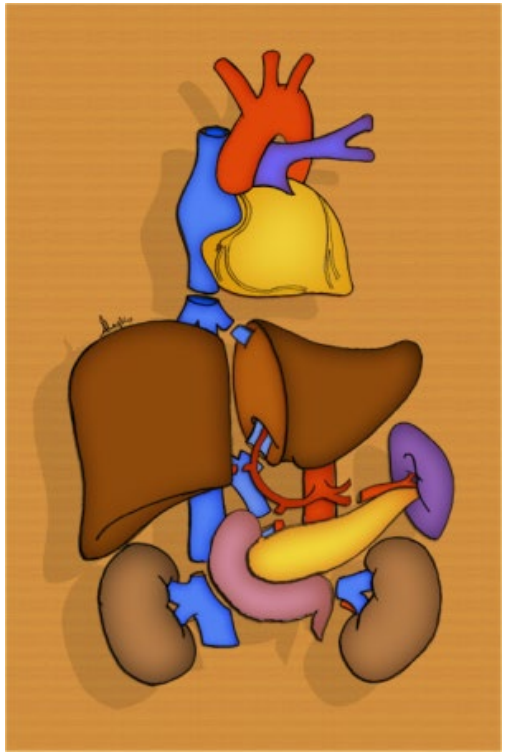
Perfusione ex situ ipotermica o normotermica degli organi addominali?



Professor M. Ravaioli

Department of General Surgery and Transplantation

Policlinico Sant'Orsola Malpighi

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STATI GENERALI

20 ANNI 1999·2019

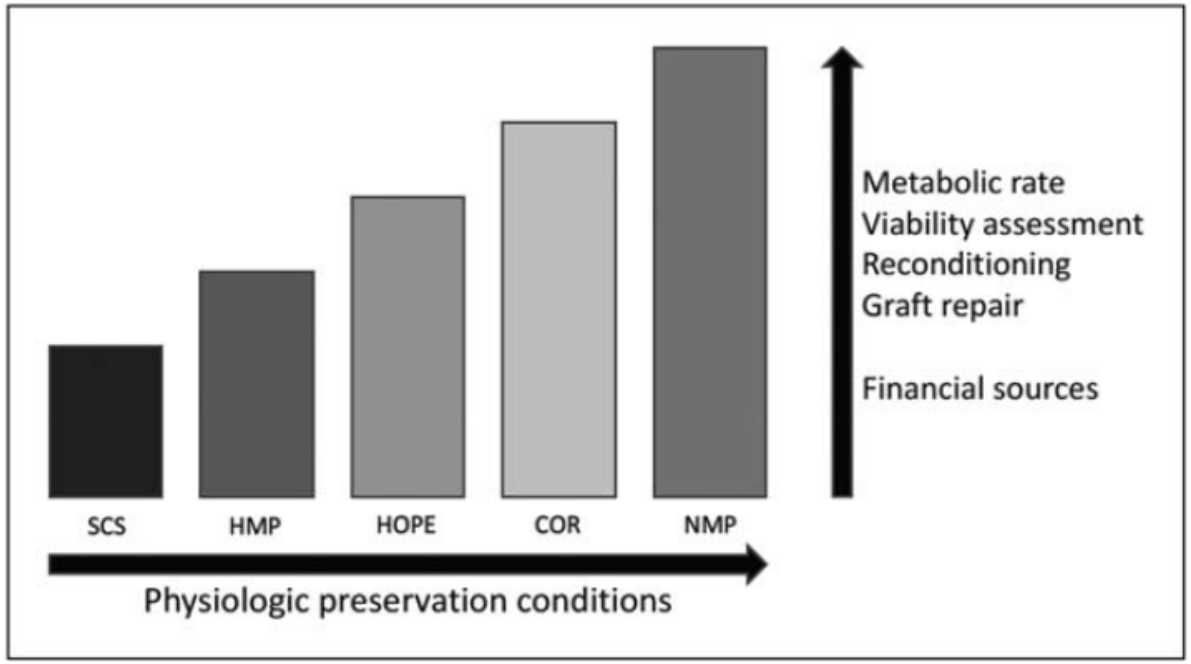
RETE NAZIONALE TRAPIANTI

6·7·8 NOVEMBRE

ROMA

Organ perfusion: cold or hot ?

