past twenty years, machine perfusion strategies have gained greater clinical traction by improving organ preservation, reducing the harmful effects of ischemia/reperfusion injury (IRI), and increasing the utilization of deceased donor organs.

Machine perfusion can be performed at different temperatures, with or without supplemental oxygen, and applied directly after procurement (continuous perfusion) or after a period of static cold storage (SCS), so called end-ischemic perfusion. A recent meta-analysis published in the Cochrane Database of Systematic Reviews[1], evaluating the effects of machine perfusion in kidney transplantation, demonstrated that compared to SCS, continuous hypothermic machine perfusion (HMP) reduces the rate of delayed graft function (DGF) and improves graft survival of deceased donor kidneys.
In contrast, this benefit over SCS was not seen with normothermic machine perfusion (NMP), nor when HMP was performed end-ischemically.

Outcome	Absolute effect		Relative effect	
	With SCS	With HMP	95% CI	GRADE**
Delayed Graft Function*	39.1%	30.5%	RR 0.78 (0.69 to 0.88)	●●●●
Graft Survival*	90.7%	95.6%	HR 0.46 (0.29 to 0.75)	●●●●
Patient Survival	94.9%	95.3%	HR 0.92 (0.17 to 5.05)	●●○○
Acute Rejection	23%	17.5%	RR 0.76 (0.49 to 1.16)	●●○○

> “Continuous HMP is superior to SCS in deceased donor kidney transplantation, reducing DGF, improving graft survival and proving cost-effective. This is true for both DBD and DCD kidneys.”
>
> Tingle et al., 2024

*Continuous HMP only, **Certainty of evidence
1. Tingle SJ, et al. *Normothermic and hypothermic machine perfusion preservation versus static cold storage for deceased donor kidney transplantation*. Cochrane Database Syst Rev. 2024;7(7):CD011671.

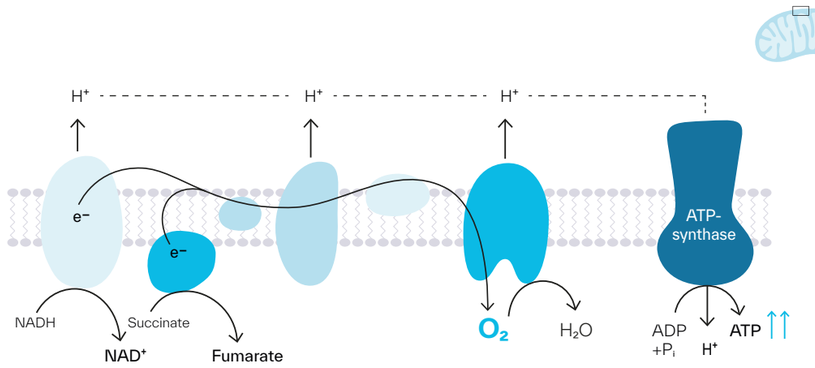
The power of oxygen

Mitochondria are often referred to as the powerhouses of the cell, creating more than 90% of the energy (ATP) needed to sustain life and support a myriad of cellular processes. This ATP production is dependent on the availability of oxygen.

Every cell in every organ of the body needs a constant supply of oxygen to work properly. This is also true for donated organs. While hypothermia slows down cellular metabolism and reduces the need for oxygen, ATP-demanding processes continue, albeit at a lower rate, leading to a delay, but not an absence of damage.

Active oxygenation of the nutrient-rich perfusate supports the residual metabolic activity of hypothermic cells during the entire perfusion procedure. Oxygen delivery helps to preserve mitochondrial function, promote ATP synthesis, and reduce oxidative stress at the time of reperfusion during transplantation.

Preclinical data using Kidney Assist Transport have shown that the high oxygen concentrations provided by the oxygenator during HOPE leads to better restoration of tissue ATP content, lower levels of oxidative stress, improved renal function, and fewer signs of kidney injury compared to non-oxygenated cold preservation strategies[1].



Simplified depiction of the mitochondrial electron transport chain and the generation of ATP in the presence of oxygen.

Under normal conditions (i.e., when oxygen is available) electrons (e^-) are passed from one complex to another, protons (H^+) are pumped out of the matrix, forming a membrane gradient, which eventually drives the synthesis of ATP.

When oxygen is not available (during ischemia) the ETC is halted resulting in depletion of ATP and accumulation of toxic byproducts. The rapid re-oxygenation of the ischemic organ during reperfusion in the recipient causes a surge of reactive oxygen species (ROS), leading to immune cell activation, endothelial damage and cell death.

