Conseil
Supérieur de la Santé

Préservation des organes *ex situ*

Décembre 2025
N° 9784

Droits d'auteur

Conseil Supérieur de la Santé
Avenue Galilée, 5 bte 2
B-1210 Bruxelles

Tél.: 02/524 97 97
E-mail: info.hgr-css@health.fgov.be

Tous droits d'auteur réservés.
Veuillez citer cette publication de la façon suivante :
Conseil Supérieur de la Santé. Préservation des organes *ex situ*. Bruxelles : CSS; 2025. Avis n° 9784.

La version intégrale de l'avis peut être téléchargée à partir de la page web: www.conseilsuperieurdelasante.be

Avec le support du :
Service Public Fédéral Santé publique, Sécurité de la Chaîne alimentaire et Environnement

Cette publication ne peut être vendue.

Conseil
Supérieur de la Santé

AVIS DU CONSEIL SUPERIEUR DE LA SANTE N° 9784

Préservation des organes *ex situ*

In this scientific advisory report, which offers guidance to public health policy-makers, the Superior Health Council of Belgium provides specific recommendations on ex situ organ preservation for organ transplantation.

Version validée par le Collège de
05/11/2025[1]

RÉSUMÉ

Le présent avis du CSS 9784 intitulé « Préservation ex situ des organes » est une mise à jour de l'avis précédent CSS 8711 « Perfusion sur machine versus conservation à froid », qui date de 2011. Au cours de la dernière décennie, les besoins en matière de transplantation d'organes (cœur, reins, foie et poumons) ont augmenté, tandis que la disponibilité d'organes de bonne qualité en quantité suffisante a diminué en raison de l'évolution du profil des donneurs. L'augmentation de l'âge des donneurs et le passage du don après mort cérébrale (DBD) au don après mort circulatoire (DCD) se traduisent par des organes plus à risque, nécessitant une préservation optimale.

Parallèlement, d'importantes avancées ont été réalisées ces dernières années dans les systèmes disponibles pour la préservation des organes. Bien que les données diffèrent quelque peu selon les types d'organes, le corpus de preuves scientifiques ne cesse de s'étoffer quant à l'utilité et à l'efficacité des techniques de préservation ex situ pour limiter les lésions d'ischémie-reperfusion et optimiser la qualité des organes. Leur utilisation dans la pratique clinique, bien qu'encore limitée en raison des coûts financiers, semble permettre d'augmenter le nombre d'organes utilisables et d'améliorer les résultats pour les patients transplantés. Ces résultats ont été observés pour tous les types d'organes.
De plus, quelques études évaluant le coût et le rapport coût-efficacité ont mis en évidence non seulement une augmentation importante du taux de transplantation, mais aussi un bilan économique favorable, y compris après prise en compte des coûts liés au dispositif de préservation et à son utilisation. Des résultats similaires ont été observés dans la récente convention de l'INAMI relative à la perfusion sur machine hypothermique (HMP), qui prévoit le remboursement de la perfusion sur machine de

[1] Le Conseil se réserve le droit de pouvoir apporter, à tout moment, des corrections typographiques mineures à ce document. Par contre, les corrections de sens sont d'office reprises dans un erratum et donnent lieu à une nouvelle version de l'avis..

tous les reins DCD et DBD prélevés en Belgique chez des donneurs à critères élargis (extended criteria donor, ECD) et conservés en conditions d'HMP, en vue d'être transplantés en Belgique. Ces résultats positifs ont conduit à une utilisation de plus en plus généralisée et, dans de nombreux pays, à un remboursement dans le cadre de l'assurance maladie de base (par exemple aux Pays-Bas).

Compte tenu du besoin croissant en cœurs, reins, foies et poumons de bonne qualité, le CSS recommande de poursuivre la mise en œuvre progressive de la préservation ex situ des organes, reposant sur les piliers suivants :

1. Application systématique de la perfusion sur machine pour tous les organes DCD et ECD :
   - La préservation ex situ des organes doit être appliquée à tous les greffons DCD et ECD dans l'ensemble des centres de transplantation belges.
   - Le type de préservation dynamique utilisé doit être choisi sur la base des données les plus récentes (par exemple, perfusion sur machine normothermique ou hypothermique pour les cœurs issus de DCD) ainsi que de l'expérience du centre avec une technique de préservation considérée.

2. Personnel formé et infrastructure performante :
   - Une infrastructure adéquate, comprenant des dispositifs de perfusion et un large éventail de consommables, est essentielle mais ne suffit pas.
   - Il est important de disposer d'une équipe pluridisciplinaire (comprenant des perfusionnistes cliniques) ayant une expérience et un savoir-faire pratique suffisants, car ces appareils/dispositifs ne se gèrent pas tout seuls.

3. Cadre de remboursement adéquat :
   - Afin de garantir que le coût n'entrave pas la mise en œuvre systématique des technologies de préservation ex situ des organes DCD et ECD, un système national de remboursement devrait être mis en place pour couvrir les coûts de la préservation ex situ de tous les types d'organes (et pas seulement des reins) dans ces indications.
   - Lors de la mise en place d'un tel cadre de remboursement, il convient de prendre en compte non seulement le coût du dispositif lui-même, mais aussi les coûts connexes, tels que l'utilisation du bloc opératoire et la mobilisation de professionnels de santé spécialisés.

4. Suivi des résultats cliniques :
   - Un registre devrait être mis en place afin de suivre de manière systématique les résultats cliniques liés à la perfusion sur machine, tels que la survie des patients et des greffons, les complications post-transplantation, mais aussi l'impact de la préservation ex situ des organes sur le taux de transplantation.
   - Une collecte continue de données contribuera à améliorer les pratiques et à garantir que les bénéfices de la perfusion sur machine soient constamment réalisés dans l'ensemble des centres de transplantation.

En mettant en œuvre ces recommandations, la Belgique pourra maintenir son rôle de premier plan en matière de transplantation d'organes et de résultats post-transplantation, en promouvant un accès équitable aux techniques de préservation de pointe, en augmentant le nombre d'organes disponibles, en réduisant la mortalité sur liste d'attente et en offrant aux patients des transplantations plus sûres, plus fiables et véritablement salvatrices.

TABLE DES MATIERES

I. INTRODUCTION ET QUESTION

The current advice SHC 9784 on "Ex situ organ preservation" is an update of the previous advice SHC 8711 on "Machine perfusion versus Cold storage", that dates from 2011.[1]
Due to changes in the donor profile and the growing need for organs, the need for optimal organ preservation is greater than ever. Meanwhile, there have been important developments in the available systems for organ preservation in recent years, with an ever-growing scientific evidence concerning the usefulness and effectiveness of these techniques. And their clinical use, although still limited due to financial burdens, appears to result in an increased number of usable organs.
Therefore, the permanent Working Group of the SHC on Cells, Tissues and Organs of the SHC considered it appropriate to review the former advice on machine perfusion (SHC 8711[1]*) and to make a comprehensive scientific advice on this topic, with updated recommendations for the Belgian authorities.*

Specifically, the SHC wanted to formulate an answer to the following questions:
- *What is the recent evolution and current status of organ donation and transplantation in Belgium?*
- *Is there a need for ex situ organ preservation systems?*
- *Which systems are currently (or in the near future) available to preserve organs and what is their added value?*
- *What is known about the costs and cost-effectiveness of the current systems in Belgium and/or in other countries?*
- *What can be recommended to the government to increase the number and quality of available donor organs in the future?*

II. METHODOLOGY

Afin de fournir une réponse appropriée à ces questions, un groupe de travail *ad hoc* a été constitué, au sein duquel des expertises des disciplines suivantes étaient représentées : transplantation abdominale et thoracique, néphrologie, chirurgie cardiaque, hépatologie, recherche sur la transplantation, coordination des transplantations, perfusion d'organes. Les experts de ce groupe ont rempli une déclaration générale et *ad hoc* d'intérêts et la Commission de Déontologie a évalué le risque potentiel de conflits d'intérêts.

L'avis est basé sur une revue de la littérature scientifique, publiée à la fois dans des journaux scientifiques et des rapports d'organisations nationales et internationales compétentes en la matière (*peer-reviewed*), ainsi que sur l'opinion des experts.

Une fois que l'avis a été approuvé par le groupe de travail *ad hoc* et examiné par les pairs par le groupe de travail permanent sur les cellules, tissus et organes du CSS, il a finalement été validé par le Collège.

Liste des abréviations utilisées (Anglais)

ABCP	*American Board of Cardiovascular Perfusion*
ACHD	*Adult Congenital Heart Disease*
ALT	*Alanine-aminotransferase*
A-NRP	*Abdominal Normothermic regional perfusion*
AST	*Aspartate aminotransferase*
ATP	*Adenosine triphosphate*
BOS	*Bronchiolitis obliterans syndrome*
CCI	*Comprehensive complication index*
CCP	*Certified Clinical Perfusionists*
CHS	*Controlled hypothermic storage*
COR	*Controlled oxygenated rewarming*
DBD	*Donation after brain death*
DCD	*Donation after circulatory death*
DGF	*Delayed graft function*
D-HOPE	*Dual-hypothermic Oxygenated Machine Perfusion*
DP	*Direct procurement*
DRI	*Donor risk index*
EAD	*Early Allograft Dysfunction*
EBCP	*European Board of Cardiovascular Perfusion*
ECD	*Extended criteria donors*
eGFR	*Estimated Glomerular Filtration Rate*
ESRD	*End stage renal disease*
ET	*Eurotransplant*
EU	*European Union*
EVLP	*Ex vivo lung perfusion*
FMN	*Flavin mononucleotide*
GNFB	*Groupement des Néphrologues Francophones de Belgique*

HMP	*Hypothermic Machine Perfusion*
HMP O_2	*Oxygenated Hypothermic Machine Perfusion*
HOPE	*Hypothermic machine perfusion*
HRD	*Higher risk donor*
IC	*Ischemia-cholangiopathy*
IFLT	*Ischemia-free liver transplantation*
INAMI	*Institut national d'assurance maladie-invalidité*
IRI	*Ischemia-reperfusion injury*
ISHLT	*International Society for Heart & Lung Transplantation*
L-GrAFT7	*Liver graft assessment following transplantation*
LT	*Liver transplantation*
MEAF	*Model for early allograft function*
MP	*Machine perfusion*
NADH	*Nicotinamide adenine dinucleotide hydride*
NAS	*Non-Anastomotic Strictures*
NBVN	*Nederlandstalige Belgische Vereniging voor Nefrologie*
NMP	*Normothermic machine perfusion*
NRP	*Normothermic regional perfusion*
OCS	*Organ Care System*
OLT	*Orthotopic liver transplantation*
PAP	*Pulmonary arterial pressure*
PGD	*Primary graft dysfunction*
PGD-3	*Grade 3 primary graft dysfunction*
PNF	*Primary non-function*
pNMP	*Prolonged Normothermic machine perfusion*
PRS	*Post-reperfusion syndrome*
PVR	*Pulmonary vascular resistance*
QALY	*Quality-adjusted life year*
RCT	*Randomized controlled trial*
RIZIV	*Rijksinstituut voor Ziekte- en Invaliditeitsverzekering*
SCD	*Standard criteria donors*
SCS	*Static cold storage*
SCTS	*SherpaPak Cardiac Transport System*
SHC	*Superior Health Council*
siRNA	*Small interfering ribonucleic acid*
TA-NRP	*Thoraco-abdominal Normothermic regional perfusion*
USA	*United States of America*
USRDS	*United States Renal Data System*
WIT	*Warm ischemic time*
WL	*Waiting list*
XHAT	*XVIVO Heart Assist Transporter*
XPS	*XVIVO Perfusion System*

III. ELABORATION ET ARGUMENTATION

For all types of organs, there are increasing numbers of patients with end-stage organ failure. On the other hand, the supply of organs is decreasing and the donor profile is changing to a higher risk profile, resulting in a larger amount of organs which do not meet the standard criteria.
The need for organ preservation strategies that can optimize the number and quality of organs for transplantation, which is common for all organs, will be illustrated in the first two introductory chapters.

1. Current status of organ transplantation: numbers of donations and procured and transplanted organs

The following figures regarding donation and transplantation, both in Belgium and more broadly in the Eurotransplant zone, presented in a first introductory chapter, illustrate the nature and extent of the problem.

1.1. Allocation of donor organs

The allocation of donor organs in Belgium is organized within the Eurotransplant (ET) Region (Figure 1),[2] composed of eight countries (Belgium, The Netherlands, Luxemburg, Germany, Austria, Croatia, Hungary, Slovenia).

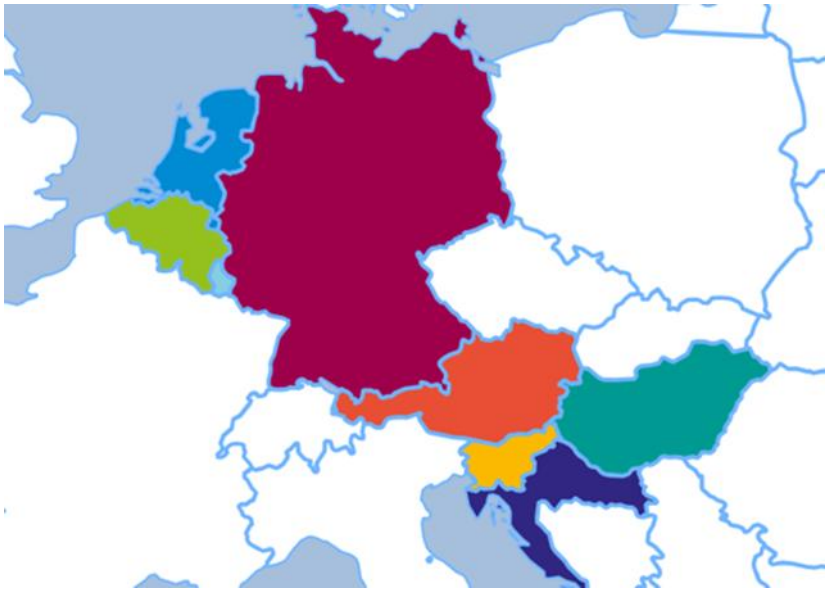
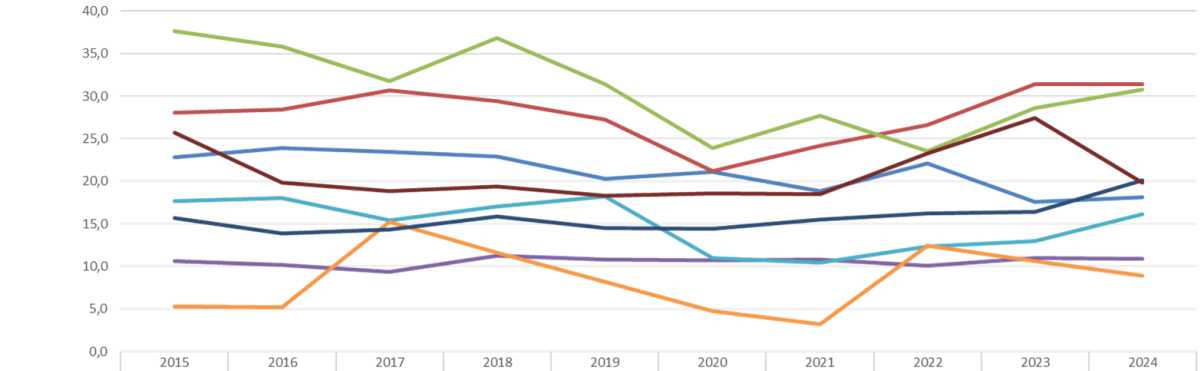


Figure 1 : Eurotransplant zone

1.2. Opting out legislation



	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Austria	22,8	23,9	23,5	22,9	20,3	21,1	18,8	22,1	17,6	18,1
Belgium	28,0	28,4	30,7	29,4	27,2	21,2	24,2	26,6	31,4	31,4
Croatia	37,6	35,8	31,8	36,8	31,4	23,9	27,7	23,5	28,6	30,8
Germany	10,6	10,1	9,3	11,3	10,8	10,7	10,8	10,1	11,0	10,9
Hungary	17,7	18,0	15,4	17,1	18,2	11,0	10,4	12,3	13,0	16,1
Luxembourg	5,3	5,2	15,2	11,6	8,1	4,8	3,2	12,4	10,6	8,9
Netherlands	15,7	13,8	14,3	15,9	14,5	14,4	15,5	16,2	16,4	20,1
Slovenia	25,7	19,9	18,9	19,4	18,3	18,6	18,5	23,3	27,4	19,8

Figure 2 : Deceased donor per million inhabitants, divided by country

Since June 13th 1986, Belgium has a legislation concerning the procurement and transplantation of organs. This law is based on implicit or presumed consent, also called 'opting out'. Belgium has the highest number of organ donors per million inhabitants (31.4 in 2023) within the ET zone. Nationwide, the total number of deceased organ donors in 2024 was 372.

Table 1 : Deceased donors used in ET zone

Deceased donors used in All ET, by year, by donor type, by organ										
DBD	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
kidney	1606	1553	1437	1624	1470	1288	1324	1333	1375	1361
heart	605	587	548	616	665	578	545	619	597	628
lung	548	584	566	627	609	570	542	501	504	541
liver	1475	1449	1387	1493	1377	1250	1277	1272	1315	1410
pancreas	605	587	548	616	665	578	545	619	597	628
any organ	1814	1803	1696	1890	1772	1568	1598	1624	1681	1732
DCD	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
kidney	222	183	210	233	222	227	249	253	311	357
heart				3	4	8	27	25	49	70
lung	61	64	62	68	89	79	82	97	133	137
liver	131	118	132	150	159	170	186	211	266	300
pancreas				3	4	8	27	25	49	70
any organ	250	218	246	269	270	269	299	314	398	449
statistics.eurotransplant.org : 1098P_All ET : 10.02.2025										

1.3. Donor profile

In general, there are two categories of deceased organ donors:
1/ In donation after brain death (DBD), the donor has irreversible and fatal cerebral damage, assessed by clinical and/or radiological evaluation.
2/ In donation after circulatory death (DCD), the donor does not meet the criteria for brain death, but further supportive therapy is considered futile for a variety of reasons. Stopping supportive treatment is expected to lead to circulatory failure and the declaration of death based on cardiocirculatory criteria in contrast with DBD donors where death is based on the Harvard criteria of brain death.[3]
During the last decade, a shift of the donor profile has been observed, with a decline/stabilisation in DBD donors which was replaced by an increase in DCD donors. This trend is observed in the whole ET zone (Table 1), but even more in Belgium (Table 2 and Figure 3).

Table 2 : Deceased donors used in Belgium

Deceased donors used in Belgium, by year, by donor type, by organ										
DBD	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
kidney	180	181	188	189	160	111	126	136	123	139
heart	81	72	82	79	84	52	55	63	57	67
lung	85	97	98	90	82	59	52	59	55	66
liver	181	197	214	207	183	126	135	153	155	175
pancreas	81	72	82	79	84	52	55	63	57	67
any organ	210	226	245	237	206	142	159	174	169	189
DCD	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
kidney	80	65	72	70	68	71	83	91	131	112
heart				3	3	6	6	7	12	23
lung	34	35	31	33	32	28	32	32	67	52
liver	82	73	71	78	84	89	103	116	167	157
pancreas				3	3	6	6	7	12	23
any organ	105	95	103	98	106	103	121	135	200	182
statistics.eurotransplant.org : 1098P_Belgium : 10.02.2025										

The percentage of DCD donors is higher in Belgium than in the ET zone and has increased from 34 % of the donor pool in 2019 to 54 % in 2023, making it the primary source of organ donation nationwide at that moment. While these figures vary among individual centers—with some local donor pools exhibiting even higher rates of DCD donation— this trend is reflected in almost all organs. In 2024 the percentage of DCD donors was nearly 50 %. This compensation of the loss of DBD donors by DCD donors was only possible by the introduction of ex situ preservation/ perfusion of organs in clinical practice.

In summary, the DCD vs. DBD ratio has evolved to approximately 50-50 % over the past decade.

1.4. Donor age and extended criteria donation

One of the current major challenges in organ transplantation is the increasing number of organs with a higher risk profile due to the increasing use of organs from older donors and donation after cardiocirculatory death (DCD), as seen in Figure 3.[4]
This increase of organs of donors with a higher age and a higher risk profile (HRD), results in an increased decline of organs.

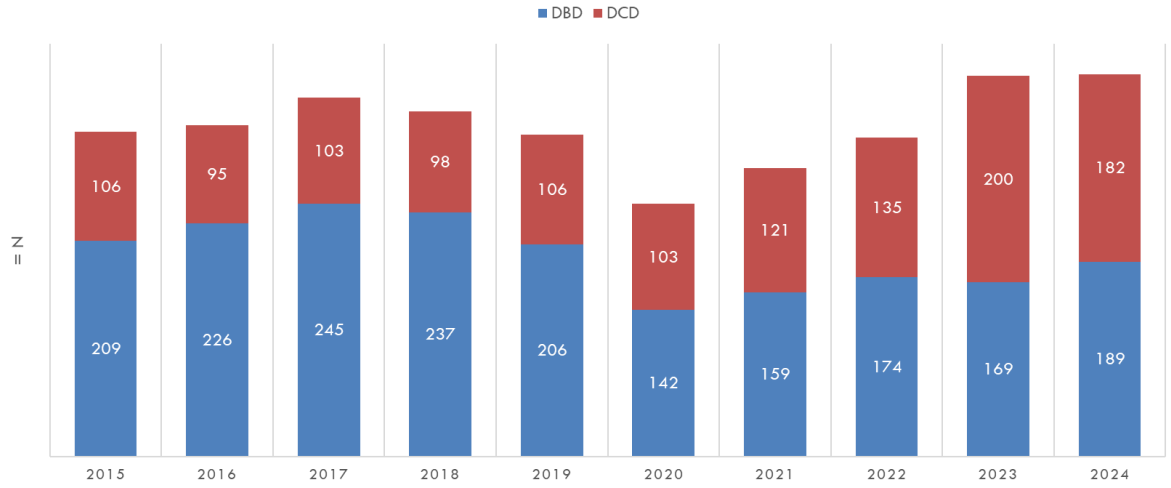


Figure 3 : DCD vs. DBD donors in Belgium

Over the years, the donor age at the moment of donation has increased, as shown in Figure 4. In 2024, 47 % of the donors is more than 60 years old.