Metabolic graft rate and cost



Hamar M, Selzner M Curr Opin Organ Transplant. 2018 Jun;23(3):369-374

Normothermic vs. hypothermic ± oxygenated

Normo-thermic oxygenation

Hypo-thermic oxygenation

Improve graft function with machine perfusion

Hypothermic perfusion

Hypothermic oxygenated perfusion

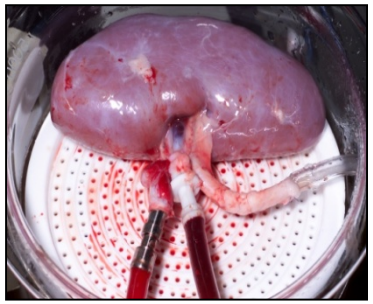
Normothermic perfusion

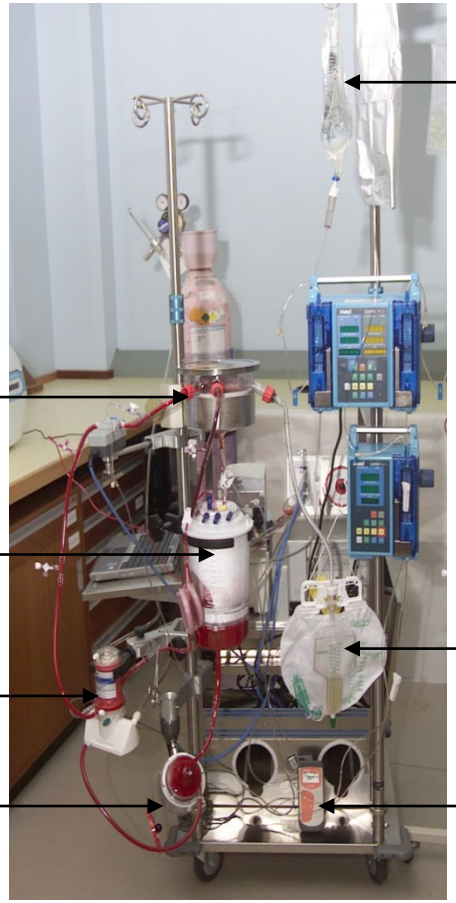
RAPID COMMUNICATIONS

First in Man Renal Transplantation After Ex Vivo Normothermic Perfusion

Sarah A. Hosgood and Michael L. Nicholson

(*Transplantation* 2011;92: 735–738)