1. Venema LH, et al. *Effects of Oxygen During Long-term Hypothermic Machine Perfusion in a Porcine Model of Kidney Donation After Circulatory Death*. Transplantation. 2019;103(10):2057-64.

HOPE for improved outcomes

Hypothermic oxygenated perfusion (HOPE) involves perfusing a donor kidney with an oxygenated, acellular, and nutrient-rich machine perfusion solution at temperatures of 12°C or below. During HOPE, an external oxygenator or gas exchange system is used to maintain a steady flow of oxygen to the perfusion solution. It mimics the function of the lungs by actively enriching the solution with oxygen and removing carbon dioxide. The oxygenator also ensures that the oxygen content is replenished throughout the perfusion procedure and does not diminish over time. Perfusion pressure, oxygen levels, and flow rates are monitored to optimize the preservation conditions.

HOPE IN DCD

Oxygenated versus standard cold perfusion preservation in kidney transplantation (COMPARE): a randomised, double-blind, paired, phase 3 trial

Jochmans I, Brat A, Davies L, Hofker HS, van de Leemkolk FEM, Leuvenink HGD, Knight RS, Pirenne J, Ploeg RJ, on behalf of the COMPARE Trial Collaboration and Consortium for Organ Preservation in Europe (COPE).

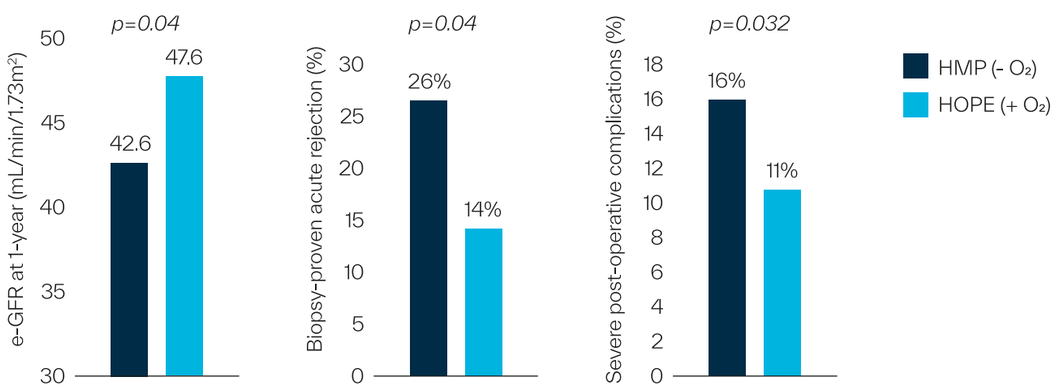
The Lancet / 2020 / doi: 10.1016/S0140-6736(20)32411-9

This international, multicenter, double-blind, randomized controlled trial (RCT) studied the effect of supplemental oxygen during continuous hypothermic machine perfusion (HMP) of kidneys from donors aged 50 years or older, donated after circulatory death (DCD).

In this paired analysis, one kidney from each donor was randomly assigned to HOPE (n=106) while the contralateral kidney was assigned to standard HMP (n=106).

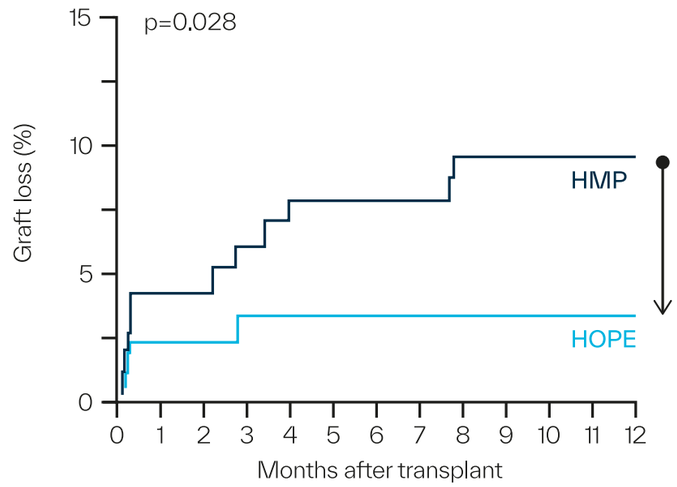
Kidney Assist Transport was used for both HOPE and HMP and clinicians were masked to treatment allocation through the use of empty dummy oxygen bottles in the control group.