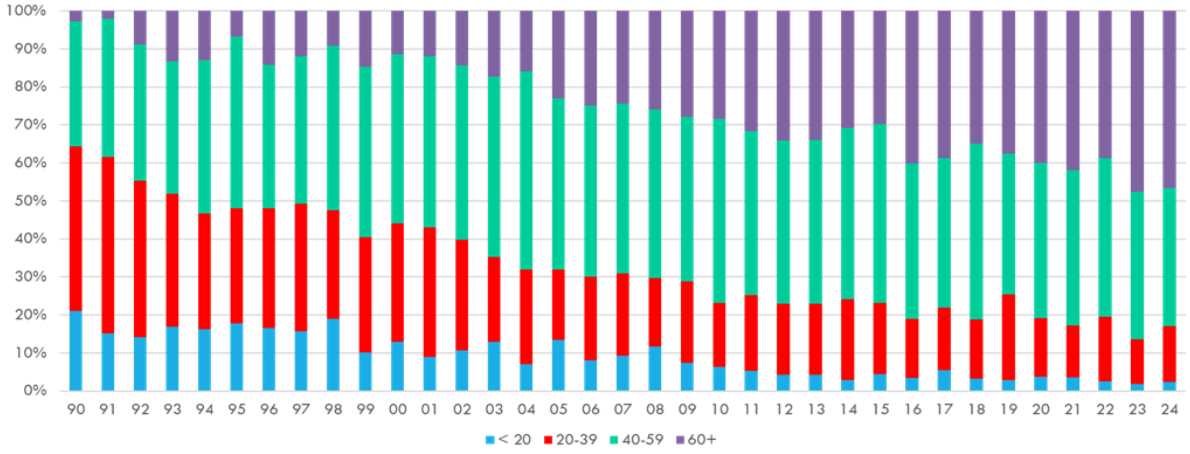


Figure 4 : Donor age at moment of donation

The constantly growing gap between the number of available organs and the increasing population of patients on the waiting list justifies the use of organs of older donors with a higher risk profile, under certain conditions.[5-6]
As compared to the standard criteria donor (defined as a brain death donor <50 years old), organs of 'higher-risk' donors (HRD) are nowadays commonly accepted for transplantation. These are organs originating from either DCD, or DBD with expanded criteria donation (ECD). ECD criteria are not uniformly defined, these criteria may vary

for different types of organs. But for kidneys, in the Belgian reimbursement system, ECD donors are defined as
1) DBD donors between 50 and 60 years old with at least 2 of the 3 following criteria: serum creatinine > 1.5 mg/dl, a history of arterial hypertension or death due to cerebrovascular accident, and
2) DBD donors older than 60 years.

Due to the increasing donor age and the related increase in HRD and ECD, the use of state-of-the-art organ perfusion and transport systems is necessary to overcome loss of organs and to prevent a decrease of transplant activity, and an even longer waiting time for potential recipients.

1.5. Evolution of transplanted organs in the past 10 years

In each of the following figures Figure 5 : Heart transplantation in Belgium*(Figures 5-8), the number of transplanted organs (Tx) is shown per year (from 2015 up till 2024). Moreover, the number of patients on the active waiting list (WL) is presented, as well as the number of patients that died while being on the WL.*

1.5.1. Heart transplantation

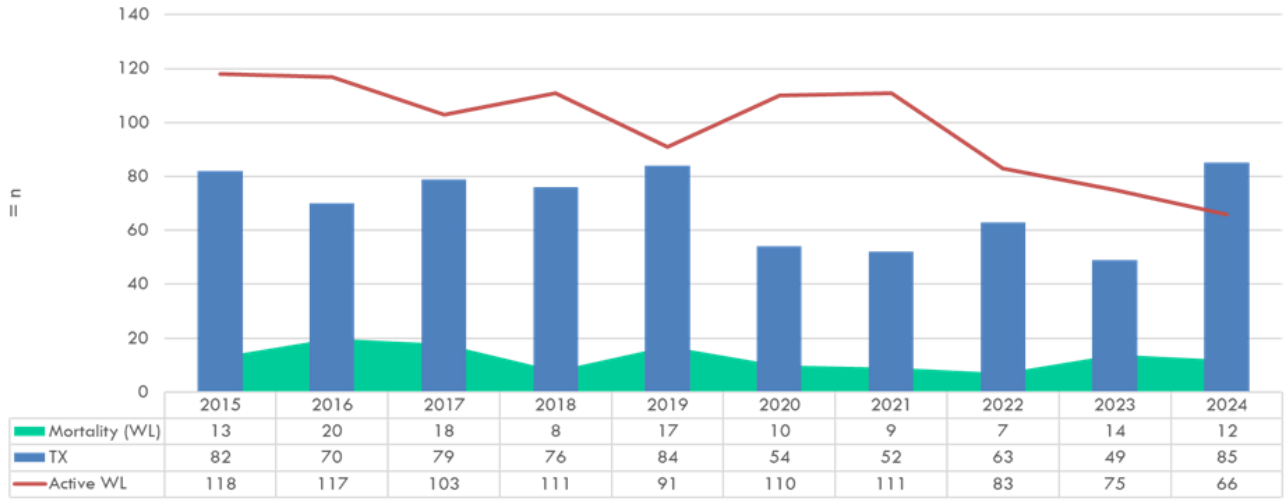
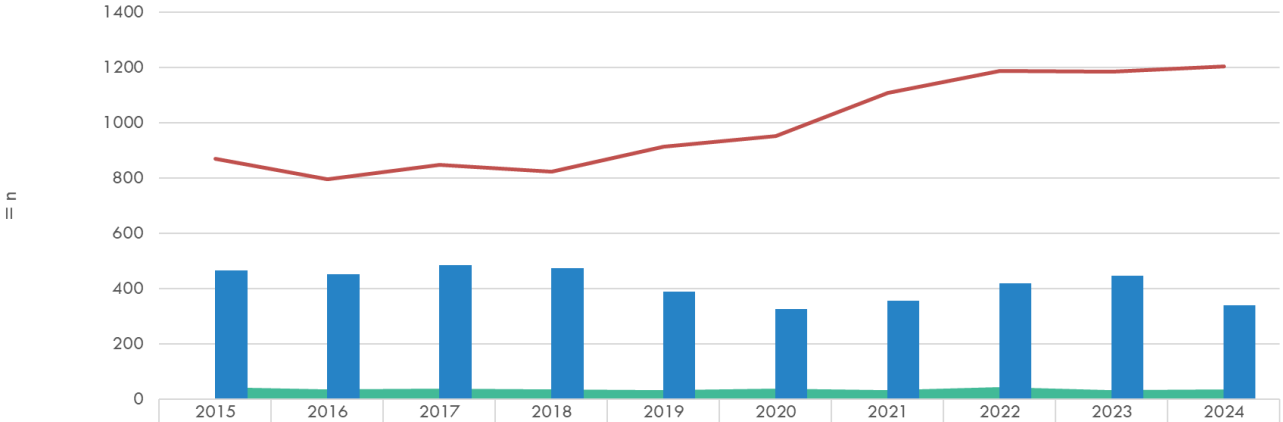


Figure 5 : Heart transplantation in Belgium

The increase in the number of transplanted hearts, despite the increase of the DCD/DBD rate was possible by the introduction of machine perfusion and the optimalisation of organ preservation.

1.5.2. Kidney transplantation

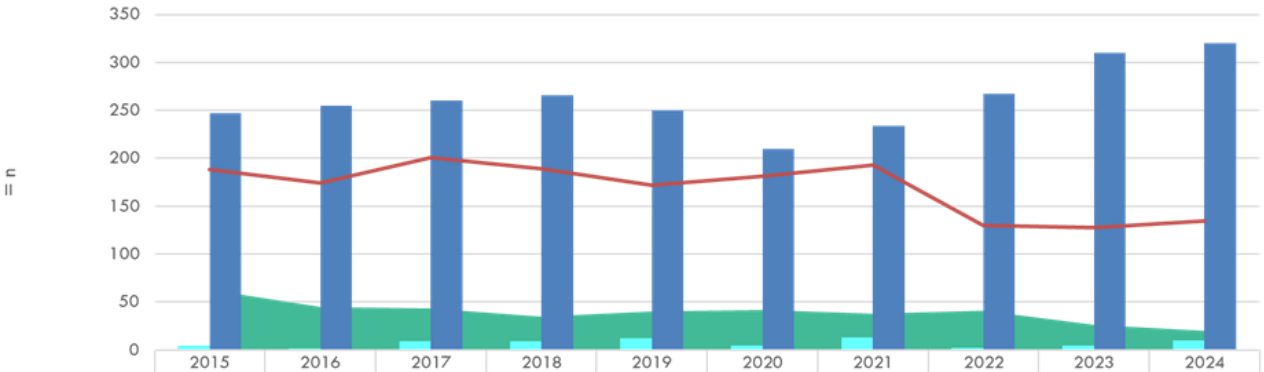


	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Mortality (WL)	44	35	38	36	32	38	34	45	34	37
Kidney en bloc	4	0	0	0	0	0	1	4	3	2
Kidney Tx	467	453	485	474	389	326	357	419	446	339
Active WL	871	797	849	824	914	952	1108	1189	1186	1203

Figure 6 : Kidney transplantation in Belgium

These figures concerning kidney transplantations in 2024 do not mention the 82 living donor transplants that were realized that year. They only reflect the transplantations performed with kidneys from deceased donors.
Kidneys from very young pediatric donors are often procured en bloc. These dual kidney transplants offer comparable to superior graft survival and outcomes as compared to single kidney transplants from donors of the same weight.[7]

1.5.3. Liver transplantation

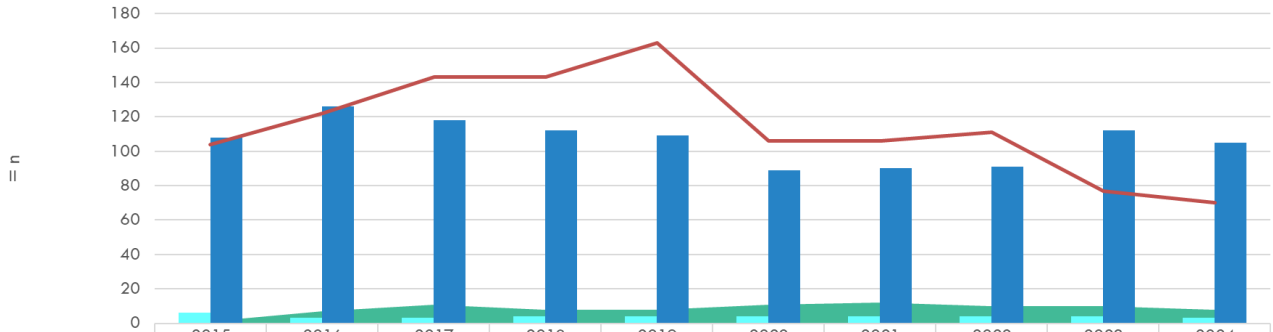


	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Mortality (WL)	63	45	43	35	40	42	38	41	26	20
Split Liver Tx	4	1	9	9	12	4	13	2	4	10
Full Liver Tx	247	255	260	266	250	210	234	267	310	320
Active WL	188	174	201	189	172	181	193	130	128	135

Figure 7 : Liver transplantation in Belgium

Also for the liver transplantation, the increase in the number of transplanted organs, was only possible by the introduction of machine perfusion to optimize the quality of the organs.

1.5.4. Lung transplantation



	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Mortality (WL)	1	7	11	8	8	11	12	10	10	8
Single Lung	6	3	3	4	4	4	4	4	4	3
Double Lung	108	126	118	112	109	89	90	91	112	105
Active WL	104	122	143	143	163	106	106	111	77	70

Figure 8 : Lung transplantation in Belgium

Lung transplantation is a standard life-saving treatment for patients suffering from end-stage respiratory failure unresponsive to other medical or surgical interventions. In 2024 in Belgium, 108 lung transplants were performed (3 single lung transplantations, 105 double lung transplantations), however 70 patients remained on the active waitlist, and 8 patients died while waiting for a lung transplant.

1.6. Waiting list

The total number of patients on the waiting list for an organ has increased slightly over the last decade and remains high, as seen in Table 3.

Table 3 : Active waiting list per organ

Active waiting list (at year-end) in Belgium, by year, by organ										
Active waiting list	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**
kidney	871	797	849	824	914	952	1108	1189	1186	1203
heart	118	117	103	111	91	110	111	83	75	66
lung	104	122	143	143	163	106	106	111	77	70
liver	188	174	201	189	172	181	193	130	128	135
pancreas	68	65	61	57	51	48	45	34	31	37
Total patients	**1288**	**1217**	**1292**	**1269**	**1341**	**1350**	**1514**	**1504**	**1453**	**1470**

2. Need for optimization of number and quality of donor organs

Based on the figures on donation, it is clear that the number of donors and especially DBD has decreased over the years, resulting in a reduced supply of organs (both quantitative and qualitative), which is insufficient to meet the current need.
Therefore, the use of organs from older donors with higher risk and more associated donor comorbidity (e.g., arterial hypertension, diabetes, death due to cerebrovascular accident, donor peak serum creatinine above 1.5 mg/dl, ..) is justified.

However, organ outcome from this type of donors is inferior when preserved by static cold storage (SCS), as compared to standard criteria donors (defined as brain death donors younger than 50 years old).
Since the 1960s, SCS was and still is in many countries, the 'gold standard' to preserve organs because of its simplicity (i.e., during procurement and transport of the organ), low cost and excellent graft outcome in case of young 'high-quality' standard criteria donors (SCD) after brain death (DBD).
The main principle of cold preservation is to suppress metabolic processes to reduce cellular oxygen demand and adenosine triphosphate (ATP) depletion.[8] Under hypothermic conditions (4 °C), oxygen consumption is reduced by 90-95 % compared to that at normal body temperature.[9-10]
The main disadvantage of the SCS preservation technique is that hypothermia worsens ischemic injuries through:

1) *reduction of ATP synthesis and metabolic activity*
2) *reduced Na^+-K-ATPase activity, which induces osmotic perturbation*
3) *mitochondrial perturbations*
4) *decreased cell survival*
5) *endothelial activation*

With the increasing acceptance of 'higher-risk' organs, another major disadvantage of SCS is the lack of viability assessment during and after preservation to evaluate "transplantability", and limited organ resuscitation capacities.

Due to technological evolution over the past twenty years, machine perfusion strategies have gained greater clinical interest to improve organ preservation, viability assessment, organ utilization, and to decrease the harmful effects of ischemia related injuries. It also opens future perspectives in the direction of regenerative medicine and therapeutic procedures during the preservation period.
A variety of different perfusion techniques have been described but the most widely used are normothermic and hypothermic machine perfusion.

Ex-situ normothermic machine perfusion (NMP) is an emerging technique that uses cardiopulmonary bypass technology with extra-corporal membrane oxygenation to perfuse organs with a warmed and oxygenated red-cell based plasma-free solution or full blood (Figure 9a-b).[11] This maintains an organ in a 'near-physiological' state, restoring function ex-situ, and therefore, allowing functional testing. NMP also enables a degree of metabolic resuscitation by replenishing ATP levels that have been depleted because of a combination of warm and cold ischemia.[12] In addition, there is the opportunity for delivery of novel therapeutics to enhance organ preservation and reconditioning, thus decreasing the harmful effects of ischemic reperfusion injury (IRI) after the anoxic hypothermic conditions of SCS or traditional hypothermic machine perfusion.[13-14] Because of complexity, demanding logistics, high costs, and high risk of organ loss in case of pump failure, this preservation technique is not yet widely implemented and applied in only a few transplant centres worldwide.

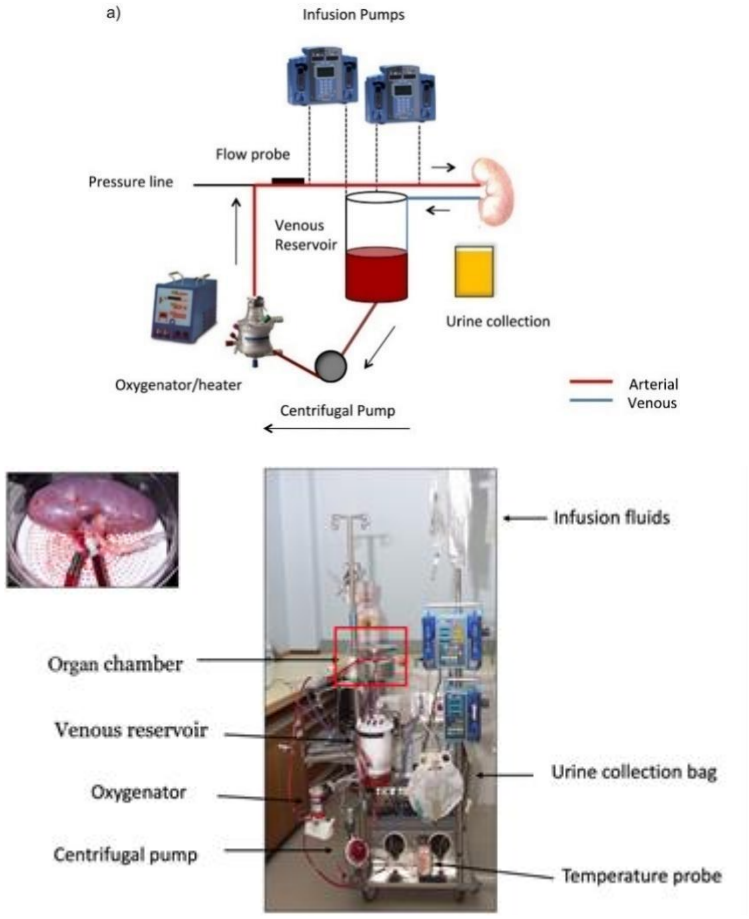


Figure 9 : Schematic overview of the ex-vivo normothermic perfusion system (a, top) and a clinical image of the 'homemade' Cambridge model (b, bottom)(courtesy by Hosgood SA). The renal artery and vein and ureter were cannulated, and the kidney was perfused with 1 unit of compatible packed red blood cells mixed with a priming solution. The kidney was perfused at a mean arterial pressure of 60 mmHg and temperature of 35°C for 60 min.

In contrast, HMP is less complex, cheaper, and the risk of organ loss due to device failure is minimal. The organ is connected by a cannula to a perfusion pump and the continuous perfusion of the graft with a cold acellular or cellular (with packed cells) preservation solution (4-10 °C) results in a continuous flush of the microcirculation and prevents accumulation of toxic metabolites. The exact working mechanism of HMP is probably multifactorial and mainly determined by a flow-related mechanical vasodilatation and a molecular vasoprotection.

Normothermic regional perfusion (NRP) involves in situ reperfusion of the organs in donation after circulatory death. This can involve NRP in thoraco-abdominal organs (TA-NRP) or only abdominal organs (A-NRP). After declaration of death, the donor is canulated and normothermic oxygenated circulation is restored to the potentially transplantable organs in a delineated region of the body using an extracorporeal circuit with pump (centrifugal/roller, oxygenator, heater-cooler unit with or without reservoir). Once the organ has recovered sufficiently, evaluation of the organ is possible in situ. If accepted for transplantation, the organ is procured and stored using either machine perfusion or static cold storage. Although this technique, first performed by Messer, et

al. [15], has gained popularity over the years, the in situ NRP technique will not be dealt with in the current scientific advice.
All possible organ preservation techniques are mentioned in Figure 10. This Advice (SHC 9784) is meant to review the former advice (SHC 8711) and will focus on ex-situ machine perfusion of organs intended for transplantation. The ex-situ preservation techniques included in this report are in dark colour in Figure 10.

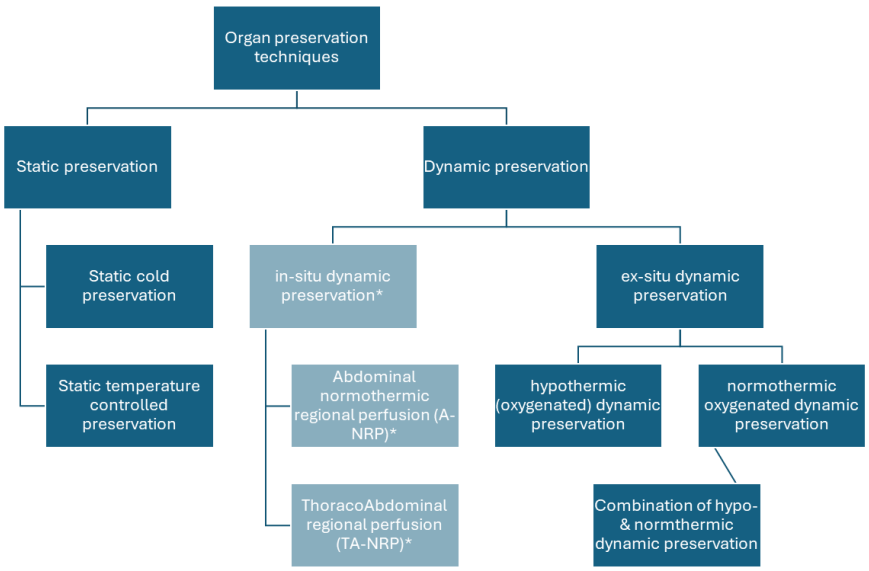


*Figure 10 : General overview of organ preservation techniques. *not included in the scope of this document*

The following chapters discuss ex situ preservation/perfusion for each type of organ more in detail. In each chapter the following aspects will be discussed:
1/ specific needs related to the organ involved
2/ existing systems for ex vivo organ perfusion
3/ effectiveness and added value compared to static cold storage of the use of the different systems
4/ cost-effectiveness analysis of the use (if available)
5/ current reimbursement system if applicable
6/ future perspectives

3. *Ex situ machine preservation/perfusion in heart transplantation*

3.1. *Specific needs in Heart Transplantation*

In 2023, the lowest amount of heart transplantations was observed in Belgium, even less than during the COVID pandemic.
The number of patients on the waiting list is decreasing slightly, but remains higher than the number of transplantations performed. This leads to longer waiting times and thus an increased waiting list mortality. Bearing these facts in mind, there might be a reluctancy to put patients on the waiting list for heart transplantation. For a recipient with blood type O e.g., the average waiting time is now more than two years. In 2023, fourteen patients died on the waiting list.
As it is the case for other organs there are two types of donors from which hearts are harvested.