Infusion fluids

Organ chamber

Venous Reservoir

Membrane oxygenator

Urinometer

Centrifugal Pump

Temperature probe

ARTICLE

https://doi.org/10.1038/s41586-018-0047-9

A randomized trial of normothermic preservation in liver transplantation

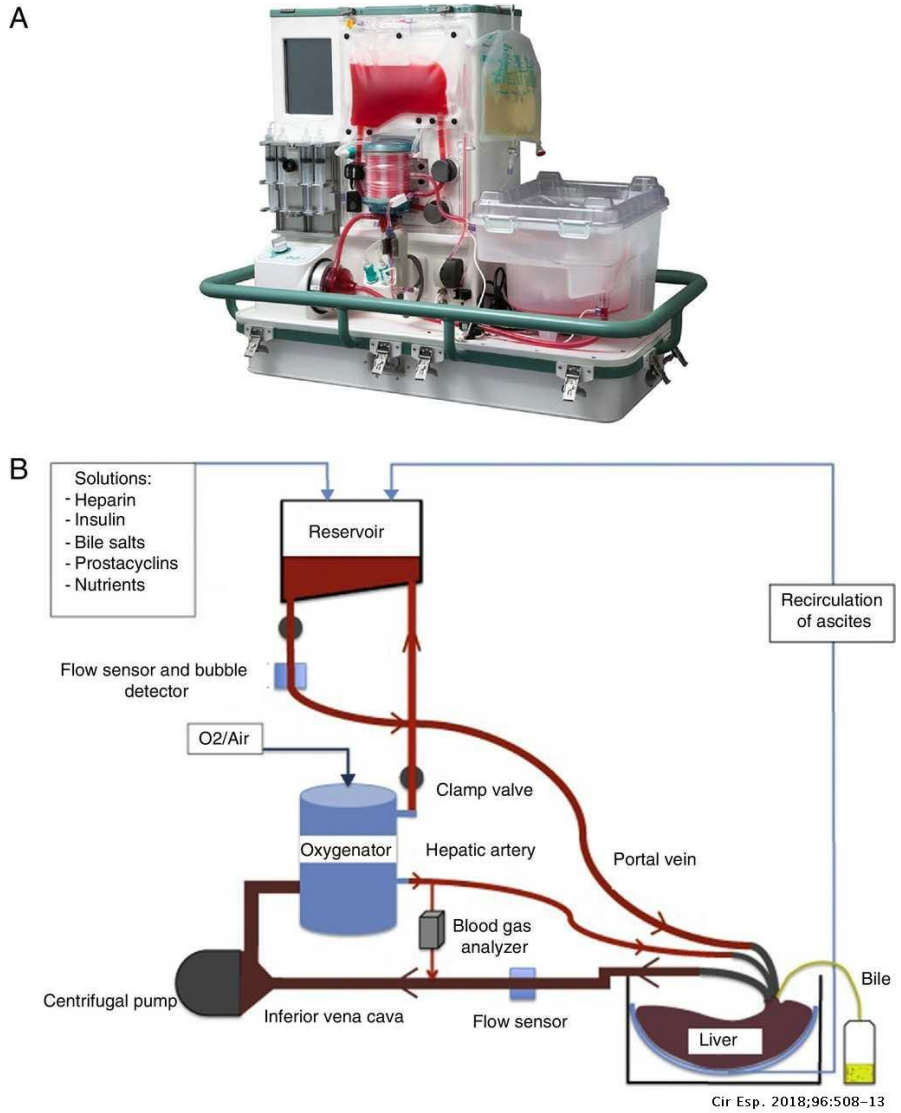
David Nasralla[1*], Constantin C. Coussios[2*], Hynek Mergental[3], M. Zeeshan Akhtar[1,4], Andrew J. Butler[5,20], Carlo D. L. Ceresa[1], Virginia Chiocchia[6,7], Susan J. Dutton[8], Juan Carlos García-Valdecasas[9], Nigel Heaton[10], Charles Imber[11], Wayel Jassem[10], Ina Jochmans[12,13], John Karani[10,14], Simon R. Knight[1,15], Peri Kocabayoglu[16], Massimo Malagò[11], Darius Mirza[3], Peter J. Morris[1,15], Arvind Pallan[17], Andreas Paul[16], Mihai Pavel[9], M. Thamara P. R. Perera[3], Jacques Pirenne[12,13], Reena Ravikumar[1], Leslie Russell[18], Sara Upponi[19], Chris J. E. Watson[5,20], Annemarie Weissenbacher[1], Rutger J. Ploeg[1], Peter J. Friend[1*] for the Consortium for Organ Preservation in Europe

Liver transplantation is a highly successful treatment, but is severely limited by the shortage in donor organs. However, many potential donor organs cannot be used; this is because sub-optimal livers do not tolerate conventional cold storage and there is no reliable way to assess organ viability preoperatively. Normothermic machine perfusion maintains the liver in a physiological state, avoids cooling and allows recovery and functional testing. Here we show that, in a randomized trial with 220 liver transplantations, compared to conventional static cold storage, normothermic preservation is associated with a 50% lower level of graft injury, measured by hepatocellular enzyme release, despite a 50% lower rate of organ discard and a 54% longer mean preservation time. There was no significant difference in bile duct complications, graft survival or survival of the patient. If translated to clinical practice, these results would have a major impact on liver transplant outcomes and waiting list mortality.

Nasralla D, Coussios CC, Mergental H, et al.