The study demonstrates that, compared to non-oxygenated HMP, HOPE significantly improves renal function (eGFR: 47.6 vs. 42.6 ml/min/1.73m2; p=0.035) up to 1 year post-transplant and reduces the risk of biopsy-proven acute rejection by 44% (14% vs. 26%; RR 0.56, 95% CI 0.31-0.98; p=0.040).



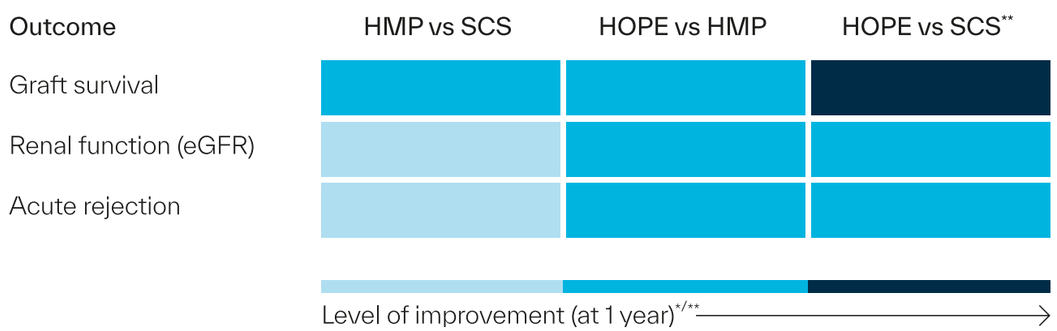
HOPE was also shown to reduce the risk of graft failure by 73% (3% vs. 10%; HR 0.27, 95% CI 0.07-0.95; p=0.028) and recipients of HOPE-treated kidneys experienced fewer serious post-operative complications (Clavien-Dindo grade ≥IIIb) than their contralateral non-oxygenated counterparts (11% vs 16%; p=0.032).

The authors conclude that HOPE provides a clinically relevant benefit compared with standard HMP, not only by reducing severe complications but alsoby reducing diagnostic procedures and hospital readmissions associated with acute rejection, and most importantly, by improving graft survival and reducing the cost of chronic dialysis.



REDUCED RISK OF GRAFT LOSS
73%
compared to standard HMP in DCD KTx

> "/.../ the simple addition of oxygen to continuous HMP further improves graft survival, kidney function and acute rejection rate compared to non- oxygenated HMP*."
>
> Tingle SJ et al., 2024



* In DCD ≥50 years ** Indirect treatment comparison

List of publications

Brat A, et al. *Hypothermic Machine Perfusion as a National Standard Preservation Method for Deceased Donor Kidneys*. Transplantation. 2022;106(5):1043-50.*

Buitrago LF, et al. *Renal Resistance During Hypothermic Machine Perfusion: A Scoping Review of Variability and Determinants, with a Meta-Analysis of Predictive Value for Transplant Outcomes*. medRxiv. 2025;25326058(preprint).

Husen P, et al. *Oxygenated End-Hypothermic Machine Perfusion in Expanded Criteria Donor Kidney Transplant: A Randomized Clinical Trial*. JAMA Surg. 2021;156(6):517-25.

Jochmans I, et al. *Oxygenated versus standard cold perfusion preservation in kidney transplantation (COMPARE): a randomised, double-blind, paired, phase 3 trial*. Lancet. 2020;396(10263):1653-62.

Meister FA, et al. *Decrease of renal resistance during hypothermic oxygenated machine perfusion is associated with early allograft function in extended criteria donation kidney transplantation*. Sci Rep. 2020;10(1):17726.

Meister FA, et al. *Hypothermic oxygenated machine perfusion-Preliminary experience with end-ischemic reconditioning of marginal kidney allografts*. Clin Transplant. 2019;33(10):e13673.

Mulvey JF, et al. *Perfusate Proteomes Provide Biological Insight Into Oxygenated Versus Standard Hypothermic Machine Perfusion in Kidney Transplantation*. Ann Surg. 2023;278(5):676-82.

Tingle SJ, et al. *Normothermic and hypothermic machine perfusion preservation versus static cold storage for deceased donor kidney transplantation*. Cochrane Database Syst Rev. 2024;7(7):CD011671.*/**

van de Leemkolk FEM, et al. *The role of flavin mononucleotide (FMN) as a potentially clinically relevant biomarker to predict the quality of kidney grafts during hypothermic (oxygenated) machine perfusion*. PLoS One. 2023;18(6):e0287713.

*Publication includes other devices in addition to the XVIVO Kidney Assist Transport.
**Systematic Review and Meta-analysis.

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

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