In DBD donors, the heart is procured and routinely stored using static cold storage (SCS). It is known that cold ischemic times longer than 3-4 hours are an important risk factor for early morbidity and mortality after heart transplantation.[16]
In DCD donors, the heart has undergone obligatory warm ischemia prior to cold flush. It is generally advised to foresee a period of cardiac reperfusion after the declaration of death and prior to transplantation.[17-18]
For both DBD and DCD donors, different possibilities exist to preserve the heart.

3.2. *Existing systems for heart preservation*

3.2.1. *Preservation without perfusion of the heart*

Static cold storage on ice in a coolbox continues to be the most widespread used preservation technique.
There are two commercial cooling systems available where the cooling process is more controlled and where the frost damage is prevented by avoiding to cool deeper than 4 degrees.
*Since 2018, the use of the temperature controlled static preservation or **SherpaPak Cardiac Transport System®** (SCTS) (Paragonix, Waltham, MA, USA) has been reported as an alternative to SCS on ice in DBD donors.[19] It is a static storage device designed to provide superior temperature-control while avoiding freezing of the ex-situ heart. This is accomplished by attaching the heart to a container filled with preservation fluid, which is specifically designed to prevent physical trauma. A phase change material is used to maintain the temperature between 4 °C and 8 °C without the need for ice.*
***Vitalpack®** is a Class IIa medical device (E3 Cortex – www.e3cortex.fr) that is able to preserve and securely transport organs between 2 and 8 degrees C.*

3.2.2. *Preservation with continuous perfusion of the heart*

3.2.2.1. Normothermic ex vivo machine perfusion Organ Care Systems

The Organ Care System® (OCS) (TransMedics, Inc., Andover, MA, USA) is currently the only commercially available normothermic ex-situ heart perfusion platform. After infusion of cardioplegia and extraction of the donor heart, a cannula is inserted into the ascending aorta. [20]

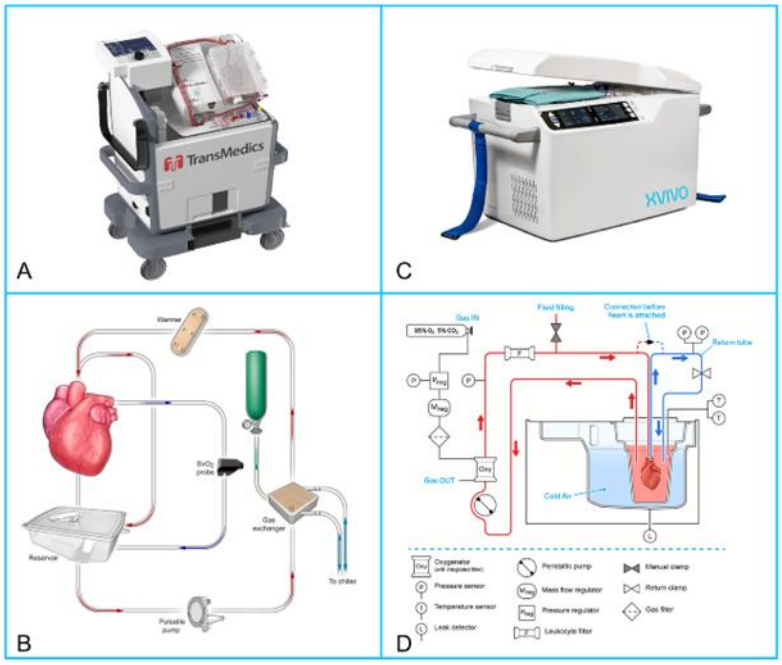


Figure 11 : Machine perfusion devices A: The Transmedics Organ Care System (OCS). B: Schematic overview of the perfusion in the OCS device. C: The XVIVO Heart Box (XHB). D: Schematic overview of the perfusion in the XHB.

Once this has been attached to the device, continuous antegrade perfusion of the coronary arteries is initiated with a donor blood enriched, normothermic, oxygenated perfusate (Figure 11). Sinus rhythm resumes either spontaneously, or with the aid of a direct current shock. Blood from the coronary sinus drains into the reservoir, is oxygenated and then returned once more to the aortic root of the isolated beating donor heart. The arterial and venous lactate profiles, perfusion pressure, visual contractility, and coronary flows are regularly monitored throughout the perfusion, contributing to the decision whether the heart is suitable for transplantation at the end of the preservation.

3.2.2.2. Hypothermic ex vivo machine perfusion XHAT® (XVIVO Heart Assist Transporter)

*The **XVIVO Heart Assist Transporter®** (XHAT (Gothenburg, Sweden)) enables pressure-controlled oxygenated ex situ perfusion of the arrested donor heart at 8 °C. An aortic cannula is inserted in the ascending aorta after cardiectomy, and antegrade perfusion of the coronary arteries is commenced once the heart has been attached (Figure 8). The perfusate consists of a hyperoncotic cardioplegic nutritive solution, containing hormones and erythrocytes. This technique is also referred to as hypothermic oxygenated perfusion (HOPE).[21]*

3.3. *Effectiveness and added value compared to static cold storage*

3.3.1. *Optimized hypothermic preservation SherpaPak Cardiac Transport System® (SCTS)*

Reports indicate that heart transplantation using SCTS may reduce primary graft dysfunction (PGD) and extend the tolerable ischemic time. A retrospective, non-

predetermined chart review with propensity matching by Shudo et al. demonstrated a significantly lower rate of severe PGD (12 % in the ice-cold storage group vs 4 % in the SCTS group, p 0.011).[22] A single-center retrospective analysis in a propensity-matched cohort by Zhu et al. showed no difference in PGD and 1 year mortality, though the total allograft ischemic time was significantly longer (246.2 ± 54.0 versus 227.4 ± 52.9 min; p = 0.01).[23]
There are no scientific reports available on the use of the Vitalpack system.

3.3.2. *Hypothermic ex vivo machine perfusion XVIVO Heart Assist Transporter® (XHAT)*

Results of a randomized controlled multi-center trial comparing this technique to SCS using hearts from brain death donors has shown a clinically meaningful risk reduction of 61 % for PGD in favour of the XHB (28 % for CS vs 11 % for XHB).[24] A recent trial exploring whether HOPE could safely prolong the preservation time, reported a mean preservation time of 414 minutes in 29 heart transplants.[25] The longest preservation time was 8 hours and 47 minutes. Of note, 10 % (n=3) of the long preservation time recipients were adult congenital heart disease (ACHD) patients. Recently the one-year outcome was reported showing a statistical significant better outcome in the HOPE group.[26]

3.3.3. *Normothermic ex situ machine perfusion Organ Care System® (OCS)*

Many reports have already highlighted the benefits of the OCS® machine,[15, 18, 27] including improved outcomes after transplantation in congenital heart disease patients.[28-29] In a meta-analysis by Langmuur and colleagues, OCS® outcomes, for both DBD and DCD hearts, appeared similar as for static cold storage.[25]

3.4. Cost/ cost-effectiveness analysis of the use of preservation/perfusion systems

No cost-effectiveness studies are available for any of the discussed preservation systems.
However, an Australian case report describes a patient receiving a heart preserved with the Organ Care System® (OCS, a type of machine perfusion) who had a significantly lower hospital cost (AU$56,658) compared to a patient with static cold storage (AU$234,160), largely due to a shorter hospital stay.[30]
In Belgium, 2024 was a record year when it comes to the number of hearts used for transplantation (n = 90). 23 of these hearts came from DCD donors. In the setting of direct procurement, machine perfusion is the only way possible to preserve these hearts. The use of machine perfusion made it possible to increase the number of hearts, available for transplantation.

3.5. *Current reimbursement system if applicable*

At this moment there is no reimbursement for ex situ organ preservation/ perfusion of hearts for transplantation in Belgium. When machine perfusion is used, the extra costs are borne by the hospital.

3.6. *Future perspectives*

Over the past decade, the field of organ preservation has undergone significant advancements, a trend that is expected to continue in the years ahead. It is likely that within the next ten years, the use of ice for heart preservation will phase out significantly. Additionally, the use of DCD hearts is anticipated to increase in order to stabilize and even increase the number of heart transplantation. As ex situ preservation/ perfusion techniques are essential for DCD heart preservation, these techniques will become standard of care in heart transplantation.

4. Ex situ machine preservation/perfusion in kidney transplantation

4.1. *Specific needs in Kidney Transplantation*

The increasing waiting list for kidney transplantation results in the death of patients awaiting transplantation (see also Figure 6). In addition, each additional year that a patient is on dialysis his/her life expectancy decreases as compared to transplanted patients.[31-32]

The increasing number of older donors and DCD donors has a detrimental impact on the outcomes after kidney transplantation. In 2024 the number of Belgian donors older than 60 has reached nearly 50 % (Figure 4) and more than half of all donors were DCD (see also Figure 3).
Kidneys of ECD donors are more susceptible to IRI, which is a well-known risk factor for primary nonfunction (PNF), delayed graft function (DGF) and graft failure.[33-36] DGF is defined as the need for dialysis during the first week after transplantation and results in a prolonged hospitalization and associated risk for complications (e.g., infection, rejection, …). A systematic review and meta-analysis of Rijkse et al published in 2021 demonstrated that DCD kidneys have 13 % increased risk of 1-year graft failure after transplant.[37] The DCD kidney function 1 year after transplantation is similar as compared to DBD.[37] For that reason, DCD kidneys are a valuable option to increase the donor pool.
A recent analysis from the Netherlands found that only 50 % of recipients of older DBD donors were alive with a functioning graft at 5 years after transplantation and this was the case in only 40 % of recipients of older DCD donor kidneys.[38] In addition, those surviving with a functioning graft had severe renal insufficiency (eGFR <30 ml/min) in about half of the patients.[38] Survival of ≥65 years old recipients of older DBD or DCD donor kidneys was not improved as compared to patients of the same age remaining on dialysis therapy. An analysis of the Belgian French-speaking (GNFB) and Dutch-Speaking (NBVN) end stage renal disease (ESRD) registries by Hellemans R et al. provided similar results.[39] Mortality during follow up of ≥65 years old recipients transplanted with suboptimal kidneys was 20.5 % which did not differ significantly from the 24.6 % mortality of patients who had remained on the waiting list.[39] These unacceptable results are the reason that many transplant professionals in Belgium are reluctant to accept older donor kidneys, in particular from DCD donors, for transplantation.
This is not only the case in Belgium as a recent retrospective analysis of the United States Renal Data System (USRDS) registry showed that approximately 35 % of DCD donor kidneys older than 50 years were discarded in the US.[40]

In Belgium many donors older than 65 years are discarded or kidneys from these donors are exported to other Eurotransplant countries such as Germany. Belgium has a net negative export balance of about 30 kidneys per year, which are exclusively older DBD and DCD donor organs. The number of kidneys exported without compensation has reached a cumulative total of 134 in June 2024 (Belgian Transplantation Society and Eurotransplant data). This causes a stagnating number of transplants and contributes to an increase of patients on the waiting list from 800 to 1200 between 2018 and 2023 and thereby to a significant prolongation of waiting time for transplantation with a deceased donor kidney (see also Figure 8).

Faced with the older donor population and the increasing number of DCD donors deceased donor kidney transplantation with acceptable waiting times is only possible when older DBD and DCD donors can be transplanted with a reasonable chance for adequate long-term patient and graft outcomes. This can only be achieved with major improvements in donor management and organ preservation to reduce early graft injury and dysfunction, which play a key role in the increased risk of failure and dysfunction of donor kidneys. Increasing use of machine perfusion during organ preservation is undoubtedly a key strategy to achieve this objective.
Nowadays, a significant number of kidneys are discarded in the pretransplant period due to the lack of objective criteria to assess organ quality and the perceived limitations of organ resuscitation and repair during preservation.[41-45] However, ex-situ organ perfusion technology has been posed as a platform to improve kidney preservation (and therefore functional graft outcome) and a tool for pretransplant organ viability assessment.

4.2. *Existing systems for ex situ kidney preservation/perfusion*

In kidney transplantation, NMP is not widely used yet, because of complexity, demanding logistics, high costs, and high risk of organ loss in case of device failure. In addition, there is no evidence at this moment that NMP is equal or superior to SCS (or HMP).
Besides 'homemade' models (e.g., Cambridge group), only 2 portable devices are at this moment commercially available and under evaluation in clinical trials: the Kidney Assist® (XVIVO, Gothenburg, Sweden) and the ARK Kidney® (Ebers Medical Technology, SL, Zaragoza, Spain).

In contrast, HMP is currently worldwide the most established perfusion technique for deceased donor kidneys.
Regarding HMP perfusion devices, numerous portable devices are commercially available including the Kidney Assist Transporter® (XVIVO BV, Groningen, The Netherlands), the WAVES machine® (Institut Georges Lopez, Lissieu, France) and the LifePort Kidney Transporter® (Organ Recovery Systems, USA).
Otherwise, some companies developed non-portable ones like the RM3 device® (Waters Medical Systems, Rochester, MN, USA) and the VitaSmart® (Bridge to Life, Northbrook, IL, USA).

To improve metabolic/mitochondrial activity during kidney preservation, some HMP devices incorporated active oxygenation as standard, while others can easily be modified to include an oxygenator.[46]

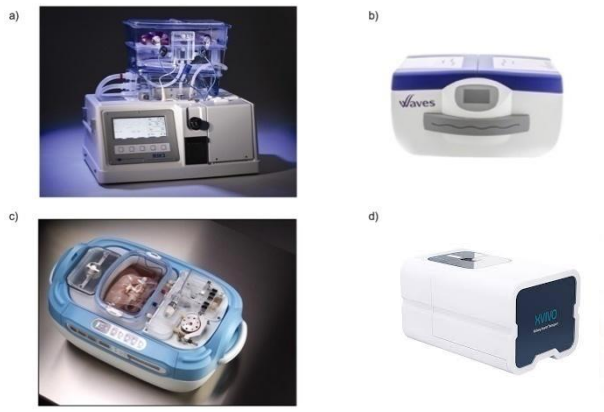


Figure 12 : Most used commercially available hypothermic machine perfusion devices for clinical kidney preservation: a) RM3® Kidney Perfusion System (Waters Medical systems, Birmingham, AL, USA), b) WAVES® transportable Kidney Perfusion (Waters Medical systems, Birmingham, AL, USA), c) LifePort Kidney Transporter® (Organ Recovery Systems, Itasca, IL, USA), d) Kidney Assist® (XVIVO, Groningen, the Netherlands).

4.3. *Effectiveness and added value compared to static cold storage*

4.3.1. *Hypothermic Machine Perfusion*

The meta-analysis of randomized clinical trials published in 2024, included 16 studies comparing HMP with SCS.[47] *The risk of DGF was lower with HMP (risk ratio (RR) 0.77, 95 % CI 0.69 to 0.86), even in kidneys after circulatory death (RR 0.78, 0.68 to 0.90) or brain death (RR 0.73, 0.63 to 0.84). Continuous HMP, from the moment of procurement until the transplantation, decreased the risk of DGF (RR 0.69, 0.60 to 0.79), whereas end-ischemic HMP (in house) after SCS for organ transport did not (RR 0.92, 0.69 to 1.22).*

The 10 years follow-up of the ET MP trial demonstrated that the ten-year graft survival overall (n=818) was significantly better for machine-perfused kidneys (78 % vs. 72.6 %; adjusted hazard ratio for graft failure, 0.73; P=0.027). In a subgroup analysis, 10-year graft survival after machine perfusion was superior for kidneys from expanded criteria donors (adjusted hazard ratio 0.64, P=0.036). Graft survival after HMP was better in both DCD and DBD subgroups but only reached statistical significance in kidneys from DBD donors (adjusted hazard ratio 0.73, P=0.049).[48-49]

These results are in line with the meta-analysis of S. Tingle et al that demonstrated the superiority of HMP-kidneys compared to SCS showing reduced rates of PNF and DGF and an improved one-year graft survival (OR:1.61 95 % CI: 1.02 to 2.53, p=0.04).[50-51] *This was also concordant with another meta-analysis published in 2019 demonstrating superiority of HMP over SCS for both DBD and DCD kidneys.*[51] *Based on these meta-analyses, continuous HMP is superior to SCS preservation. Even when applied for cold ischemia times (<10 hours), HMP demonstrated proven superiority over SCS alone.*[52] *However, HMP should be applied for the entire cold ischemic period, as end-ischemic application after a preceding period of SCS has not*

demonstrated any clinical benefit (used for only 2 hours, but currently not yet explored with longer end-ischemic times).[53-54]

4.3.2. *Oxygenated Hypothermic Machine Perfusion (HMP O2)*

Currently, six clinical trials studied the effect of active oxygenation during HMP, with a variety of O_2 administration strategies.[55] *The strongest evidence for active oxygenation during HMP is derived from a recent multicenter randomized controlled trial (RCT) from DCD Maastricht category III donors older than 50 years applying either oxygenated or non-oxygenated HMP during the entire preservation period. This study failed to demonstrate an improvement in 12-month eGFR, but the graft failure rate was significantly lower in the oxygenated group (3 % versus 10 %, p=0.028).*[56] *These positive findings were not replicated in two matched-case studies and one RCT, where oxygenated HMP was performed as an end-ischemic preservation strategy for extended criteria donors of donation after brain death kidneys after a preceding period of static cold storage.*[46, 55, 57-59]

4.3.3. *Normothermic Machine Perfusion*

NMP today is mostly used as an end-ischemic preservation strategy following a preceding SCS or HMP period. The only RCT at this moment, published by S. Hosgood et al in 2023 was conducted to compare the outcome of DCD kidney transplants after conventional SCS alone or SCS plus 1h-NMP.[60] *A total of 338 kidneys were randomly allocated to SCS (n=168) or NMP (n=170), and 277 kidneys were included in the final intention-to-treat analysis. The rate of DGF, as primary endpoint, was 82 of 135 (60.7 %) in NMP kidneys versus 83 of 142 (58.5 %) in SCS kidneys (adjusted odds ratio (95 % confidence interval) 1.13 (0.69–1.84); P = 0.624). NMP was not associated with any increase in transplant thrombosis, infectious complications or any other adverse events. A 1-h period of NMP after a longer period of standard SCS preservation did not improve the initial function of the transplanted kidney (did not reduce the rate of DGF in DCD kidneys).*

4.3.4. *Assessment tool: HMP(O_2) vs NMP*

Markers of graft injury and function as well as perfusion parameters have been investigated as possible viability markers during ex-situ HMP(O_2) and NMP.[55, 61] *As described above, HMP(O_2) improves the kidney preservation and early and late kidney graft outcome but has no conditioning effect on the kidney graft. It does not improve kidney quality but rather slows down the detrimental effects occurring during the cold time and helps maintain kidney quality. This implies that HMP does not allow a safe extension of the preservation time before transplantation. In addition, injury markers and perfusion parameters during HMP have a low predictive value and do not allow their use as predictive tools in clinical decision making. In contrast, NMP, during which the kidney remains fully metabolically active, seems a more promising platform for true viability assessment. Therefore, both preservation techniques must be considered as complementary techniques.*

4.4. *Cost-effectiveness analysis of the use of preservation/perfusion systems*

4.4.1. *Hypothermic Machine Perfusion*

HMP is proven to result in an overall cost savings as compared to SCS preservation at 1 year after transplantation (European setting).[62-63]

4.4.2. *Normothermic machine perfusion*

Because of the low implementation rate of NMP, no reports exist at this moment on the cost-effectiveness of ex-situ NMP as compared to SCS.