A randomized trial of normothermic preservation in liver transplantation.

Nature. 2018; 557:50-56



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 1, 2009 VOL. 360 NO. 1

Machine Perfusion or Cold Storage in Deceased-Donor Kidney Transplantation

Hypothermic oxygenated

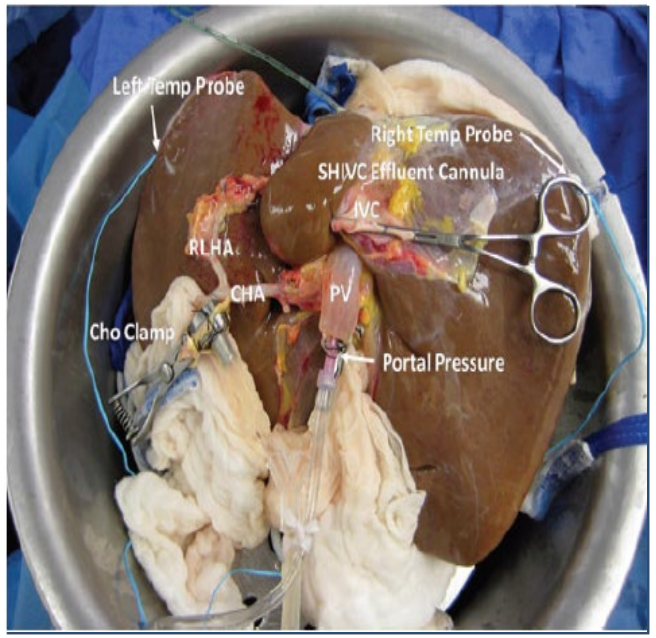
Hypothermic Machine Perfusion or Cold Storage in Deceased-Donor Liver Transplantation

J. V. Guarrera[a,*], S. D. Henry[a], B. Samstein[a], R. Odeh-Ramadan[a], M. Kinkhabwala[d], M. J. Goldstein[a], L. E. Ratner[a], J. F. Renz[c], H. T. Lee[b], R. S. Brown, Jr.[a] and J. C. Emond[a]

[a]*Center for Liver Disease and Transplantation, Department of Surgery and* [b]*Department of Anesthesiology, Columbia University Medical Center, New York, NY*
[c]*Division of Transplantation, University of Arizona, Tuscon, AZ*
[d]*Division of Transplantation, Montefiore Medical Center, Bronx, New York, NY*
**Corresponding author: James V. Guarrera, jjg46@columbia.edu or liverpreservation@gmail.com*

Hypothermic Machine Preservation in Human Liver Transplantation: The First Clinical Series