4.5. *Current reimbursement criteria for HMP(O_2) in Belgium and initial results*

The rationale to reimburse HMP was to increase the national transplantation rate of high-risk kidneys (for delayed graft function, primary nonfunction and graft- and patient survival) procured and transplanted in Belgium and to decrease the export of these kidneys. A 3-year test period of this reimbursement was foreseen by an HMP convention of the RIZIV/INAMI (signed by all Belgian transplant centers) from September 2022 until August 2025. The reimbursement criteria included all DCD (independent of donor age) and DBD ECD kidneys procured in Belgium and preserved by HMP conditions with the intent to be transplanted in Belgium. DBD ECD was defined as a DBD donor between 50 and 60 years old with at least 2/3 criteria (history of arterial hypertension, donor serum creatinine ≥1.5 mg/dL, and death due to cerebrovascular accident/stroke) or any DBD donor ≥ 60 years old. The reimbursement condition is per kidney of each donor. This implicates that also for dual kidney transplantation in one recipient both kidneys can be preserved by HMP conditions within the reimbursement criteria of the convention.
Therefore, the Belgian Transplantation Society created a workgroup with representatives of all Belgian transplant centers who set-up and implemented a national machine perfusion service for kidneys which was launched in October 2022.
*A recent interim analysis demonstrated that the reimbursement and nationwide implementation of HMP for kidneys procured in Belgium, resulted in an important increase of the national transplantation rate of DCD kidneys from 90 to 175 ($p<0.0001$) and ECD kidneys (from 45 to 54 per year ($p=0.02965$) without affecting kidney export (Figure 13**Erreur ! Source du renvoi introuvable.**), with excellent functional outcome as compared to RCTs (Table 4).*
Therefore, based on an estimated 240 procedures per year, the saving of dialysis costs for the health insurance was -3.592.265€ per year with a half-cycle correction (i.e. reducing the annual saving by 50 % in order to correct for the timing effect of the transplant procedure during the year) of 1.376.132€ per year (based on costs of HMP (3.500€/procedure) and dialysis (44.932€/year/patient). The profit percentage accounts 163.8 % versus the costs of machine perfusion.
In addition, the cost-effectiveness was 3.592.265€ saved on dialysis costs per year after its implementation (based on costs of HMP (3500€/procedure and dialysis (44.932€/year/patient)) but excluding hospitalization and immunosuppressive treatment costs during the first year)

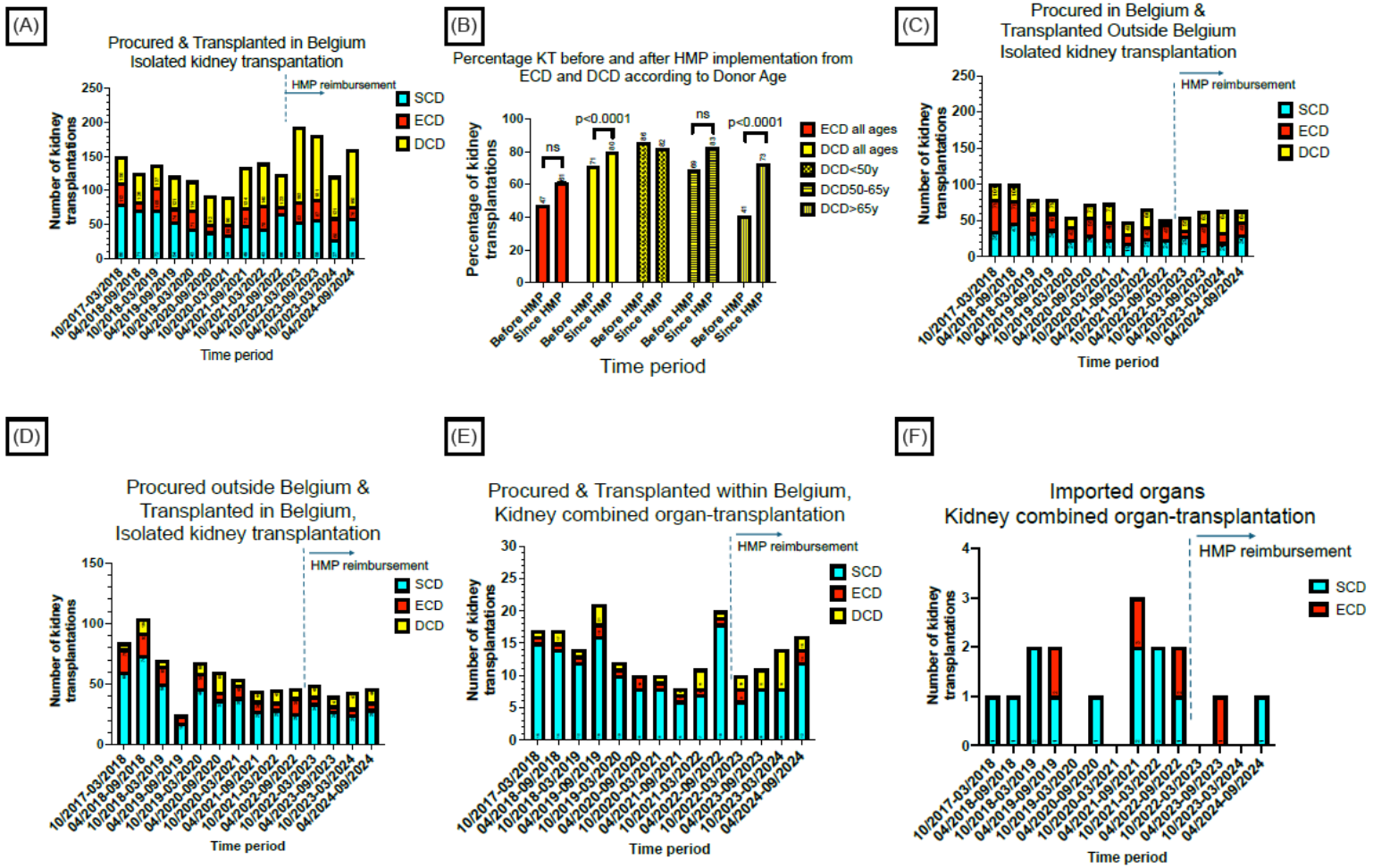


Figure 13 : The national implementation of HMP on kidney utilization rate in Belgium between October 2017 and March 2024 resulted in an increase of total number of kidney transplantations originated from Belgian DCD and ECD donors regardless of donor age (A). The observed increase was more pronounced in the donor age groups between 50 and 65 years old and above 65 years, but not for DCD kidneys with donor age below the age of 50 (B). The numbers of kidney transplantations from exported (C) and imported kidneys in Belgium (D) did not change after the introduction of HMP. A mild increase of kidney combined organ-transplantation from especially ECD and DCD was observed (E). Import in Belgium of a kidney for combined organ transplantation is rare (F).

*Table 4 : The functional 1-year outcome with 1 year of follow-up of 242 HMP kidneys procured and transplanted in Belgium from October 2022 until September 2023 demonstrates and low incidence of delayed graft function and excellent estimated glomerular filtration rate, organ rejection rate and death-censored graft survival at 1 year after transplantation. Outcome of the ET MP and Compare trial are illustrative and to place the Belgian data in context of current published data. * Cyril Moers et al, NEJM 2009 and NEJM 2012, ** Jochmans Ina et al, Lancet 2020*
$HMP n=63 ; HMPO2 n=14; $$HMP n=2; HMPO2 n=114

	1-year functional outcome of HMP-kidneys according to donor type					ET MP trial*		COPE-COMPARE Trial**	
Donor type	DBD ECD DBD ESP DCD	DBD ECD	DCD	DCD<50y	DCD>50yrs	DBD SCD&ECD DCD		DCD>50yrs	
Type of kidney preservation (HMP, HMPO2, SCS)	HMP(O2) (n=242)	HMP (n=49)	HMP (n=193)	HMP(O2)$ (n=77)	HMP(O2) $$ (n=116)	HMP (n=336)	SCS (n=336)	HMPO2 (n=83)	HMP (n=83)
DGF, %	14.35%	9.14%	16.67%	9.46%	19.64%	20.8%	26.5%	36%	36%
Mean eGFR @1y, ml/min/1.73m2	54.25	52.03	54.69	61.10	49.73	NA	NA	48.8	44.4
Organ rejection @1y, %	10.05%	2.33%	12.82%	8.96%	14.00%			14%	28%
Graft survival @1y, %	94.63%	100%	94.82%	97.40%	92.24%	94%	90%	97%	90%
Death-censored graft survival @1y, %	96.28%	100%	94.34%	97.40%	93.97%				
Patient survival @1y, %	98.34%	95.91%	98.96%	100%	98.28%				

Based on this interim analysis, HMP will become standard of care for high-risk kidneys and a second HMP convention (09-2025 until 08-2030) is approved by the INAMI/RIZIV). In collaboration with the RIZIV and the Belgian Transplantation Society, the current reimbursement criteria will be enlarged to 1) DBD standard criteria donors <50 yrs with a peak serum creatinine above 1.5 mg/dl before procurement and for all combined organ with kidney transplantation (e.g., combined liver-kidney, heart-kidney, pancreas-kidney transplantation, ..), and 2) transborder exchange of HMP kidneys from the Netherlands to Belgium in a first step (and vice versa in a second step).

4.6. *Future perspectives*

Although machine perfusion is gradually making the transition to clinical practice, reconditioning therapies have not yet progressed beyond the experimental setting, pointing towards a translational gap. Our expectations are that in the next decade the focus will be on the treatment of ischemia reperfusion injury to improve graft quality by targeting reperfusion damage. Single target (e.g., anti-oxidant/anti-inflammatory therapies, anti-thrombotics) and multi-target (e.g., gases, gene therapy and genetic engineering, cell therapy & extracellular vesicles) therapies will be the focus in future clinical trial using MP, from the spectrum of HMP, subnormothermic and NMP.[64] Dual kidney transplantation in a single recipient is another successful strategy in using older donor kidneys while maintaining good outcomes.[65] The allocation process of older donor kidneys in Belgium will integrate allocation of HLA-matched dual kidneys as an additional measure to increase the use of older donor kidneys.

The future research focus for HMP will be:

1) *the added value of active oxygenation,*
2) *the usefulness of HMP as a treatment platform to reduce the effects of ischemia reperfusion injury (single target (e.g., anti-oxidant/anti-inflammatory therapies, anti-thrombotics), and multi-target (e.g., gases, gene therapy and genetic engineering, cell therapy & extracellular vesicles), and*
3) *the added value of HMP for DBD donors <50years old as compared to SCS alone preservation.*

The future research focus for NMP will be:

1) *the implementation as a continuous preservation strategy alone or for longer end-ischemic use after SCS preservation to extent preservation time,*
2) *the use of NMP as a viability assessment platform pre-transplant, and*
3) *the use of NMP as a treatment platform to reduce the effects of ischemia reperfusion injury (as described above, single vs multi-target therapies).*

5. Ex situ machine preservation/perfusion in liver transplantation

5.1. *Specific needs in Liver Transplantation*

Liver transplantation (LT) is a life-saving procedure offering patients with irreversible liver failure excellent survival rates of 90 % at 1-year and 70–80 % at 5-years post-transplantation. Consistently favorable post-transplant outcomes have expanded the range of indications eligible for LT.[66-67] Despite the high donation rate in Belgium, the demand for liver transplants continues to exceed supply. In 2023, 314 liver transplants were performed, yet 128 patients remained on the active waitlist, and 26 died while waiting for an organ. This contributed to a national waitlist mortality rate of ~30 %, reflecting the ongoing critical organ shortage.

In line with a global trend, most Belgian centers now increasingly use so-called "extended criteria donors" (ECD) and -since the early 2000s- donation after circulatory death (DCD) donors. ECD involve donors previously considered unsuitable for LT, including donors having severe macro-vesicular steatosis, hypernatremia, hypotension and inotropic support, prolonged intensive care stay, prolonged period of cold preservation, or aged 60 or older.

DCD represents another form of ECD donation. While the use of ECD and DCD has significantly expanded the donor pool, it comes with notable challenges. DCD liver grafts, in particular, face a higher risk of post-transplant complications due to warm ischemic time (WIT)—the period of ischemia experienced at body temperature during circulatory arrest.

This results in significant ischemic injury before organ preservation begins, leading to elevated risks of graft failure and complications post-transplantation. A meta-analysis by Jay et al. highlighted that recipients of DCD liver grafts face a 2.1-fold higher risk of graft failure, a 1.6-fold increased risk of mortality within the first year, and a 10.8-fold increased likelihood of developing post-transplant biliary complications.[68]

These elevated risk of post-transplant failure and complications in ECD and DCD liver transplants are primarily due to Ischemia-Reperfusion Injury (IRI) that occurs when the oxygen supply, interrupted at donation, is suddenly restored during transplantation.

A well-established positive correlation exists between the duration of ischemic time and IRI severity, and between IRI severity and the risk of immediate graft failure, Early Allograft Dysfunction (EAD), and Non-Anastomotic Strictures (NAS) of the biliary tree. Moreover, donor-specific characteristics such as advanced age and hepatic steatosis exacerbate IRI severity.

Static Cold Storage (SCS), the current standard method for organ preservation, has proven inadequate in preventing ischemic injury in high-risk grafts. SCS involves rapidly cooling the organ to reduce metabolism. But even under hypothermic conditions, metabolism continues, leading to cellular energy depletion, oxidative stress, and mitochondrial impairment. These processes intensify upon reperfusion with warm, oxygenated blood, leading to a cascade of inflammatory damage, particularly affecting DCD grafts, which experience both warm and cold ischemic injuries.

Clinically, IRI may manifest in varying degrees, from unnoticed (immediate graft function with minimal or no damage), EAD (affecting 10-30 % of grafts), or result in immediate graft loss (in <5 % of grafts). EAD, marked by hepatocellular injury and necrosis, is associated with a seven-fold increase in the risk of graft loss and a ten-fold increase in mortality compared to transplants without EAD.

Grafts from older donors are particularly prone to EAD, which is often linked to acute kidney injury and poorer long-term outcomes.[69] The biliary epithelium is particularly susceptible to IRI, and the severity of bile duct epithelial injury on histological examination correlates with NAS development.[70-72]
Post-transplant biliary complications affect up to 40% of DCD liver transplant recipients, with 21-33 % developing the more severe complication of diffuse NAS.[73] The pathogenesis of NAS is not fully understood, but risk factors include prolonged warm and cold ischemia times, inadequate preservation, injury to the peri-biliary glands and vascular plexus, and IRI.[70] Therapeutic options for NAS are limited: minimally invasive treatments such as radiological or endoscopic dilation of strictures typically offer only short-term relief, necessitating repeated procedures and increasing morbidity (recurrent cholangitis and biliary sepsis) and financial burden.[74] NAS often necessitates re-transplantation and is associated with a mortality rate of 15 %. Despite the growing reliance on ECD and DCD grafts, the limitations of SCS remain a barrier to optimizing outcomes. The inability to assess graft viability during preservation forces surgeons to make decisions with limited information, leading to the frequent rejection of high-risk organs that might have functioned adequately post-transplant.[75]
Over the past decade, the clinical application of ex situ dynamic preservation or machine perfusion has emerged,[76] rapidly becoming the standard of care for ECD/DCD graft preservation.[77-89] More specifically, normothermic machine perfusion (NMP), hypothermic oxygenated machine perfusion (HOPE), and combined approaches have emerged as the dominant modalities. Beyond their specific differences, the main advantages of these techniques include the reduction of IRI,[76] the safe extension of preservation times,[85, 90] the evaluation of organ viability,[91-93] and the potential for ex-situ interventions to address organ repair and regeneration.[94]

5.2. *Existing systems for ex situ liver preservation/perfusion*

During ex situ dynamic preservation, the liver graft is connected to an isolated circuit via its blood vessels, which pumps and recirculates a perfusion solution through the organ. Preservation can be conducted at body temperature (NMP) using a red blood cell-based perfusion solution, or at lower temperatures (hypothermic oxygenated perfusion, HOPE) with an acellular oxygenated solution (Figure 14).

5.2.1. *Normothermic Machine Perfusion (NMP)*

NMP aims to create a near-to-physiology environment for the liver. The graft is perfused at 37°C with a red blood cell-based solution to provide oxygen and nutrients, supporting its metabolism ex situ.[76] Thanks to transportable devices, NMP can begin at the donor hospital ("upfront" or "continuous" NMP) or later at the recipient hospital after SCS, termed "end-ischemic" or "back-to-base" NMP.

5.2.2. *Hypothermic Oxygenated Machine Perfusion (HOPE)*

HOPE combines reduced metabolism with active oxygenation to protect the graft by supporting aerobic mitochondrial respiration. This approach has been better characterized in terms of protection against IRI compared to NMP.[76]
HOPE is typically conducted at 10-12°C, either through portal perfusion alone or both arterial and portal (dual-HOPE, D-HOPE), with no definitive evidence of superiority between the two methods.[95]

5.2.3. *Combined MP approaches*

In order to take advantage of the beneficial effects of each MP modality, some centers started to explore the possibility of combining different preservation techniques. Controlled oxygenated rewarming (COR) involves the sequential use of D-HOPE and NMP. This strategy integrates the protective effects of D-HOPE with a comprehensive viability assessment during NMP.[96]

5.3. *Effectiveness and added value compared to static cold storage*

5.3.1. *Normothermic Machine Perfusion (NMP)*

Clinical evidence of NMP

The majority of clinical evidence favoring NMP over SCS comes from studies using upfront NMP (Table 5). The first 20 cases of LT following NMP, published in 2016, demonstrated reduced post LT aspartate aminotransferase (AST) peaks compared to a matched SCS cohort.[97] This laid the foundation for a first multicenter RCT that confirmed reduced AST peaks and showed a 12 % increase in organ utilization with NMP.[77]

A separate multicenter RCT (PROTECT) also found lower rates of EAD in the NMP group. Notably, NMP grafts exhibited fewer cases of ischemic cholangiopathy (IC), although the study's IC definition included bile leaks.[78]

More recently, the results from the second RCT comparing NMP and SCS were published, showing unexpected comparable rates of EAD and IC among groups.[80] However, in this USA cohort, donor risk profiles and preservation times were much lower than previous trials and the authors concluded that the study was underpowered to identify a protective effect of NMP in this cohort.

In contrast, the only RCT on end-ischemic NMP found no clinical advantage over SCS preservation of elderly liver grafts.[98] This suggests that the primary benefit of this approach may lie in viability assessment rather than actual reconditioning of the organ.[99]

Viability assessment during NMP

Since the liver is metabolically active during NMP, it enables a more precise evaluation of graft function, improving the objectivity to accept or decline a donor liver for transplantation. While gross appearance and liver consistency are commonly assessed, these subjective measures can be supplemented by surrogate markers measured in the perfusate such as lactate, pH, and glucose levels, which correlate with early graft function after LT.[76]

Long-term outcomes of the VITTAL trial demonstrated that recipients of high-risk ECD grafts accepted after viability assessment achieved five-year graft and survival rates of 72 % and 82 %, respectively.[91] However, 18 % of these recipients required re-transplantation due to IC, underscoring the challenge posed by this complication.

Efforts to improve biliary viability assessment during NMP have focused on bile production and composition, as bile synthesis is an ATP-dependent process requiring functional hepatocytes and cholangiocytes. Although bile production is considered necessary for graft acceptance,[100-101] especially in the case of DCD,[102] its total volume does not predict post-LT IC.[103] Instead, bile pH, bicarbonate, and glucose levels have

emerged as better predictors of NAS. [103-104] As bile composition during NMP is affected by the perfusate, viability criteria were refined to include perfusate/bile ratios[104] which correlate with biliary injury and regeneration.[105]
Notably, applying this biliary viability assessment to 42 discarded DCD livers led to 25 successful transplants, with only one case of IC.[105] NMP viability assessment has driven a paradigm shift in LT, with acceptance rates for previously discarded ECD grafts ranging from 47 % to 100 %.[106]
However, comparing protocols is challenging due to variations in biomarker timing and perfusion devices. A study by Mergental et al. highlighted this issue by applying three different viability protocols to the same ECD cohort, resulting in conflicting acceptance rates of 0 %, 3 %, and 77 %, emphasizing the need for standardized criteria. [107] In the future, analyzing bioenergetic performance, cytokine expression, and proteomics during NMP could provide more detailed assessments of organ quality, but time and cost considerations will play crucial roles in their adoption.[108-109]
Certainly, time is crucial for decision-making, and extended observation during long-term NMP could both increase graft acceptance[108] and further enable safer evaluation of high-risk grafts.[99]

Prolonged NMP

Several preclinical studies have investigated prolonged NMP (pNMP), demonstrating its safety and efficacy in providing extended opportunities for assessing organ quality and viability.[110-111] pNMP not allows for a longer evaluation period compared to traditional methods, but also offers a potential platform for the repair of damaged organs in the future. There is growing evidence that pNMP is not only feasible but may also rescue donor organs that would otherwise be discarded under conventional preservation techniques.
The longest reported clinical case of pNMP, by Clavien's group, involved a successful orthotopic liver transplantation (OLT) after 3 days of perfusion, showcasing the technology's potential.[112] In some centers, pNMP is now routinely used for viability assessment of ECD grafts, or to overcome logistic challenges and safely extend preservation times in complex recipients. Extending livers preservation up to 38 hrs, omitting nighttime procedures and parallel transplantation whilst achieving excellent graft and patient survival without NAS.[90]

5.3.2. *Hypothermic Oxygenated Machine Perfusion (HOPE)*

Clinical evidence of (D)HOPE

Hypothermic dynamic preservation was the first clinical application of ex situ dynamic preservation. Most of the clinical evidence favoring (D)HOPE over SCS comes from studies using end-ischemic (D)HOPE.
Early evidence showed reduced EAD and shorter hospital stays following hypothermic preservation.[113] Later, animal studies revealed that active oxygen delivery supports mitochondrial function, leading to the clinical implementation of (D)-HOPE.[76]
A 2021 multicenter RCT showed that D-HOPE reduced EAD, post-reperfusion syndrome, and symptomatic IC in donation after circulatory death (DCD) grafts.[82] Smaller studies have also demonstrated benefits in ECD-DBD grafts.[79, 83] Ravaioli, et al. [79] and Czigany, et al. [83] reported reduced rates of EAD and graft loss in HOPE-treated ECD-DBD livers.

Table 5 : Randomized controlled trials on normothermic machine perfusion in liver transplantation

Study	Country	Donor type	Comparison [n]	Device	Perfusion protocol	Main outcomes
Nasralla et al. 2018	EU	DBD and DCD	NMP [121] vs SCS [101]	OrganOx Metra	Up-front	↓ Post-LT ALT peak (488 IU vs 965 IU) ↓ EAD (10% vs 30%) ↓ PRS (12% vs 33%) ↓ Discard rates (12% vs 24%)
Ghinolfi et al. 2018	Italy	DBD >70 years old	NMP [10] vs SCS [10]	XVivo LiverAssist	Endischemic	↓ IRI-related histological features = EAD (10% vs 20%) = biliary interventions (10% vs 0%)
Markmann et al. 2022	USA	DBD and DCD	NMP [151] vs SCS [142]	TransMedics OCS Liver	Up-front	↓ EAD (18% vs 31%) ↓ IC at 6 mo (1.3% vs 8.5%) ↓ IC at 12 mo (2.6% vs 9.9%)
Guo et al. 2023	China	DBD	NMP [32] vs SCS [33]	XVivo LiverAssist	IFLT	↓ EAD (6% vs 24%) ↓ Post-LT ALT peak (417 IU vs 1010 IU) ↓ PRS (9% vs 64%) ↓ IC at 6 mo (7% vs 28%) ↓ IC at 12 mo (8% vs 36%) ↓ CCI at 12 mo (30.5 vs 42.1)
Chapman et al. 2023	USA	DBD and DCD	NMP [192] vs SCS [191]	OrganOx Metra	Up-front	= EAD (21% vs 24%) = Biliary interventions (9.4% vs 8.7%)

However, a larger RCT did not meet its primary endpoint (Clavien >III complications), although a post-hoc analysis revealed reduced Clavien >IIIb complications.[84] This study's short HOPE duration (96 minutes) and inclusion of standard brain-dead donors (DBD) may have influenced the results. Consistently, Grat et al.[114] showed that early allograft function and post-operative complications could be improved by D-HOPE only if applied to a higher-risk donor subpopulation, thus advocating against the routine use of MP.

A recent international, multicenter cohort study, assessed long-term results of 1,202 liver transplantations using HOPE across 22 centers in 6 European countries.[115] The study demonstrated excellent 5-year death-censored graft survival rates (91 % for DBD and 81 % for DCD), with low rates of graft loss due to primary non-function or NAS supporting the routine clinical implementation of HOPE, as it shows consistent benefits across different donor risk profiles.
A recent North American RCT reported safety and non-inferiority efficacy of the first transportable D-HOPE device with continuous D-HOPE in 27 out of 63 cases, showing reduced post-LT events and improved liver graft assessment scores.[116-117]
A recent meta-analysis of randomized controlled trials confirmed with high certainty that end-ischemic HOPE improves graft survival and reduces clinically relevant ischemic biliary complications in donors after circulatory death.[51]

Viability assessment during HOPE
Assessing viability during hypothermia was traditionally viewed with skepticism, but emerging evidence suggests that released mitochondrial compounds like flavin mononucleotide (FMN) can predict graft outcomes. FMN is released when mitochondrial respiration is impaired during 5 re-oxygenation, and higher perfusate FMN levels have been associated with graft dysfunction and loss.[118-119]
The Zurich group analyzed 158 high-risk DCD LTs performed with end-ischemic HOPE and found that donor characteristics alone were insufficient to prevent severe complications.[92] In the past five years, they introduced routine assessments of mitochondrial CO_2 production, along with perfusate FMN and NADH levels. However, the cut-offs for these criteria were arbitrarily set and validated mostly on surrogate endpoints, highlighting the need for a multicenter validation study. [92, 120]
Very recently, the predictive value of flavin mononucleotide (FMN) released during HOPE was validated in an international study analyzing 473 perfusate samples from 10 centers across 7 countries.[92] Higher perfusate FMN levels were strongly associated with graft loss, cholangiopathy, kidney failure, and liver injury, outperforming traditional donor and recipient risk scores

Prolonged (D-)HOPE
While 1-2 hours of HOPE are generally sufficient to provide its protective effects, prolonged perfusion (4+ hours) has been shown to facilitate transplant logistics without compromising outcomes.[121]
On this basis, the Groningen group set up a safety and feasibility trial for prolonged D-HOPE, in which, to avoid nighttime procedures, liver grafts were allocated to short- or longterm D-HOPE depending on the timing of the donor procedure.[85] Median MP time was 9.3 hours in the prolonged D-HOPE group and all LTs were performed during daytime without an increased rate of serious adverse events. Notably, median duration of recipient surgery was almost 2 hours longer in the short-term D-HOPE group.

Similarly to long-term NMP, prolonged (D-)HOPE holds indeed the enormous potential to shift LT scheduling from an urgent procedure to a relatively more flexible one, significantly enhancing the working conditions for the entire LT team. Notwithstanding the active metabolism during NMP traditionally being considered an imperative characteristic of pharmacological reconditioning, recent evidence suggests that some therapeutic approaches, such as posttranscriptional gene regulation, can be delivered during HOPE, thus broadening the potential application of prolonged (D-)HOPE.[122]

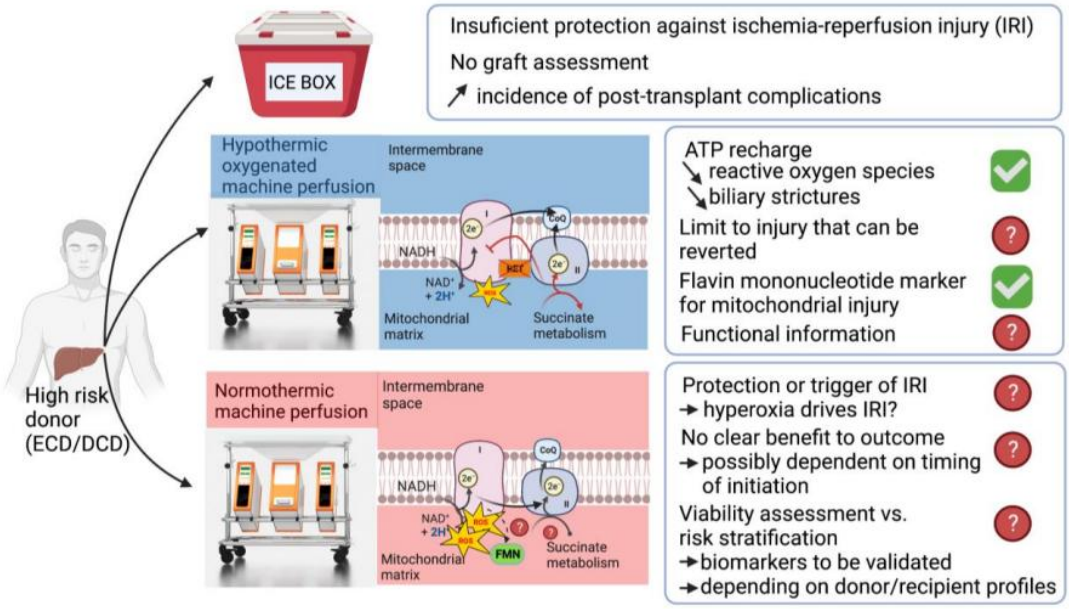


Figure 14 : Schematic overview of the potential effect of HOPE and NMP on mitochondria-driven ischemia-reperfusion injury in ECD and DCD LT

5.3.3. *Combined MP approaches*

Controlled oxygenated rewarming (COR) involving the sequential use of D-HOPE and NMP, was first reported to be feasible and safe by the groups from Essen and Bonn in Germany after they had previously shown in a preclinical porcine model that COR after SCS effectively increased energetic re-equilibration and reduced reperfusion injury.[123-124] *Notably, in their protocol livers were shortly perfused hypothermic at 10 °C, before rewarming to maximally 20 °C over a period of 60 minutes.*
In contrast, the Groningen group performed COR in their protocol of sequential DHOPE-COR-NMP. Following one hour of D-HOPE, COR is started from 20 °C and then slowly increased to body temperature.[96] *This protocol enabled successful transplantation of 33 out of 53 initially discarded DCD livers with 100 % one-year graft survival and only one patient developing NAS.*[105]

5.4. *Cost-effectiveness analysis of the use of preservation/perfusion systems*

In addition to the compelling clinical benefits of ex situ dynamic preservation, recent evidence highlights its increasing cost-effectiveness across various healthcare systems.

In France, Rayar et al. demonstrated that HOPE did not significantly increase costs when compared to a matched static cold storage (SCS) cohort.[125]
In Canada, Webb et al. found that incorporating 6 normothermic machine perfusion (NMP) into liver transplant programs resulted in greater quality-adjusted life year (QALY) gains and was cost-effective from a public healthcare perspective.[126]
Similarly, Javanbakht et al. from the UK calculated that NMP was cost-effective, with a cost of £7,800 per QALY gained—well below the UK's willingness-to-pay threshold of £20,000 per QALY.[127]
At the Cleveland Clinic in the US, Wehrle et al. demonstrated that routine NMP reduced waitlist mortality, optimized organ utilization without compromising short-term survival even with higher-risk grafts, improved waitlist management, and reduced healthcare costs, indicating the long-term economic viability of this approach.[128]
Data from the Dutch centers participating in the recent international multicenter DHOPE-DCD RCT provided evidence on the cost-effectiveness of (D)HOPE in DCD liver transplants. Among 119 patients, the trial showed that DHOPE reduced total medical costs by approximately €15,427 per patient compared to SCS, with significant savings in intensive care (28.4 %) and non-surgical intervention costs (24.3 %). Depending on the scenario, DHOPE became cost-effective after just one procedure, and even in more conservative models, remained cost-effective after 25-30 procedures annually.
In Belgium, a study by UZ Leuven (manuscript in preparation) explored the predicted cost-effectiveness of HOPE. The study analyzed 339 LT recipients from 2016-2020 and stratified costs by the occurrence of NAS. The mean total cost for patients without NAS was €9,822 versus €53,468 for those with NAS. The estimated cost per HOPE procedure was €7,500. Using HOPE, the incidence of NAS after DCD-LT could be reduced from 17 % (SCS) to 6 % (in line with the original results published by Van Rijn et al.). The Leuven study predicted that performing 120 HOPE procedures over two years would prevent significant NAS-related costs, with potential savings approaching €395,873 and breaking even at a conservative QALY gain estimate of €30,452 per QALY. Importantly, the study did not account for savings related to increased organ utilization rates and reduced waiting list times, likely underestimating the economic benefits of HOPE .

5.5. *Current reimbursement system if applicable*

At this moment there is no reimbursement for machine perfusion of livers for transplantation in Belgium.

5.6. *Future perspectives*

The advent of machine perfusion technology has allowed clinicians to transplant liver grafts that would not even be considered 10 years ago. At present, ex situ dynamic preservation allows reconditioning of the liver graft by providing oxygen and restoring energy levels in the mitochondria. Additionally, NMP is an established modality to assess organ quality before transplantation allowing us to save precious liver grafts that would otherwise be discarded. However, next to graft assessment, NMP also provides a platform for active treatment and regeneration, enabling us to repair liver that are considered too damaged to transplant. To this end, pNMP would be a requirement.
Recently the Zurich group of P. A. Clavien has successfully transplanted a donor liver that was preserved for three days with NMP. It is likely that perfusion devices allowing prolonged perfusion for multiple days will become widely available in the foreseeable future. Numerous strategies to improve liver grafts during NMP are currently being investigated such as active defatting of steatotic livers, reducing IRI of older livers with senolytic drugs, as well as targeting IRI at the genetic level with small interfering RNA (siRNA) or stem cell derived extracellular vesicles.

6. Ex situ machine preservation/perfusion in lung transplantation

6.1. *Specific needs in lung transplantation*

Lung transplantation is a standard life-saving treatment for patients suffering from end-stage respiratory failure unresponsive to other medical or surgical interventions. In 2024 in Belgium, 108 lung transplants were performed (3 single lung transplantations, 105 double lung transplantations), however 70 patients remained on the active waiting list, and 8 patients died while waiting for a lung transplant.

Donor-lung utilization continues to increase with the use of extended criteria donors, careful evaluation, active donor optimization, and ex vivo assessment.
Organ transport represents a critical step in the lung transplantation process. The primary objective is to minimize injury to the organ during ex vivo preservation. Traditionally, this is achieved by rapidly cooling the lungs and storing them in an ice-filled container at 0 °C to 2 °C. This method is known as ***static cold storage (SCS)****.*
Although SCS remains the global standard, the duration of preservation must be strictly limited, as prolonged exposure to ice can result in significant lung tissue damage.[129]
To alleviate this time constraint and improve transplant outcomes, several innovative preservation techniques have been developed in recent years. These can be broadly categorized into two approaches [130]*:*

1. ***Machine Perfusion (MP):*** *In this technique, the lungs are continuously ventilated and perfused with perfusate or blood at normothermic temperatures (35 °C–37 °C) (NMP) or at low temperatures (HMP) outside the body (ex vivo lung perfusion and ventilation).*
2. ***Controlled Hypothermic Storage (CHS):*** *This method involves storing the lungs in a specially designed container under stable, controlled hypothermic conditions (6 °C–10 °C).*

6.2. *Existing systems for ex situ lung preservation/perfusion*

6.2.1. *Machine Perfusion*

To implement machine perfusion (MP) in clinical practice, commercial devices have been developed that enable either normothermic or hypothermic perfusion. These systems are, however, costly to acquire and require the use of specific consumables, which increases the overall cost. As a result, some lung transplant centers opt for custom-built systems, such as the Toronto-based model, which is more cost-effective but demands greater technical expertise.
Currently, two commercially available systems are most widely used:

- ***OCS Lung® (Organ Care System, TransMedics, Andover, MA, USA,):*** *Allows for normothermic perfusion and ventilation during transport.*
- ***XPS® platform (XVIVO Perfusion System, XVIVO, Gothenburg, Sweden,*** *Figure 15**):*** *Operates under controlled conditions at room temperature or slightly elevated temperatures in a stationary setting using ex vivo perfusion and ventilation. The XPS® system utilizes a standardized perfusion protocol (Steen Solution®, dextran, albumin, and antibiotics) and ventilates the lungs for 4 to 6 hours at physiological temperature. This system is designed to clinically assess and optimize marginal donor lungs prior to transplantation*

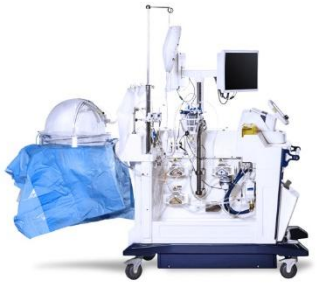


Figure 15 : XPS®

6.2.2. *Controlled Hypothermic Storage*

Traditionally, donor lungs are transported in a cooler filled with ice, and transplantation is performed immediately upon arrival at the transplant center. However, recent research has demonstrated that ice storage is too cold for organs and poses a risk of freezing injury to the tissue. Consequently, the safe preservation time at ice temperature is limited to a maximum of 6 to 8 hours.[131]
*This has translated into the concept of **controlled hypothermic storage (CHS)** for lung transplantation. This approach involves storing organs at a temperature between 6 °C and 10 °C.*

Figure 16 : LUNGguard®

***LUNGguard®** (Paragonix, Waltham, MA, USA, Figure 16) is one of the devices designed to maintain donor lungs within a temperature range of 6 °C-8 °C for 48 hours. A monitor displays the ambient temperature of the lungs, and during transport, both the temperature and location of the lungs can be tracked in real time via a software application accessible to the entire transplant team. A prospective worldwide registry (including UZ Leuven) compares the outcome of LUNGguard preserved organs versus ice-preserved.*
*Another commercial device is the **VITALPACK® EVO** (E3 Cortex, France) which maintains lung grafts between 2 °C-6 °C. No clinical data on outcome is available.*

In follow-up of the LungGUARD®, a next-generation approach to ex situ lung preservation is BAROguard® Donor Lung Preservation System integrating active airway pressure control with controlled hypothermic storage. Unlike conventional cold-storage in ice, BAROguard® maintains a stable inflation pressure (e.g. ~ 15 cm H_2O) to prevent barotrauma or under-inflation, while continuously regulating temperature within safe limits.[132]
During transport - including altitude changes - this dual control ensures that donor lungs remain mechanically and thermally protected. The system also features real-time data monitoring and remote reporting, enabling transplant teams to track internal pressure and temperature throughout the cold ischemic interval.[132-133]

6.3. *Effectiveness and added value compared to static cold storage*

6.3.1. *Effectiveness and added value of Machine perfusion*

Effectiveness and added value of the OCS Lung® System

- ***INSPIRE Trial:** A randomized, controlled study comparing normothermic MP with standard static cold storage (SCS) in standard-criteria donors. The results confirmed that the OCS system is safe and effective, with a lower incidence of grade 3 primary graft dysfunction (PGD-3) within the first 72 hours post-transplantation.[134]*
- ***EXPAND Trial:** A single-arm pivotal study evaluating the use of OCS in lungs from extended-criteria donors, including donation after circulatory death (DCD) donors. Successful transplantation was achieved in 87 % of cases, often involving lungs previously declined by other centers. The study suggested that normothermic MP can significantly expand the donor organ pool.[135]*

Effectiveness and added value XPS® System and Ex Vivo Lung Perfusion (EVLP)

- ***NOVEL Trial (North American Observational Study of EVLP)[136]:*** *A prospective, multicenter, observational study conducted in North America using the XPS system to evaluate lungs initially deemed unsuitable for direct transplantation. The study demonstrated that a substantial number of these "marginal" lungs could be safely transplanted following successful EVLP, with 30-day and 1-year survival rates comparable to those of standard donor lungs.*
- ***HELP Trial (High-risk Extended Lung Preservation)[137]:*** *Focused on lungs from extended-criteria donors, including DCD and older donors, evaluated with XPS-EVLP for 4 to 6 hours. The results showed improved oxygenation indices and a reduced incidence of PGD-3 post-transplantation in selected cases.*
- ***European Experience and Scandinavian Data (Gothenburg Cohort):*** *Several Scandinavian transplant centers, particularly in Sweden and Norway, have extensive experience with the XPS system. Multiple cohort studies and national registries have reported that the use of EVLP with XPS significantly increases the number of transplants without compromising short- or mid-term outcomes*

6.3.2. *Effectiveness and added value of Controlled Hypothermic Storage (CHS): Comparison of Controlled Hypothermic Storage (CHS) with Classical Ice Storage (SCS) and Its Potential Added Value*

<u>Historical and Experimental Evidence</u>
In 1989, Wang et al. (Toronto, Canada) developed an ex vivo rabbit model to evaluate post-ischemic lung function after preservation at various temperatures. They compared 4 °C, 10 °C, 15 °C, 23 °C, 34 °C, and 38 °C, measuring parameters such as arterial oxygen tension (PaO_2), pulmonary arterial pressure (PAP), and oxygen uptake. Lungs preserved at 10 °C for 12 hours demonstrated superior gas exchange, hemodynamic stability, and reduced edema compared to those stored at 4 °C. Moreover, lungs in the 10 °C group tolerated ischemic times of 18–24 hours without significant functional loss.[138]
In 1992, Date et al. (St. Louis, Missouri) confirmed these findings in a canine model of orthotopic left lung transplantation. Lungs preserved at 10 °C for 18 hours showed improved oxygenation and lower pulmonary vascular resistance (PVR) compared to the 4 °C group.[139] That same year, Nakamoto et al. (Japan) concluded in a comparative rabbit model that the optimal temperature range is 8–9 °C. They reported increased vascular obstruction at 4 °C and damage to the alveolocapillary membrane at 15 °C.[140]
Additional experimental evidence came from Toronto[141-142] and from Steen et al.[143], who reported similar findings in a porcine model. Despite this robust experimental foundation, clinical implementation of CHS remained limited for many years due to technological and logistical challenges.

<u>Renewed Interest and Clinical Translation</u>

In 2021, CHS regained attention through the work of Cypel, Ali, and colleagues (Toronto), who developed a porcine model in which lungs were preserved at 10 °C for 36 hours, followed by ex vivo lung perfusion (EVLP). The 10 °C group demonstrated superior compliance, oxygenation, and reduced edema compared to the 4 °C group. Importantly, mitochondrial function was preserved, and inflammatory markers such as IL-6 and TNF-α were significantly lower.[144]
These findings were subsequently translated into clinical practice. In a prospective study, five patients received lung transplants using organs preserved at 10 °C for 10.4 to 12.1 hours. None of the patients developed PGD-3 at 72 hours, and the median duration of mechanical ventilation was reduced.[145] *In 2022, further studies confirmed that CHS can also successfully preserve marginal donor lungs (e.g., DCD or lungs with mild abnormalities).*[146] *The underlying hypothesis is that mild hypothermia activates protective cellular mechanisms, including inhibition of apoptosis, preservation of mitochondrial integrity, and reduction of oxidative stress.*

<u>Clinical Evidence and Real-World Data</u>
A global comparative study demonstrated that CHS using the LUNGguard system can safely extend donor lung preservation time to over 15 hours, compared to 6–8 hours with conventional ice storage. This enables evening procurement, overnight storage under CHS at the transplant center, and planned transplantation the following morning—a strategy referred to as "night-to-day bridging." This strategy was successfully implemented in Belgium since 2023.[147-148]

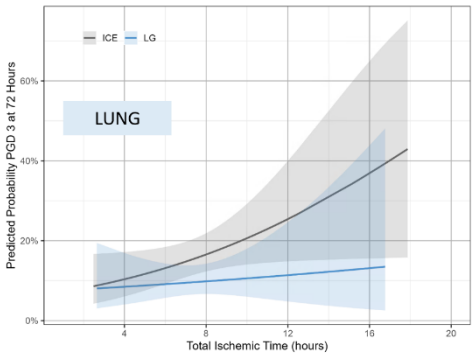


Figure 17 : Probability of primary graft dysfunction grade 3 in relation to ischemic time comparing ice (grey line) versus Lungguard (blue line); unpublished data

At the International Society for Heart & Lung Transplantation (ISHLT) 2025 annual meeting, data from 420 lung transplants in the GUARDIAN-LUNG registry were presented, comparing CHS with LUNGguard to conventional static ice storage (SIS). CHS was associated with a significant reduction in severe primary graft dysfunction (PGD3) (Figure 17), improved one-year survival, and reduced need for ECMO and renal replacement therapy. These findings confirm that CHS not only improves clinical outcomes but also offers logistical advantages for transplant teams.[149-150]
Additionally, the BAROGUARD system (Paragonix Technologies) was introduced in a cohort of 75 lung transplants. This device maintains both temperature and intrapulmonary pressure, resulting in more stable oxygen tension. The results showed a significant reduction in post-transplant pulmonary edema and a lower incidence of PGD-3 within the first 72 hours compared to conventional preservation methods. Early graft function was also improved, as evidenced by higher PaO_2/FiO_2 ratios.

Early clinical use in the US, suggests that this controlled approach may reduce incidences of graft injury associated with fluctuating pressures or thermal stress, especially over longer transport times.[133]

Logistical Advantages and Impact on Healthcare Teams

CHS enables planned daytime transplant procedures. Nighttime surgeries are associated with an increased risk of medical errors and poorer outcomes. In a cohort study of 563 lung transplant recipients, reperfusion between 4:00 and 8:00 a.m. was associated with higher rates of PGD-3. A propensity-matched analysis comparing 187 nighttime and 187 daytime transplants revealed that nighttime transplantation was linked to worse five-year survival and faster progression to bronchiolitis obliterans syndrome (BOS).[151]

For healthcare providers, CHS reduces the need for nighttime surgeries, improves work-life balance, and lowers the risk of burnout. An international survey of 7,900 surgeons found that frequent night shifts were associated with lower career satisfaction. CHS thus contributes to the retention of experienced personnel and the recruitment of young physicians and surgeons for transplantation surgery.

6.4. *Cost/ cost-effectiveness analysis of the use of preservation/perfusion systems*

To date, no specific cost or implementation studies have been conducted regarding the use of CHS. Nevertheless, it is evident that, in addition to the clinical cost savings associated with improved outcomes—such as reduced incidence of PGD, decreased need for dialysis, and less frequent use of ECMO—the most substantial benefit lies in the human cost savings for transplant teams by avoiding nighttime transplant procedures. This human factor has become increasingly critical in today's healthcare landscape.

6.5. *Current reimbursement system if applicable*

At this moment there is no reimbursement for machine perfusion or controlled hypothermic storage devices in Belgium.

6.6. Future Perspectives

An international randomized controlled trial (RCT) on CHS, led by the Toronto group, is currently underway. This study aims to compare CHS (10 °C, transport using the Xport system) with standard SCS, focusing on outcomes such as PGD3 incidence, one-year survival, logistical planning, and team dynamics.

***CHS** represents a paradigm shift in lung transplantation: it enables safe extension of preservation time, offers greater logistical flexibility, maintains donor lung quality, and improves working conditions for healthcare professionals—without compromising clinical outcomes.*

***EVLP** has transformed lung transplantation by allowing functional assessment of donor lungs outside the body. It is increasingly used as a therapeutic platform to improve graft quality before transplant (Figure 18). Advances in machine perfusion now enable targeted delivery of drugs, anti-inflammatory agents, and regenerative therapies during EVLP, reducing injury and dysfunction. Integrating genetic modulation techniques like RNA interference and CRISPR into EVLP offers promising ways to modify donor lungs, lowering immunogenicity and enhancing repair. As precision medicine advances, EVLP enables personalized graft optimization tailored*

to donor and recipient.[152-153] Ongoing research, including the 2025 Europe-based LifeLUNG consortium led by L. Ceulemans (KU Leuven) under a Marie Curie Horizon project, aims to validate these novel approaches for clinical use.

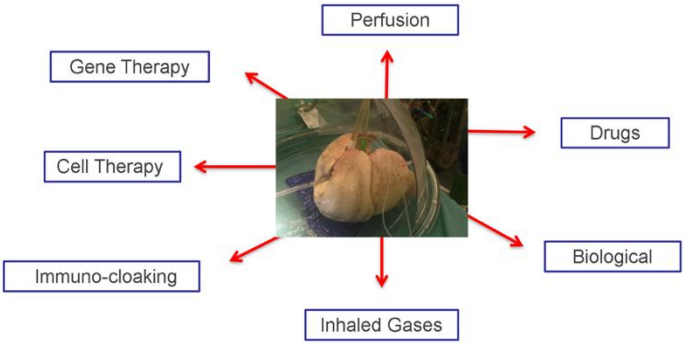


Figure 18 : Ex vivo lung perfusion as a therapeutic platform for targeted delivery

7. Conclusions and recommendations

Due to the limited availability of viable donor organs and the growing reliance on DCD and ECD grafts, there is an increasing need to improve organ preservation. Current evidence supports the routine use of machine perfusion strategies to minimize ischemia-reperfusion injury and enhance post-transplant outcomes. Moreover, clinical use of organ preservation systems resulted in an important increase of the national transplantation rate of ECD and DCD organs with excellent functional outcome. This was also shown in the recent analysis of the outcome of the RIZIV/INAMI reimbursement initiative of HMP for kidneys procured in Belgium.

In light of this, the SHC recommends a further progressive implementation of ex situ organ preservation, based on the following pillars:
1/ systematic application of ex situ preservation in all DCD and ECD grafts
2/ trained staff and high performance infrastructure
3/ adequate reimbursement framework
4/ monitoring of clinical outcomes

7.1. *Systematic application of machine perfusion for all DCD and ECD Grafts*

To ensure that all organ transplant recipients benefit from the best possible outcomes, ex situ organ preservation should be available to all DCD and ECD grafts in every Belgian transplant center. This approach ensures equity in care, providing equal access to optimized grafts, regardless of the transplant center.
The type of dynamic preservation used should be based on the most recent evidence, while also considering the center's experience with specific preservation techniques. This allows flexibility in applying the most suitable methods based on expertise, within the framework of standardized best practices.
Based on current scientific evidence the following techniques should be considered as minimum standard for ex situ preservation of DCD and ECD hearts, kidneys, livers and lungs:

a. Heart

For DCD hearts, static cold storage is not a viable option following direct procurement (DP), yielding inferior transplant outcomes. Machine perfusion is necessary for DCD hearts that have been directly procured. Both normothermic machine perfusion (NMP) as well as hypothermic machine perfusion (HOPE) have shown post-transplant DCD-DP outcomes similar to classic DBD.

b. Kidney

Continuous HMP is proven superior as compared to SCS alone for the preservation of 'high-risk' kidneys to improve graft outcome. Based on the growing scientific evidence in favor of HMP and also on the interim analysis of the first HMP convention in Belgium, HMP has become standard of care for high-risk kidneys. The recently approved extension of the reimbursement criteria as described above, aims to increase national kidney transplant activity in the context of an increase of dialysis patients and longer waiting lists for transplantation.
NMP is demonstrated to be feasible as an end-ischemic preservation strategy, however, without a positive influence on early graft function as compared to SCS alone. But NMP, used as a viability assessment platform pre-transplant, can increase the number of available kidneys for transplantation. At present, many kidneys are

discarded, because they are considered at risk of dysfunction based on age and other donor characteristics. A significant proportion of these organs could eventually be transplanted in case the assessment of function and histology during NMP provided reassuring results.

c. Liver

Ex situ dynamic preservation and especially dual-hypothermic Oxygenated Machine Perfusion (D-HOPE) has been shown to significantly reduce ischemic injury, early allograft dysfunction, and long-term complications, and has become the standard of care particularly for ECD/DCD grafts.
A growing body of scientific data suggests that more complex dynamic preservation techniques—such as normothermic machine perfusion or sequential hypothermic-normothermic machine perfusion— should be applied in specific contexts, such as the evaluation of very high-risk organs.

d. Lung

Based on current scientific evidence, ***controlled hypothermic storage (CHS)*** *should be adopted as the new standard for donor lung preservation, as it enables a longer preservation time, significantly reduces the risk of ice-induced injury, and allows for planned daytime transplantation.*
In parallel, ***ex vivo lung perfusion (EVLP)*** *has emerged as an essential platform in modern lung transplantation, especially in ECD lungs, as it creates a unique therapeutic window for* ***organ optimization and active modulation prior to implantation****.. As such,* ***CHS and EVLP are complementary and synergistic strategies****, indispensable for both* ***expanding the donor pool*** *and* ***improving post-transplant outcomes in lung transplantation****,*

7.2. Trained staff and high performance infrastructure

All transplant centers utilizing dynamic organ preservation techniques must be equipped with the appropriate infrastructure, including perfusion devices and trained personnel.
It is essential to establish dedicated training programs for clinical teams to ensure safe and efficient operation and monitoring of perfusion systems. Additionally, facilities must be adequately prepared to preform dynamic organ preservation technology.

Certified Clinical Perfusionists (CCP) play a central and indispensable role in this context. As highly trained professionals in extracorporeal circulation, they are uniquely qualified to manage organ perfusion devices both directly and in a supervisory role, ensuring safe and effective perfusion practices. According to the European Board of Cardiovascular Perfusion (EBCP), EBCP-CCP should be the preferred experts in all perfusion-related activities across Europe.[154-155] Similarly, the American Board of Cardiovascular Perfusion (ABCP) emphasizes CCPs are the only medical professionals formally trained in all aspects of extracorporeal technology. Their expertise covers both normothermic regional perfusion (NRP) and dynamic organ preservation techniques, that are in close relationship to the principles of extracorporeal technology and require equally deep understanding of Ex-Situ and In-Situ organ perfusion.[156] Therefore the ABCP states that a CCP serves as the primary operator of extracorporeal devices, such as oxygenators, de-oxygenators, and pumps

used to manage the physiological condition of human organs that have been isolated from the body for potential transplantation.[157]
In Belgium, clinical perfusionists hold either a Bachelor of Science or Master of Science degree, awarded by the University of Liège or KU Leuven. Organ perfusion for transplantation is already integrated into the official curriculum of these accredited higher education programs, ensuring a solid theoretical and practical foundation.

7.3. *Adequate reimbursement framework*

In the 2011 advice (SHC 8711) the SHC already mentioned that financial issues and the lack of reimbursement hindered the use of organ preservation systems at that time.

The National Health Care Institute of the Netherlands advised the Ministry of Health, Welfare and Sport (VWS) to include machine perfusion for lung and liver transplantation in the basic health insurance package starting in 2022. This means that, as of January 1, 2022, this treatment is reimbursed under the basic health insurance coverage.

In Belgium, anno 2025, the reimbursement of ex situ organs preservation is limited to the kidneys, under certain conditions.
Nowadays the HMP convention of the RIZIV/INAMI foresees a reimbursement for HMP for all DCD and DBD ECD kidneys procured in Belgium and preserved by HMP conditions with the intent to be transplanted in Belgium.
For the other organs there is no reimbursement yet for any of the available preservation systems. There are local initiatives where the cost of the device and the consumables is paid by the hospital, but this is not sustainable in the long term.
In the other cases, this means that an ex situ conservation is not available, leading to loss of the organ or a potential shift of these organs to other ET countries with a reimbursed preservation system (eg. The Netherlands).
To ensure that cost does not hinder the systematic implementation of these life changing technologies in DCD and ECD organs, a national reimbursement scheme should be established to cover costs of ex situ organ preservation in these indications.
When establishing such a reimbursement framework it is important to take into account not only the cost of the device itself but also some related costs.

Without being exhaustive, these related costs might include:

- *device related material such asl disposables, fluids and oxygenation materials*
- *extra cost of dedicated OR facility*
- *extra cost of the clinical perfusionist and other health professionals, dealing with the device*
- *costs of transport of the device (in a lot of cases an extra car is needed*
- *compensation for the cost of procedures that do not result in a transplantation of the organ, and hence lack of reimbursement, as there is no recipient*
- *administrative cost e.g. to write a public tender or for the reimbursement procedure*
- *costs linked to the monitoring and follow-up (e.g. construction of a database, time to collect the data to complete the database, analysis of the data…)*

…

As a return on investment, there will be:

- *an increase in the number of organs available for transplantation,*
- *a decrease of the time on the waiting list, and of associated complications and hospitalization periods*
- *decreased need for organ supportive therapy such as dialysis or use of ECMO*
- *better clinical outcomes and increased survival*
- *greater logistical flexibility, avoiding nighttime transplant procedures, which results in reduced costs for personnel and improves the working conditions for healthcare professionals*
- *increased knowledge on the use and efficacy of organ preservation techniques, triggering further research and optimalisation of the existing devices and procedures.*

7.4. *Monitoring of clinical outcomes*

A registry should be established to systematically monitor the clinical outcomes related to machine perfusion. Based on the positive experience of the kidney transplant programs with the ET database to register the outcomes of HMP within the RIZIV/INAMI convention, this way of monitoring might be expanded to other organs. If ET is willing to add a number of extra items in the machine perfusion template of their database as they did for the kidneys, this could be a win-win solution and avoid double registration in different databases.

This registry should track key metrics such as patient and graft survival, post-transplant complications, but also the impact of ex situ organ preservation on the transplantation rate. The content of already existing international databases (eg. ISHLT) could be used to create an optimal data set.
Continuous data collection will help improve practices and ensure the benefits of machine perfusion are consistently realized across all transplant centers. Participation in the registry should be mandatory and linked to reimbursement, requiring a minimal set of clinical data to be recorded for perfusion costs to be covered. This ensures transparency, consistency, and adherence to best practices.

By implementing these recommendations and promoting equitable access to the best available organ preservation techniques, Belgium can continue its leading role in organ transplantation and post-transplant outcomes, increase the number of available

organs, reduce waiting list mortality, by and provide patients with safer, more reliable organ transplants.

IV. RÉFÉRENCES

1. Superior Health Council, SHC 8711: Machine perfusion versus cold storage. Brussels 2011.
2. www.eurotransplant.org.
3. Evrard, P., *Donation After Circulatory Death (DCD): A Belgian Consensus*. 2021.
4. Matas, A. J.; Smith, J. M.; Skeans, M. A.; Thompson, B.; Gustafson, S. K.; Stewart, D. E.; Cherikh, W. S.; Wainright, J. L.; Boyle, G.; Snyder, J. J.; Israni, A. K.; Kasiske, B. L., OPTN/SRTR 2013 Annual Data Report: kidney. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2015,** *15 Suppl 2*, 1-34.
5. Boulet, J.; Mehra, M. R., Crossing the chasm of donor organ recovery in heart transplantation. *European Heart Journal* **2023,** *44* (44), 4675-4677.
6. Wayda, B.; Angleitner, P.; Smits, J. M.; van Kins, A.; Berchtold-Herz, M.; De Pauw, M.; Erasmus, M. E.; Gummert, J.; Hartyanszky, I.; Knezevic, I.; Laufer, G.; Milicic, D.; Rega, F.; Schulze, P. C.; van Caeneghem, O.; Khush, K. K.; Zuckermann, A. O., Disparities in donor heart acceptance between the USA and Europe: clinical implications. *European Heart Journal* **2023,** *44* (44), 4665-4674.
7. Oberparleiter, S.; Krendl, F. J.; Resch, T.; Oberhuber, R.; Esser, H.; Ponholzer, F.; Weissenbacher, A.; Breitkopf, R.; Neuwirt, H.; Schneeberger, S.; Maglione, M.; Cardini, B., En-bloc kidney transplants from very small pediatric donors: a propensity score matched analysis. *Frontiers in pediatrics* **2025,** *13*, 1570489.
8. Hendriks, K. D. W.; Bruggenwirth, I. M. A.; Maassen, H.; Gerding, A.; Bakker, B.; Porte, R. J.; Henning, R. H.; Leuvenink, H. G. D., Renal temperature reduction progressively favors mitochondrial ROS production over respiration in hypothermic kidney preservation. *J Transl Med* **2019,** *17* (1), 265.
9. Fuller, B. J.; Lee, C. Y., Hypothermic perfusion preservation: the future of organ preservation revisited? *Cryobiology* **2007,** *54* (2), 129-45.
10. Guibert, E. E.; Petrenko, A. Y.; Balaban, C. L.; Somov, A. Y.; Rodriguez, J. V.; Fuller, B. J., Organ Preservation: Current Concepts and New Strategies for the Next Decade. *Transfusion medicine and hemotherapy : offizielles Organ der Deutschen Gesellschaft fur Transfusionsmedizin und Immunhamatologie* **2011,** *38* (2), 125-142.
11. Hosgood, S. A.; Nicholson, M. L., First in man renal transplantation after ex vivo normothermic perfusion. *Transplantation* **2011,** *92* (7), 735-8.
12. Bagul, A.; Hosgood, S. A.; Kaushik, M.; Kay, M. D.; Waller, H. L.; Nicholson, M. L., Experimental renal preservation by normothermic resuscitation perfusion with autologous blood. *The British journal of surgery* **2008,** *95* (1), 111-8.
13. Hamelink, T. L.; Ogurlu, B.; De Beule, J.; Lantinga, V. A.; Pool, M. B. F.; Venema, L. H.; Leuvenink, H. G. D.; Jochmans, I.; Moers, C., Renal Normothermic Machine Perfusion: The Road Toward Clinical Implementation of a Promising Pretransplant Organ Assessment Tool. *Transplantation* **2022,** *106* (2), 268-279.
14. Elliott, T. R.; Nicholson, M. L.; Hosgood, S. A., Normothermic kidney perfusion: An overview of protocols and strategies. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2021,** *21* (4), 1382-1390.
15. Messer, S.; Ardehali, A.; Tsui, S., Normothermic donor heart perfusion: Current clinical experience and the future. *Transplant International* **2015**, 634–642.
16. Banner, N. R.; Thomas, H. L.; E, C., The importance of cold and warm cardiac ischemia for survival after heart transplantation. *Transplantation* **2008,** *86*, 542–547.
17. Siddiqi, H. K.; Trahanas, J.; Xu, M.; Wells, Q.; Farber-Eger, E.; Pasrija, C.; Amancherla, K.; Debose-Scarlett, A.; Brinkley, D. M.; Lindenfeld, J.; Menachem, J. N.; Ooi, H.; Pedrotty, D.; Punnoose, L.; Rali, A. S.; Sacks, S.; Wigger, M.; Zalawadiya, S.; McMaster, W.; Devries, S.; Shah, A.; Schlendorf, K., Outcomes of Heart Transplant Donation After Circulatory Death. *J Am Coll Cardiol* **2023,** *82* (15), 1512-1520.

18. Schroder, J. N.; Patel, C. B.; DeVore, A. D., Transplantation Outcomes with Donor Hearts after Circulatory Death. *N Engl J Med* **2023,** *388* (23), 2121–2131.
19. Radakovic, D.; Karimli, S.; K, P., First clinical experience with the novel cold storage SherpaPakTM system for donor heart transportation. *J Thorac Dis* **2020,** *12*, 7227–7235.
20. Messer, S. J.; Axell, R. G.; S, C., Functional assessment and transplantation of the donor heart after circulatory death. *Journal of Heart and Lung Transplantation* **2016,** *35*, 1443–1452.
21. McGiffin, D. C.; Kure, C. E.; Ps, M., Hypothermic oxygenated perfusion (HOPE) safely and effectively extends acceptable donor heart preservation times: Results of the Australian and New Zealand trial. *Journal of Heart and Lung Transplantation* **2024,** *43*, 485–495.
22. Shudo, Y.; Leacche, M.; H, C., A Paradigm Shift in Heart Preservation: Improved Post-transplant Outcomes in Recipients of Donor Hearts Preserved With the SherpaPak System. *ASAIO Journal* **2023,** *69*, 993–1000.
23. Zhu, Y.; Shudo, Y.; H, H., Outcomes of Heart Transplantation Using a Temperature-controlled Hypothermic Storage System. *Transplantation* **2023,** *107*, 1151–1157.
24. Rega, F.; Lebreton, G.; Para, M.; Michel, S.; Schramm, R.; Begot, E.; Vandendriessche, K.; Kamla, C.; Gerosa, G.; Berman, M.; Boeken, U.; Clark, S.; Ranasinghe, A.; Ius, F.; Forteza, A.; Pivodic, A.; Hennig, F.; Guenther, S.; Zuckermann, A.; Knosalla, C.; Dellgren, G.; Wallinder, A., Hypothermic oxygenated perfusion of the donor heart in heart transplantation: the short-term outcome from a randomised, controlled, open-label, multicentre clinical trial. *Lancet (London, England)* **2024,** *404* (10453), 670-682.
25. Langmuur, S. J. J.; Amesz, J. H.; Veen, K. M.; Bogers, A. J. J. C.; Manintveld, O. C.; Taverne, Y. J. H. J., Normothermic Ex Situ Heart Perfusion With the Organ Care System for Cardiac Transplantation: A Meta-analysis. *Transplantation* **2022,** *1;106(9):1745-1753*.
26. Rega, F.; Lebreton, G.; Para, M.; Michel, S.; Schramm, R.; Begot, E.; Vandendriessche, K.; Kamla, C.; Gerosa, G.; Berman, M.; Boeken, U.; Clark, S.; Ranasinghe, A.; Ius, F.; Forteza, A.; Pivodic, A.; Hennig, F.; Guenther, S.; Zuckermann, A.; Knosalla, C.; Dellgren, G.; Wallinder, A., (100) - Hypothermic Oxygenated Perfusion of the Donor Heart in Heart Transplantation: The One Year Outcome from a Randomized, Controlled, Open-Label, Multicenter Clinical Trial. *The Journal of Heart and Lung Transplantation* **2025,** *44* (4, Supplement), S49.
27. Chew, H. C.; Iyer, A.; Connellan, M., Outcomes of Donation After Circulatory Death Heart Transplantation in Australia. *J Am Coll Cardiol* **2019,** *73* (12), 1447–1459.
28. Isath, A.; Ohira, S.; A, L., Ex Vivo Heart Perfusion for Cardiac Transplantation Allowing for Prolonged Perfusion Time and Extension of Distance Traveled for Procurement of Donor Hearts: An Initial Experience in the United States. *Transplant Direct* **2023,** *9:E1455.*
29. Rojas S., V.; Avsar, M.; Ius, F., Ex-Vivo Preservation with the Organ Care System in High-Risk Heart Transplantation. *Life* **2022**, 12.
30. Jain, P.; Prichard, R. A.; Connellan, M. B.; Dhital, K. K.; Macdonald, P. S., Long distance heart transplantation: a tale of two cities. *Internal Medicine Journal* **2017,** *47* (10), 1202-1205.
31. Meier-Kriesche, H. U.; Port, F. K.; Ojo, A. O.; Rudich, S. M.; Hanson, J. A.; Cibrik, D. M.; Leichtman, A. B.; Kaplan, B., Effect of waiting time on renal transplant outcome. *Kidney international* **2000,** *58* (3), 1311-7.
32. Meier-Kriesche, H.-U.; Kaplan, B., Waiting time on dialysis as the strongest modifiable risk factor for renal transplant outcomes: A Paired Donor Kidney Analysis: 1. *Transplantation* **2002,** *74* (10), 1377-1381.
33. Heylen, L.; Jochmans, I.; Samuel, U.; Tieken, I.; Naesens, M.; Pirenne, J.; Sprangers, B., The duration of asystolic ischemia determines the risk of graft failure after circulatory-dead donor kidney transplantation: A Eurotransplant cohort study. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2018,** *18* (4), 881-889.
34. Hamed, M. O.; Chen, Y.; Pasea, L.; Watson, C. J.; Torpey, N.; Bradley, J. A.; Pettigrew, G.; Saeb-Parsy, K., Early graft loss after kidney transplantation: risk factors and

consequences. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2015,** *15* (6), 1632-43.
35. Saidi, R. F.; Elias, N.; Kawai, T.; Hertl, M.; Farrell, M. L.; Goes, N.; Wong, W.; Hartono, C.; Fishman, J. A.; Kotton, C. N.; Tolkoff-Rubin, N.; Delmonico, F. L.; Cosimi, A. B.; Ko, D. S., Outcome of kidney transplantation using expanded criteria donors and donation after cardiac death kidneys: realities and costs. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2007,** *7* (12), 2769-74.
36. O'Neill, S.; Srinivasa, S.; Callaghan, C. J.; Watson, C. J. E.; Dark, J. H.; Fisher, A. J.; Wilson, C. H.; Friend, P. J.; Johnson, R.; Forsythe, J. L.; Ploeg, R. J.; Mirza, D. F.; Wigmore, S. J.; Oniscu, G. C., Novel Organ Perfusion and Preservation Strategies in Transplantation - Where Are We Going in the United Kingdom? *Transplantation* **2020,** *104* (9), 1813-1824.
37. Rijkse, E.; Ceuppens, S.; Qi, H.; JNM, I. J.; Hesselink, D. A.; Minnee, R. C., Implementation of donation after circulatory death kidney transplantation can safely enlarge the donor pool: A systematic review and meta-analysis. *Int J Surg* **2021,** *92*, 106021.
38. Peters-Sengers, H.; Berger, S. P.; Heemskerk, M. B.; Al Arashi, D.; Homan van der Heide, J. J.; Hemke, A. C.; Ten Berge, I. J.; Idu, M. M.; Betjes, M. G.; van Zuilen, A. D.; Hilbrands, L. B.; de Vries, A. P.; Nurmohamed, A. S.; Christiaans, M. H.; Ernest van Heurn, L. W.; de Fijter, J. W.; Bemelman, F. J., Stretching the Limits of Renal Transplantation in Elderly Recipients of Grafts from Elderly Deceased Donors. *J Am Soc Nephrol* **2017,** *28* (2), 621-631.
39. Hellemans, R.; Kramer, A.; De Meester, J.; Collart, F.; Kuypers, D.; Jadoul, M.; Van Laecke, S.; Le Moine, A.; Krzesinski, J. M.; Wissing, K. M.; Luyckx, K.; van Meel, M.; de Vries, E.; Tieken, I.; Vogelaar, S.; Samuel, U.; Abramowicz, D.; Stel, V. S.; Jager, K. J., Does kidney transplantation with a standard or expanded criteria donor improve patient survival? Results from a Belgian cohort. *Nephrol Dial Transplant* **2021,** *36* (5), 918-926.
40. Yu, S.; Long, J. J.; Yu, Y.; Bowring, M. G.; Motter, J. D.; Ishaque, T.; Desai, N.; Segev, D. L.; Garonzik-Wang, J. M.; Massie, A. B., Survival benefit of accepting kidneys from older donation after cardiac death donors. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2021,** *21* (3), 1138-1146.
41. Mittal, S.; Adamusiak, A.; Horsfield, C.; Loukopoulos, I.; Karydis, N.; Kessaris, N.; Drage, M.; Olsburgh, J.; Watson, C. J.; Callaghan, C. J., A Re-evaluation of Discarded Deceased Donor Kidneys in the UK: Are Usable Organs Still Being Discarded? *Transplantation* **2017,** *101* (7), 1698-1703.
42. Reese, P. P.; Harhay, M. N.; Abt, P. L.; Levine, M. H.; Halpern, S. D., New Solutions to Reduce Discard of Kidneys Donated for Transplantation. *J Am Soc Nephrol* **2016,** *27* (4), 973-80.
43. Perez-Saez, M. J.; Montero, N.; Redondo-Pachon, D.; Crespo, M.; Pascual, J., Strategies for an Expanded Use of Kidneys From Elderly Donors. *Transplantation* **2017,** *101* (4), 727-745.
44. Moeckli, B.; Sun, P.; Lazeyras, F.; Morel, P.; Moll, S.; Pascual, M.; Buhler, L. H., Evaluation of donor kidneys prior to transplantation: an update of current and emerging methods. *Transpl Int* **2019,** *32* (5), 459-469.
45. De Beule, J.; Jochmans, I., Kidney Perfusion as an Organ Quality Assessment Tool-Are We Counting Our Chickens Before They Have Hatched? *Journal of clinical medicine* **2020,** *9* (3).
46. Darius, T.; Nath, J.; Mourad, M., Simply Adding Oxygen during Hypothermic Machine Perfusion to Combat the Negative Effects of Ischemia-Reperfusion Injury: Fundamentals and Current Evidence for Kidneys. *Biomedicines* **2021,** *9* (8), 993.
47. Kang, M.; Kim, S.; Choi, J. Y.; Kim, K. S.; Jung, Y. K.; Park, B.; Choi, D., Ex vivo kidney machine perfusion: meta-analysis of randomized clinical trials. *The British journal of surgery* **2024,** *111* (4).
48. Schutter, R., *Optimizing utilization and quality assessment of deceased donor kidneys*. University of Groningen: [Groningen], 2023.

49. Moers, C.; Smits, J. M.; Maathuis, M. H.; Treckmann, J.; van Gelder, F.; Napieralski, B. P.; van Kasterop-Kutz, M.; van der Heide, J. J.; Squifflet, J. P.; van Heurn, E.; Kirste, G. R.; Rahmel, A.; Leuvenink, H. G.; Paul, A.; Pirenne, J.; Ploeg, R. J., Machine perfusion or cold storage in deceased-donor kidney transplantation. *N Engl J Med* **2009,** *360* (1), 7-19.
50. Bellini, M. I.; Yiu, J.; Nozdrin, M.; Papalois, V., The Effect of Preservation Temperature on Liver, Kidney, and Pancreas Tissue ATP in Animal and Preclinical Human Models. *Journal of clinical medicine* **2019,** *8* (9).
51. Tingle, S. J.; Figueiredo, R. S.; Moir, J. A.; Goodfellow, M.; Talbot, D.; Wilson, C. H., Machine perfusion preservation versus static cold storage for deceased donor kidney transplantation. *The Cochrane database of systematic reviews* **2019,** *3* (3), CD011671.
52. Kox, J.; Moers, C.; Monbaliu, D.; Strelniece, A.; Treckmann, J.; Jochmans, I.; Leuvenink, H.; Van Heurn, E.; Pirenne, J.; Paul, A.; Ploeg, R., The Benefits of Hypothermic Machine Preservation and Short Cold Ischemia Times in Deceased Donor Kidneys. *Transplantation* **2018,** *102* (8), 1344-1350.
53. Gallinat, A.; Moers, C.; Treckmann, J.; Smits, J. M.; Leuvenink, H. G.; Lefering, R.; van Heurn, E.; Kirste, G. R.; Squifflet, J. P.; Rahmel, A.; Pirenne, J.; Ploeg, R. J.; Paul, A., Machine perfusion versus cold storage for the preservation of kidneys from donors >/= 65 years allocated in the Eurotransplant Senior Programme. *Nephrol Dial Transplant* **2012,** *27* (12), 4458-63.
54. Watson, C. J.; Wells, A. C.; Roberts, R. J.; Akoh, J. A.; Friend, P. J.; Akyol, M.; Calder, F. R.; Allen, J. E.; Jones, M. N.; Collett, D.; Bradley, J. A., Cold machine perfusion versus static cold storage of kidneys donated after cardiac death: a UK multicenter randomized controlled trial. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2010,** *10* (9), 1991-9.
55. Foguenne, M.; MacMillan, S.; Kron, P.; Nath, J.; Devresse, A.; De Meyer, M.; Michel, M.; Hosgood, S.; Darius, T., Current Evidence and Future Perspectives to Implement Continuous and End-Ischemic Use of Normothermic and Oxygenated Hypothermic Machine Perfusion in Clinical Practice. *Journal of clinical medicine* **2023,** *12* (9).
56. Jochmans, I.; Brat, A.; Davies, L.; Hofker, H. S.; van de Leemkolk, F. E. M.; Leuvenink, H. G. D.; Knight, S. R.; Pirenne, J.; Ploeg, R. J.; Collaboration, C. T.; Consortium for Organ Preservation in, E., Oxygenated versus standard cold perfusion preservation in kidney transplantation (COMPARE): a randomised, double-blind, paired, phase 3 trial. *Lancet (London, England)* **2020,** *396* (10263), 1653-1662.
57. Ravaioli, M.; De Pace, V.; Angeletti, A.; Comai, G.; Vasuri, F.; Baldassarre, M.; Maroni, L.; Odaldi, F.; Fallani, G.; Caraceni, P.; Germinario, G.; Donadei, C.; Malvi, D.; Del Gaudio, M.; Bertuzzo, V. R.; Siniscalchi, A.; Ranieri, V. M.; D'Errico, A.; Pasquinelli, G.; Morelli, M. C.; Pinna, A. D.; Cescon, M.; La Manna, G., Hypothermic Oxygenated New Machine Perfusion System in Liver and Kidney Transplantation of Extended Criteria Donors:First Italian Clinical Trial. *Scientific reports* **2020,** *10* (1), 6063.
58. Meister, F. A.; Czigany, Z.; Bednarsch, J.; Boecker, J.; Wiltberger, G.; Rohlfs, W.; Neumann, U. P.; Lurje, G., Hypothermic oxygenated machine perfusion-Preliminary experience with end-ischemic reconditioning of marginal kidney allografts. *Clinical transplantation* **2019,** *33* (10), e13673.
59. Husen, P.; Boffa, C.; Jochmans, I.; Krikke, C.; Davies, L.; Mazilescu, L.; Brat, A.; Knight, S.; Wettstein, D.; Cseprekal, O.; Banga, N.; Bellini, M. I.; Szabo, L.; Ablorsu, E.; Darius, T.; Quiroga, I.; Mourad, M.; Pratschke, J.; Papalois, V.; Mathe, Z.; Leuvenink, H. G. D.; Minor, T.; Pirenne, J.; Ploeg, R. J.; Paul, A., Oxygenated End-Hypothermic Machine Perfusion in Expanded Criteria Donor Kidney Transplant: A Randomized Clinical Trial. *JAMA Surg* **2021,** *156* (6), 517-525.
60. Hosgood, S. A.; Callaghan, C. J.; Wilson, C. H.; Smith, L.; Mullings, J.; Mehew, J.; Oniscu, G. C.; Phillips, B. L.; Bates, L.; Nicholson, M. L., Normothermic machine perfusion versus static cold storage in donation after circulatory death kidney transplantation: a randomized controlled trial. *Nat Med* **2023,** *29* (6), 1511-1519.

61. Verstraeten, L.; Jochmans, I., Sense and Sensibilities of Organ Perfusion as a Kidney and Liver Viability Assessment Platform. *Transpl Int* **2022,** *35*, 10312.
62. Groen, H.; Moers, C.; Smits, J. M.; Treckmann, J.; Monbaliu, D.; Rahmel, A.; Paul, A.; Pirenne, J.; Ploeg, R. J.; Buskens, E., Cost-effectiveness of hypothermic machine preservation versus static cold storage in renal transplantation. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2012,** *12* (7), 1824-30.
63. Gomez, V.; Galeano, C.; Diez, V.; Bueno, C.; Diaz, F.; Burgos, F. J., Economic impact of the introduction of machine perfusion preservation in a kidney transplantation program in the expanded donor era: cost-effectiveness assessment. *Transplantation proceedings* **2012,** *44* (9), 2521-4.
64. Akalay, S.; Hosgood, S. A., How to Best Protect Kidneys for Transplantation—Mechanistic Target. *Journal of clinical medicine* **2023,** *12* (5), 1787.
65. Savoye, E.; Legendre, C.; Neuzillet, Y.; Peraldi, M. N.; Grimbert, P.; Ouali, N.; Durand, M.; Badet, L.; Kerbaul, F.; Pastural, M.; Legeai, C.; Macher, M. A.; Snanoudj, R., Long-term survival benefit from dual kidney transplantation using kidneys from donors with very extended criteria-a French cohort between 2002 and 2014. *Nephrol Dial Transplant* **2022,** *37* (5), 982-990.
66. Patrono, D.; Colli, F.; Colangelo, M., How Can Machine Perfusion Change the Paradigm of Liver Transplantation for Patients with Perihilar Cholangiocarcinoma? *Journal of clinical medicine* **2023,** *12* (5).
67. Krendl, F. J.; Bellotti, R.; Sapisochin, G., Transplant oncology – Current indications and strategies to advance the field. *JHEP Rep* **2024,** *6* (2).
68. Jay, C. L.; Lyuksemburg, V.; Ladner, D. P., Ischemic Cholangiopathy After Controlled Donation After Cardiac Death Liver Transplantation: A Meta-analysis. *Ann Surg* **2011,** *253* (2).
69. Olthoff, K. M.; Kulik, L.; Samstein, B., Validation of a current definition of early allograft dysfunction in liver transplant recipients and analysis of risk factors. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc* **2010,** *16* (8).
70. Karimian, N.; Westerkamp, A. C.; Porte, R. J., Biliary complications after orthotopic liver transplantation. *Curr Opin Organ Transplant* **2014,** *19* (3), 209–216.
71. Glanemann, M.; Langrehr, J. M.; Stange, B. J., Clinical implications of hepatic preservation injury after adult liver transplantation. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg* **2003,** *3* (8), 1003–1009.
72. Brunner, S. M.; Junger, H.; Ruemmele, P., Bile duct damage after cold storage of deceased donor livers predicts biliary complications after liver transplantation. *J Hepatol* **2013,** *58* (6), 1133–1139.
73. Monbaliu, D.; Pirenne, J.; Talbot, D., Liver transplantation using Donation after Cardiac Death donors. *J Hepatol* **2012,** *56* (2), 474–485.
74. op den Dries, S.; Westerkamp, A.; Karimian, N., Injury to peribiliary glands and vascular plexus before liver transplantation predicts formation of non-anastomotic biliary strictures. *J Hepatol* **2014,** *60* (6), 1172–1179.
75. Watson, C. J. E.; Jochmans, I., From “Gut Feeling” to Objectivity: Machine Preservation of the Liver as a Tool to Assess Organ Viability. *Curr Transplant Rep* **2018,** *5* (1), 72–81.
76. Blondeel, J.; Monbaliu, D.; Gilbo, N., Dynamic liver preservation: Are we still missing pieces of the puzzle? *Artif Organs* **2023,** *47* (2), 248–259.
77. Nasralla, D.; Coussios, C. C.; Mergental, H., A randomized trial of normothermic preservation in liver transplantation. *Nature* **2018,** *557* (7703), 50–56.
78. Markmann, J. F.; Abouljoud, M. S.; Ghobrial, R. M., Impact of Portable Normothermic Blood-Based Machine Perfusion on Outcomes of Liver Transplant: The OCS Liver PROTECT Randomized Clinical Trial. *JAMA Surg* **2022,** *157* (3).
79. Ravaioli, M.; Germinario, G.; Dajti, G., Hypothermic oxygenated perfusion in extended criteria donor liver transplantation—A randomized clinical trial. *American journal of*

transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons **2022,** *22* (10), 2401–2408.
80. Chapman, W. C.; Barbas, A. S.; D'Alessandro, A. M.; Guo, Z.; Zhao, Q.; Jia, Z., Normothermic Machine Perfusion of Donor Livers for Transplantation in the United States: A Randomized Controlled Trial. *Ann Surg* **2023,** *278* (5).
81. Guo, Z.; Zhao, Q.; Jia, Z.; Huang, C.; Wang, D.; Ju, W.; Zhang, J.; Yang, L.; Huang, S.; Chen, M.; Zhu, X.; Hu, A.; Ma, Y.; Wu, L.; Chen, Y.; Han, M.; Tang, Y.; Wang, G.; Wang, L.; Li, L.; Xiong, W.; Zhang, Z.; Shen, Y.; Tang, Z.; Zhu, C.; Chen, X.; Hu, X.; Guo, Y.; Chen, H.; Ma, Y.; Zhang, T.; Huang, S.; Zeng, P.; Lai, S.; Wang, T.; Chen, Z.; Gong, J.; Yu, J.; Sun, C.; Li, C.; Tan, H.; Liu, Y.; Dong, Y.; Sun, C.; Liao, B.; Ren, J.; Zhou, Z.; Andrea, S.; Björn, N.; Cai, C.; Gong, F.; Rong, J.; Huang, W.; Guan, X.; Clavien, P. A.; Stefan, T. G.; Huang, J.; He, X., A randomized-controlled trial of ischemia-free liver transplantation for end-stage liver disease. *J Hepatol* **2023,** *79* (2), 394-402.
82. van Rijn, R.; Schurink, I.; de Vries, Y., Hypothermic Machine Perfusion in Liver Transplantation - A Randomized Trial. *N Engl J Med* **2021,** *384* (15), 1391–1401.
83. Czigany, Z.; Pratschke, J.; Froněk, J., 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), 705–712.
84. Schlegel, A.; Mueller, M.; Muller, X., A multicenter randomized-controlled trial of hypothermic oxygenated perfusion (HOPE) for human liver grafts before transplantation. *J Hepatol* **2023,** *78* (4), 783–793.
85. Brüggenwirth, I. M. A.; Lantinga, V. A.; Lascaris, B., Prolonged hypothermic machine perfusion enables daytime liver transplantation – an IDEAL stage 2 prospective clinical trial. *eClinicalMedicine* **2024,** *68* (102411).
86. Hessheimer, A. J., In Situ Normothermic Regional Perfusion in Controlled Donation After Circulatory Determination Death: Organ Utilization, Outcomes, and Elusiveness of a Randomized Clinical Trial. *Transplantation* **2023,** *107* (2), 311–312.
87. Hessheimer, A. J.; Rosa, G.; Gastaca, M., Abdominal normothermic regional perfusion in controlled donation after circulatory determination of death liver transplantation: Outcomes and risk factors for graft loss. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg* **2022,** *22* (4), 1169–1181.
88. De Carlis, R.; Schlegel, A.; Frassoni, S., 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), 2385–2396.
89. Patrono, D.; Zanierato, M.; Vergano, M., 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).
90. Cardini, B.; Oberhuber, R.; Fodor, M., Clinical Implementation of Prolonged Liver Preservation and Monitoring Through Normothermic Machine Perfusion in Liver Transplantation. *Transplantation* **2020,** *104* (9).
91. Mergental, H.; Laing, R. W.; Kirkham, A. J., Discarded livers tested by normothermic machine perfusion in the VITTAL trial: Secondary end points and 5-year outcomes. *Liver Transpl* **2024,** *30* (1), 30–45.
92. Eden, J.; Breuer, E.; Birrer, D., Screening for mitochondrial function before useroutine liver assessment during hypothermic oxygenated perfusion impacts liver utilization. *eBioMedicine* **2023,** *98* (104857).
93. Steinberg, I.; Patrono, D.; Cesaris, E., Viability assessment of livers donated after circulatory determination of death during normothermic regional perfusion. *Artif Organs* **2023,** *47* (10), 1592–1603.

94. N, D. S.; A, C.; V, N.-T.; F, R.; D, P.; R, R., State-of-the-Art and Future Directions in Organ Regeneration with Mesenchymal Stem Cells and Derived Products during Dynamic Liver Preservation. *Med Kaunas Lith* **2022,** *58* (12).
95. de Vries, Y.; Brüggenwirth, I.; Karangwa, S., Dual Versus Single Oxygenated Hypothermic Machine Perfusion of Porcine Livers: Impact on Hepatobiliary and Endothelial Cell Injury. *Transplant Direct* **2021,** *7* (9).
96. van Leeuwen, O.; Bodewes, S.; Lantinga, V. A., Sequential hypothermic and normothermic machine perfusion enables safe transplantation of high-risk donor livers. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2022,** *22* (6), 1658–1670.
97. Ravikumar, R.; Jassem, W.; Mergental, H., Liver Transplantation After Ex Vivo Normothermic Machine Preservation: A Phase 1 (First-in-Man) Clinical Trial. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg* **2016,** *16* (6), 1779–1787.
98. Ghinolfi, D.; Rreka, E.; Tata, V., Prospective Trial for Normothermic Machine Perfusion Evaluation in Liver Transplantation From Older Donors. *Liver Transpl* **2019,** *25* (3), 436–449.
99. Patrono, D.; Carlis, R.; Gambella, A., Viability assessment and transplantation of fatty liver grafts using end-ischemic normothermic machine perfusion. *Liver Transpl* **2023,** *29* (5).
100. Quintini, C.; Del Prete, L.; Simioni, A., Transplantation of declined livers after normothermic perfusion. *Surgery* **2022,** *171* (3), 747–756.
101. Watson, C. J. E.; Gaurav, R.; Fear, C., Predicting Early Allograft Function After Normothermic Machine Perfusion. *Transplantation* **2022,** *106* (12), 2391–2398.
102. Weissenbacher, A.; Bogensperger, C.; Oberhuber, R., Perfusate Enzymes and Platelets Indicate Early Allograft Dysfunction After Transplantation of Normothermically Preserved Livers. *Transplantation* **2022,** *106* (4).
103. Watson, C. J. E.; Kosmoliaptsis, V.; Pley, C., Observations on the ex situ perfusion of livers for transplantation. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2018,** *18* (8), 2005–2020.
104. Matton, A. P. M.; Vries, Y.; Burlage, L. C., Biliary Bicarbonate, pH, and Glucose Are Suitable Biomarkers of Biliary Viability During Ex Situ Normothermic Machine Perfusion of Human Donor Livers. *Transplantation* **2019,** *103* (7), 1405–1413.
105. de Jong, I.; Bodewes, S.; van Leeuwen, O., Restoration of Bile Duct Injury of Donor Livers During Ex Situ Normothermic Machine Perfusion. *Transplantation* **2023,** *107* (6).
106. Patrono, D.; Lonati, C.; Romagnoli, R., Viability testing during liver preservation. *Curr Opin Organ Transplant* **2022,** *27* (5), 454–465.
107. Mergental, H.; Laing, R. W.; Hodson, J., Introduction of the Concept of Diagnostic Sensitivity and Specificity of Normothermic Perfusion Protocols to Assess High-Risk Donor Livers. *Liver Transpl* **2022,** *28* (5).
108. Hofmann, J.; Meszaros, A. T.; Buch, M. L., Bioenergetic and Cytokine Profiling May Help to Rescue More DCD Livers for Transplantation. *Int J Mol Sci* **2023,** *24* (11).
109. Thorne, A. M.; Wolters, J. C.; Lascaris, B., Bile proteome reveals biliary regeneration during normothermic preservation of human donor livers. *Nat Commun* **2023,** *14* (1).
110. Eshmuminov, D.; Becker, D.; Bautista Borrego, L., An integrated perfusion machine preserves injured human livers for 1 week. *Nat Biotechnol* **2020,** *38* (2), 189–198.
111. Lau, N. S.; Ly, M.; Dennis, C., Long-term normothermic perfusion of human livers for longer than 12 days. *Artif Organs* **2022,** *46* (12), 2504–2510.
112. Clavien, P.-A.; Dutkowski, P.; Mueller, M.; Eshmuminov, D.; Bautista Borrego, L.; Weber, A.; Muellhaupt, B.; Sousa Da Silva, R. X.; Burg, B. R.; Rudolf von Rohr, P.; Schuler, M. J.; Becker, D.; Hefti, M.; Tibbitt, M. W., Transplantation of a human liver following 3 days of ex situ normothermic preservation. *Nature Biotechnology* **2022,** *40* (11), 1610-1616.
113. Guarrera, J. V.; Henry, S. D.; Samstein, B., Hypothermic Machine Preservation in Human Liver Transplantation: The First Clinical Series. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2010,** *10* (2).

114. Grąt, M.; Morawski, M.; Zhylko, A., Routine End-ischemic Hypothermic Oxygenated Machine Perfusion in Liver Transplantation From Donors After Brain Death: A Randomized Controlled Trial. *Ann Surg* **2023,** *278* (5).
115. Eden, J.; Brüggenwirth, I. M. A.; Berlakovich, G., 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. Published online July* **2024,** *3* (24), 02341–9.
116. Panayotova, G. G.; Lunsford, K. E.; Quillin, R. C., 3rd; Rana, A.; Agopian, V. G.; Lee-Riddle, G. S.; Markovic, D.; Paterno, F.; Griesemer, A. D.; Amin, A.; Alonso, D.; Rocca, J. P.; Borja-Cacho, D.; Hernandez-Alejandro, R.; Fung, J. J.; Pelletier, S. J.; Shah, S. A.; Guarrera, J. V., Portable hypothermic oxygenated machine perfusion for organ preservation in liver transplantation: A randomized, open-label, clinical trial. *Hepatology (Baltimore, Md.)* **2024,** *79* (5), 1033-1047.
117. Agopian, V. G.; Harlander-Locke, M. P.; Markovic, D., Evaluation of Early Allograft Function Using the Liver Graft Assessment Following Transplantation Risk Score Model. *JAMA Surg* **2018,** *153* (5).
118. Muller, X.; Schlegel, A.; Kron, P., Novel Real-time Prediction of Liver Graft Function During Hypothermic Oxygenated Machine Perfusion Before Liver Transplantation. *Ann Surg* **2019,** *270* (5), 783–790.
119. Patrono, D.; Roggio, D.; Mazzeo, A. T., Clinical assessment of liver metabolism during hypothermic oxygenated machine perfusion using microdialysis. *Artif Organs* **2022,** *46* (2), 281–295.
120. Eden, J.; Thorne, A. M.; Bodewes, S. B., Assessment of liver graft quality during hypothermic oxygenated perfusion: the first international validation study. *J Hepatol. Published online September* **2024,** *7*.
121. Brüggenwirth, I. M. A.; Mueller, M.; Lantinga, V. A., Prolonged preservation by hypothermic machine perfusion facilitates logistics in liver transplantation: A European observational cohort study. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2022,** *22* (7), 1842–1851.
122. Bonaccorsi-Riani, E.; Gillooly, A. R.; Iesari, S., Delivering siRNA Compounds During HOPE to Modulate Organ Function: A Proof-of-concept Study in a Rat Liver Transplant Model. *Transplantation* **2022,** *106* (8), 1565–1576.
123. Minor, T.; Efferz, P.; Fox, M.; Wohlschlaeger, J.; Lüer, B., Controlled oxygenated rewarming of cold stored liver grafts by thermally graduated machine perfusion prior to reperfusion. *Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg* **2013,** *13* (6), 1450–1460.
124. Hoyer, D. P.; Mathé, Z.; Gallinat, A., Controlled Oxygenated Rewarming of Cold Stored Livers Prior to Transplantation: First Clinical Application of a New Concept. *Transplantation* **2016,** *100* (1), 147–152.
125. Rayar, M.; Beaurepaire, J. M.; Bajeux, E., Hypothermic Oxygenated Perfusion Improves Extended Criteria Donor Liver Graft Function and Reduces Duration of Hospitalization Without Extra Cost: The PERPHO Study. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc* **2021,** *27* (3), 349–362.
126. Webb, A. N.; Lester, E. L. W.; Shapiro, A. M. J.; Eurich, D. T.; Bigam, D. L., Cost-utility analysis of normothermic machine perfusion compared to static cold storage in liver transplantation in the Canadian setting. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons* **2022,** *22* (2), 541–551.
127. Javanbakht, M.; Mashayekhi, A.; Trevor, M.; Branagan-Harris, M.; Atkinson, J., Costutility analysis of normothermic liver perfusion with the OrganOx metra compared to static cold storage in the United Kingdom. *J Med Econ* **2020,** *23* (11), 1284–1292.
128. Wehrle, C. J.; Hong, H.; Gross, A., The impact of normothermic machine perfusion and acuity circles on waitlist time, mortality, and cost in liver transplantation: A multicenter

experience. *Liver Transplant Off Publ Am Assoc Study Liver Dis Int Liver Transplant Soc. Published online June* **2024,** *5*.
129. Cenik, I.; Van Slambrouck, J.; Barbarossa, A.; Jin, X.; Provoost, A. L.; Patel, P.; Churchill, L.; Bulka, B.; Haney, J.; Ceulemans, L. J., Temperature Dynamics of Porcine and Human Lungs During Static Ice Storage: Ice Is Not 4 C. *Journal of clinical medicine* **2025,** *20;14(6):2127*.
130. Van Raemdonck, D.; Van Slambrouck, J.; Ceulemans, L., Donor lung preservation for transplantation—where do we go from here? *J Thorac Dis* **2022,** *14* (9), 10 21037 –22–949.
131. Cenik, I.; Van Slambrouck, J.; Provoost, A. L.; Barbarossa, A.; Vanluyten, C.; Boelhouwer, C.; Vanaudenaerde, B. M.; Vos, R.; Pirenne, J.; Van Raemdonck, D. E.; Ceulemans, L. J., Controlled Hypothermic Storage for Lung Preservation: Leaving the Ice Age Behind. *Transpl Int* **2024,** *37* (12601).
132. Stukov, Y.; Jacobs, J. P.; Bleiweis, M. S.; Aladaileh, M.; Peek, G. J.; Kugler, L.; Bilgili, A.; Schecter, M. G.; Rackauskas, M., First Pediatric Lung Transplant Using the Paragonix BAROguard Preservation System. *Pediatric transplantation* **2025,** *29* (7), e70179.
133. Nakata, K.; Alderete, I.; Arnold, C. J.; Hartwig, M. G., Overview of novel donor lung preservation system mediating stable organ temperature and airway pressure. *Expert review of medical devices* **2024,** *21* (12), 1057-1059.
134. Warnecke, G.; Van Raemdonck, D.; Smith, M. A.; Massard, G.; Kukreja, J.; Rea, F.; Loor, G.; Robertis, F.; Nagendran, J.; Dhital, K. K.; Moradiellos Díez, F. J.; Knosalla, C.; Bermudez, C. A.; Tsui, S.; McCurry, K.; Wang, I. W.; Deuse, T.; Lesèche, G.; Thomas, P.; Tudorache, I.; Kühn, C.; Avsar, M.; Wiegmann, B.; Sommer, W.; Neyrinck, A.; Schiavon, M.; Calabrese, F.; Santelmo, N.; Olland, A.; Falcoz, P. E.; Simon, A. R.; Varela, A.; Madsen, J. C.; Hertz, M.; Haverich, A.; Ardehali, A., Normothermic ex-vivo preservation with the portable Organ Care System Lung device for bilateral lung transplantation (INSPIRE): a randomised, open-label, non-inferiority, phase 3 study. *Lancet Respir Med* **2018,** *May;6(5):357-367*.
135. Loor, G.; Warnecke, G.; Villavicencio, M. A.; Smith, M. A.; Kukreja, J.; Ardehali, A.; Hartwig, M.; Daneshmand, M. A.; Hertz, M. I.; Huddleston, S.; Haverich, A.; Madsen, J. C.; Van Raemdonck, D., Portable normothermic ex-vivo lung perfusion, ventilation, and functional assessment with the Organ Care System on donor lung use for transplantation from extended-criteria donors (EXPAND): a single-arm, pivotal trial. *Lancet Respir Med* **2019,** (v;7(11):975-984).
136. Gouchoe, D. A.; Sanchez, P. G.; D'Cunha, J.; Bermudez, C. A.; Daneshmand, M. A.; Davis, R. D.; Hartwig, M. G.; Wozniak, T. C.; Kon, Z. N.; Griffith, B. P.; Lynch, W. R.; Machuca, T. N.; Weyant, M. J.; Jessen, M. E.; Mulligan, M. S.; D'Ovidio, F.; Camp, P. C.; Cantu, E.; Whitson, B. A.; N.o.v.e.l; Investigators, N. O. V. E. L. E. T., Ex vivo lung perfusion in donation after circulatory death: A post hoc analysis of the Normothermic Ex Vivo Lung Perfusion as an Assessment of Extended/Marginal Donors Lungs trial. *J Thorac Cardiovasc Surg* **2024,** *734* (e7).
137. Cypel, M.; Yeung, J. C.; Mingyao, L., Normothermic ex vivo lung perfusion in clinical lung transplantation. *N Engl J Med* **2011,** *364* (15), 1431–1440.
138. Wang, L. S.; Yoshikawa, K.; Miyoshi, S.; Nakamoto, K.; Hsieh, C. M.; Yamazaki, F.; Guerreiro Cardoso, P. F.; Schaefers, H. J.; Brito, J.; Keshavjee, S. H.; et al., The effect of ischemic time and temperature on lung preservation in a simple ex vivo rabbit model used for functional assessment. *J Thorac Cardiovasc Surg* **1989,** *98* (3), 333-42.
139. Date, H.; Lima, O.; Matsumura, A.; Tsuji, H.; d'Avignon, D. A.; Cooper, J. D., In a Canine Model, Lung Preservation at 10° C Is Superior to That at 4° C: A Comparison of Two Preservation Temperatures on Lung Function and on Adenosine Triphosphate Level Measured by Phosphorus 31-Nuclear Magnetic Resonance. *J Thorac Cardiovasc Surg* **1992,** *103* (4), 773–80.
140. Nakamoto, K.; Maeda, M.; Taniguchi, K.; Tsubota, N.; Kawashima, Y., A Study on Optimal Temperature for Isolated Lung Preservation. *Ann Thorac Surg* **1992,** *53* (1), 101–8.

141. Keshavjee, S. H.; Yamazaki, F.; Cardoso, P. F.; McRitchie, D. I.; Patterson, G. A.; Cooper, J. D., A Method for Safe Twelve-Hour Pulmonary Preservation. *J Thorac Cardiovasc Surg* **1989,** *98* (4), 529–34.
142. Mayer, E.; Puskas, J. D.; Cardoso, P. F. G.; Shi, S.; Slutsky, A. S.; Patterson, G. A., Reliable Eighteen-Hour Lung Preservation at 4 Degrees and 10 Degrees C by Pulmonary Artery Flush After High-Dose Prostaglandin E1 Administration. *J Thorac Cardiovasc Surg* **1992,** *103* (6), 1136–42.
143. Steen, S.; Sjöberg, T.; Massa, G.; Ericsson, L.; Lindberg, L., Safe Pulmonary Preservation for 12 Hours With Low-Potassium-Dextran Solution. *Ann Thorac Surg* **1993,** *55* (2), 434–40.
144. Ali, A.; Wang, A.; Ribeiro, R. V. P.; Beroncal, E. L.; Baciu, C.; Galasso, M., Static lung storage at 10°C maintains mitochondrial health and preserves donor organ function. *Sci Transl Med* **2021,** *13* (611).
145. Ali, A.; Hoetzenecker, K.; Cruz, J. C.; Schwarz, S.; Barturen, M. G.; Tomlinson, G., *Extension of cold static donor lung preservation at 10°C*. NEJM Evid: 2023; Vol. 2.
146. Abdelnour-Berchtold, E.; Ali, A.; Baciu, C.; Beroncal, E. L.; Wang, A.; Hough, O., Evaluation of 10°C as the Optimal Storage Temperature for Aspiration-Injured Donor Lungs in a Large Animal Transplant Model. *J Heart Lung Transplant* **2022,** *41* (12), 1679–88.
147. Novysedlak, R.; Provoost, A. L.; Langer, N. B.; Van Slambrouck, J.; Barbarossa, A.; Cenik, I.; Van Raemdonck, D.; Vos, R.; Vanaudenaerde, B. M.; Rabi, S. A.; Keller, B. C.; Svorcova, M.; Ozaniak Strizova, Z.; Vachtenheim, J., Jr.; Lischke, R.; Ceulemans, L. J., Extended ischemic time (>15 hours) using controlled hypothermic storage in lung transplantation: A multicenter experience. *J Heart Lung Transplant* **2024,** *43* (6), 999-1004.
148. Provoost, A. L.; Novysedlak, R.; Van Raemdonck, D.; Van Slambrouck, J.; Prisciandaro, E.; Vandervelde, C. M.; Barbarossa, A.; Jin, X.; Denaux, K.; Leyn, P.; Veer, H.; Depypere, L.; Jansen, Y.; Pirenne, J.; Neyrinck, A.; Bouneb, S.; Ingels, C.; Jacobs, B.; Godinas, L.; Sadeleer, L.; Vos, R.; Svorcova, M.; Vajter, J.; Kolarik, J.; Tavandzis, J.; Havlin, J.; Ozaniak Strizova, Z.; Pozniak, J.; Simonek, J.; J, V., Jr.; Lischke, R.; Ceulemans, L. J., Lung transplantation following controlled hypothermic storage with a portable lung preservation device: first multicenter European experience. *Front Cardiovasc Med* **2024,** *11* (1370543).
149. Haney, J.; Hartwig, M.; Langer, N.; Sanchez, P.; Bush, E., 68) Not too warm, not too cold: real-world multi-center outcomes with elevated hypothermic preservation of donor lungs. *J Heart Lung Transplant* **2023,** *42:S39-40*.
150. Langer, N.; Kukreja, J.; Carrott, P.; Ceulemans, L.; Sanchez, P.; Forest, S.; Bush, E.; Schwartz, G.; Shigemura, N.; Huang, H.; Hartwig, M., Real-World Outcomes Using Controlled Moderate Hypothermia at 4-8°C for Lung Transplant: An Update from the Guardian-Lung Registry. *The Journal of Heart and Lung Transplantation* **2025,** *44* (4), S193-S194.
151. Cunningham, P. S.; Maidstone, R.; Durrington, H. J.; Venkateswaran, R. V.; Cypel, M.; Keshavjee, S., Incidence of Primary Graft Dysfunction After Lung Transplantation Is Altered by Timing of Allograft Implantation. *Thorax* **2019,** *74* (4), 413–6.
152. Van Slambrouck, J.; Carlon, M.; Van Raemdonck, D.; Ceulemans, L., Genetic modualtion in lung transplantation: epic odyssey of vector transduction and transgene experession. *J Thorac Cardiovasc Surg* **2023,** *Jul;166(1):e50-e51*.
153. Figueiredo, C.; Chen-Wacker, C.; Salman, J.; Carvalho-Oliveira, M.; Monthé, T. S.; Höffler, K.; Rother, T.; Hacker, K.; Valdivia, E.; Pogozhykh, O.; Hammer, S.; Sommer, W.; Yuzefovych, Y.; Wenzel, N.; Haverich, A.; Warnecke, G.; Blasczyk, R., Knockdown of swine leukocyte antigen expression in porcine lung transplants enables graft survival without immunosuppression..Sci Transl Med. **2024,** *17;16(756):eadi9548*.
154. Merkle, F.; Mata Forcades, M. T.; Pomar, J. L.; Seeberger, M.; Wahba, A., Statement on the qualification of cardiovascular perfusionists. *Interactive cardiovascular and thoracic surgery* **2014,** *18* (4), 409-10.

155. Debeuckelaere, G.; Bauer, A.; Lemmers, A.; De Somer, F., The European Board of Cardiovascular Perfusion statement on organ perfusion. *Interdisciplinary CardioVascular and Thoracic Surgery* **2025,** *40* (2).
156. American Board of Cardiovascular Perfusion *Position Statement on Organ Perfusion*; 2024.
157. American Board of Cardiovascular Perfusion *Annual report reference sheet*; 2023.

V. COMPOSITION DU GROUPE DE TRAVAIL

La composition du Bureau et du Collège ainsi que la liste des experts nommés par arrêté royal se trouvent sur le site Internet du CSS (page : Qui sommes-nous).

Tous les experts ont participé ***à titre personnel*** au groupe de travail. Leurs déclarations générales d'intérêts ainsi que celles des membres du Bureau et du Collège sont consultables sur le site Internet du CSS (page : conflits d'intérêts).

Les experts suivants ont participé à l'élaboration et à l'approbation de l'avis. Le groupe de travail a été présidé par **Hilde BEELE** et **Eric HOSTE** et le secrétariat scientifique a été assuré par Stijn BOODTS et Stijn EVERAERT.

BEELE Hilde	Dermatologie, Transplantation,Banques d'organes, de tissus et de cellules	UZ Gent
CEULEMANS Laurens	Chirurgie thoracique, transplantation pulmonaire	KULeuven
DARIUS Tom	Chirurgie abdominale et transplantation	UCLouvain
DE SOMER Filip	Chirurgie cardiaque et perfusion	UZ Gent
DEGEZELLE Karlien	Perfusion clinique	UZ Leuven
EKER Hasan	Chirurgie de transplantation abdominale	UZGent
GILBO Nicholas	Chirurgie de transplantation abdominale	CHU Liège
HOSTE Eric	Néphrologie et traumatologie	UZ Gent
LEDOUX Didier	Transplantation	CHU Liège
LEMMERS Andreas	Perfusion clinique	UZA
MARTENS Thomas	Chirurgie cardiaque	UZ Gent
MASTRUBUONI Stefano	Transplantation cardiaque	UC Louvain
MEYNS Bart	Chirurgie cardiaque	UZ Leuven
MIKHALSKI Dimitri	Chirurgie de transplantation	HUB
MONBALIU Diethard	Chirurgie de transplantation abdominale	UZ Leuven
NAESENS Maarten	Néphrologie et transplantation	UZ Leuven
PHILIPSEN Tine	Chirurgie et transplantation cardiaque	UZ Gent
PIRENNE Jacques	Chirurgie de transplantation abdominale	UZ Leuven
RANDON Caren	Chirurgie thoracique et de transplantation	UZ Gent
ROEYEN Geert	Transplantation hépatobiliaire et chirurgie endocrinienne	UZA
TCHANA SATO Vincent	Chirurgie cardiaque	ULiège
TULLENEERS-THEVISSEN Daniel Jacobs	Chirurgie de transplantation abdominale	UZ Brussel
VAN BEERSEL Dieter	Anesthésiologie	UZ Leuven
VAN RAEMDONCK Dirk	Chirurgie thoracique, transplantation pulmonaire	KULeuven
VANDENDRIESSCHE Katrien	Chirurgie cardiaque	UZ Leuven
VANDER KUYLEN Maarten	Chirurgie thoracique, transplantation pulmonaire	Hôpital Erasme
VANDEVOORDE Kristof	Perfusion clinique	UZ Leuven
VANDEWIELE Korneel	Perfusion clinique	UZ Gent
WISSING Karl Martin	Néphrologie et transplantation	UZBrussel

YSEBAERT Dirk	Chirurgie de transplantation abdominale	UZA

Le groupe de travail permanent en charge du domaine « Cellules, tissus et organes d'origine humaine et animale" a approuvé l'avis. Le groupe de travail permanent a été présidé par **Hilde BEELE** et le secrétariat scientifique a été assuré par Alexandra COUTTENIER.

ECTORS Nadine	Pathologie anatomique	KULeuven
LEWALLE Philippe	Hématologie et transplantation	IJB-HUB

Les experts suivants ont été entendu mais n'ont pas participé à l'approbation de l'avis:

JOCHMANS Ina	Chirurgie abdominale et transplantation	UZ Leuven
REGA Filip	Chirurgie cardiaque et transplantation	UZ Leuven

Les administrations et/ou cabinets ministériels suivants ont été entendus :

SÉNÉPART Isabelle	SPF Santé publique
COLENBIE Luc	SPF Santé publique

Au sujet du Conseil Supérieur de la Santé (CSS)

Le Conseil Supérieur de la Santé est un organe d'avis fédéral dont le secrétariat est assuré par le Service Fédéral Santé publique, Sécurité de la Chaîne alimentaire et Environnement. Il a été fondé en 1849 et rend des avis scientifiques relatifs à la santé publique aux ministres de la Santé publique et de l'Environnement, à leurs administrations et à quelques agences. Ces avis sont émis sur demande ou d'initiative. Le CSS s'efforce d'indiquer aux décideurs politiques la voie à suivre en matière de santé publique sur base des connaissances scientifiques les plus récentes.

Outre son secrétariat interne composé d'environ 25 collaborateurs, le Conseil fait appel à un large réseau de plus de 500 experts (professeurs d'université, collaborateurs d'institutions scientifiques, acteurs de terrain, etc.), parmi lesquels 300 sont nommés par arrêté royal au titre d'expert du Conseil. Les experts se réunissent au sein de groupes de travail pluridisciplinaires afin d'élaborer les avis.

En tant qu'organe officiel, le Conseil Supérieur de la Santé estime fondamental de garantir la neutralité et l'impartialité des avis scientifiques qu'il délivre. A cette fin, il s'est doté d'une structure, de règles et de procédures permettant de répondre efficacement à ces besoins et ce, à chaque étape du cheminement des avis. Les étapes clé dans cette matière sont l'analyse préalable de la demande, la désignation des experts au sein des groupes de travail, l'application d'un système de gestion des conflits d'intérêts potentiels (reposant sur des déclarations d'intérêt, un examen des conflits possibles, et une Commission de Déontologie) et la validation finale des avis par le Collège (organe décisionnel du CSS, constitué de 30 membres issus du pool des experts nommés). Cet ensemble cohérent doit permettre la délivrance d'avis basés sur l'expertise scientifique la plus pointue disponible et ce, dans la plus grande impartialité possible.

Après validation par le Collège, les avis sont transmis au requérant et au ministre de la Santé publique et sont rendus publics sur le site internet (www.hgr-css.be). Un certain nombre d'entre eux sont en outre communiqués à la presse et aux groupes cibles concernés (professionnels du secteur des soins de santé, universités, monde politique, associations de consommateurs, etc.).

Si vous souhaitez rester informé des activités et publications du CSS, vous pouvez envoyer un mail à l'adresse suivante : info.hgr-css@health.belgium.be.

Cette publication ne peut être vendue

www.conseilsuperieurdelasante.be

Avec le soutien administratif du SPF

Santé publique
Sécurité de la Chaîne alimentaire
Environnement