American Journal of Transplantation 2010; 10: 372–381

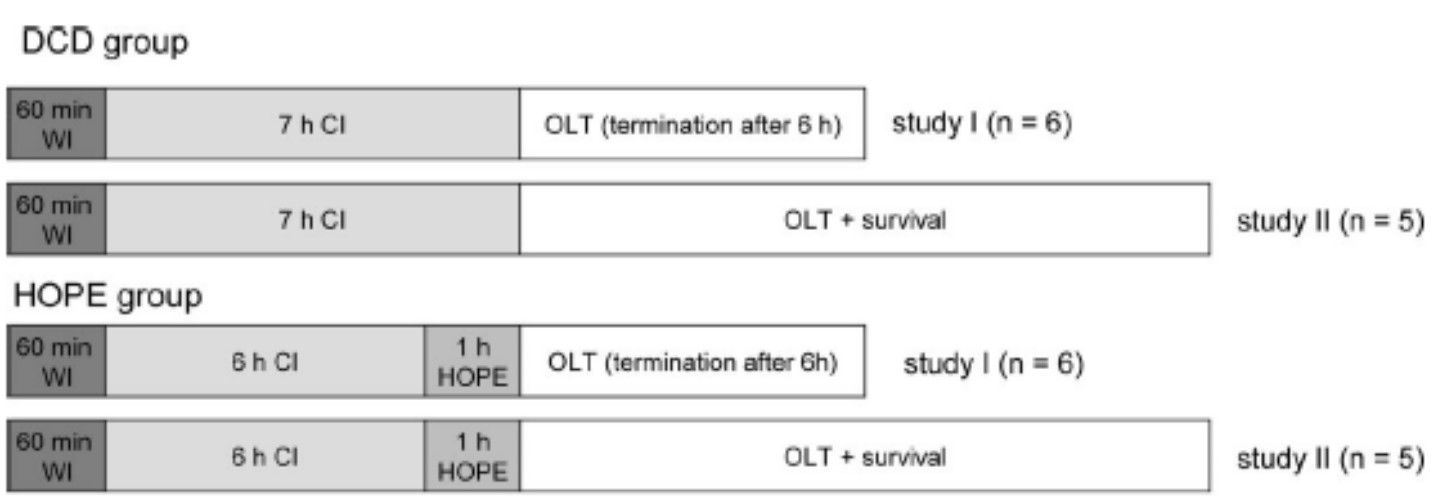


Hypothermic Oxygenated Perfusion

One Hour Hypothermic Oxygenated Perfusion (HOPE) Protects Nonviable Liver Allografts Donated After Cardiac Death

Olivier de Rougemont, MD, Stefan Breitenstein, MD,* Boris Leskosek,* Achim Weber, MD,† Rolf Graf, PhD,* Pierre-Alain Clavien, MD, PhD,* and Philipp Dutkowski, MD**

(*Ann Surg* 2009;250: 674–683)



Ex vivo Organ Perfusion Technique
Differences

	Advantages	Disadvantages
Hypothermic Machine Perfusion	▪ Simple ▪ Graft improvement ▪ Simultaneous use of therapeutic agents	▪ Partial organ assessment (Flow, resistance, lactate)
Hypothermic Oxygenated Perfusion	▪ Simple ▪ Graft improvement ▪ Simultaneous use of therapeutic agents	▪ Partial organ assessment (Flow, resistance, lactate, oxygen consumption)
Normothermic Machine Perfusion	▪ Organ viability assessment ▪ Graft improvement ▪ Organ recovery ▪ Simultaneous use of therapeutic agents	▪ Complex ▪ Harmful (if machine perfusion failure)

Side events and perfusion

Preliminary Single-Center Canadian Experience of Human Normothermic *Ex Vivo* Liver Perfusion: Results of a Clinical Trial

M. Bral[1,2], B. Gala-Lopez[1,2], D. Bigam[1], N. Kneteman[1,2], A. Malcolm[1,2], S. Livingstone[1], A. Andres[1], J. Emamaullee[1], L. Russell[3], C. Coussios[4], L. J. West[1,2], P. J. Friend[5] and A. M. J. Shapiro[1,2,*]

American Journal of Transplantation 2017; 17: 1071–1080

Ten donor liver grafts were procured, four (40%) from donation after circulatory death (DCD), of which nine were transplanted.

One liver did not proceed because of a technical failure with portal cannulation and was discarded

Applications

1) Check graft quality and function (selection)?

2) Improve graft early and long term (treatment)?

Applications

1) Check graft quality and function (selection)?

2) Improve graft early and long term (treatment)?

Protocol of a randomised controlled, open-label trial of ex vivo normothermic perfusion versus static cold storage in donation after circulatory death renal transplantation

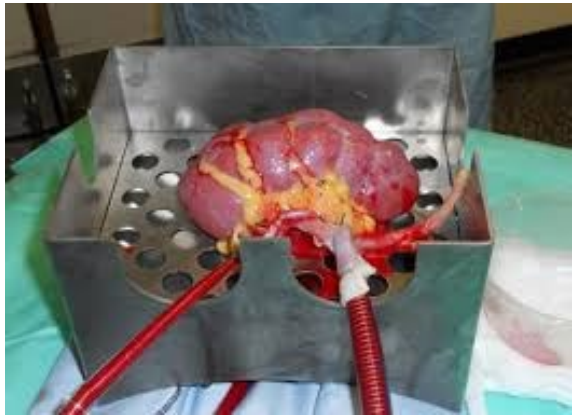


Figure 1: Trial design

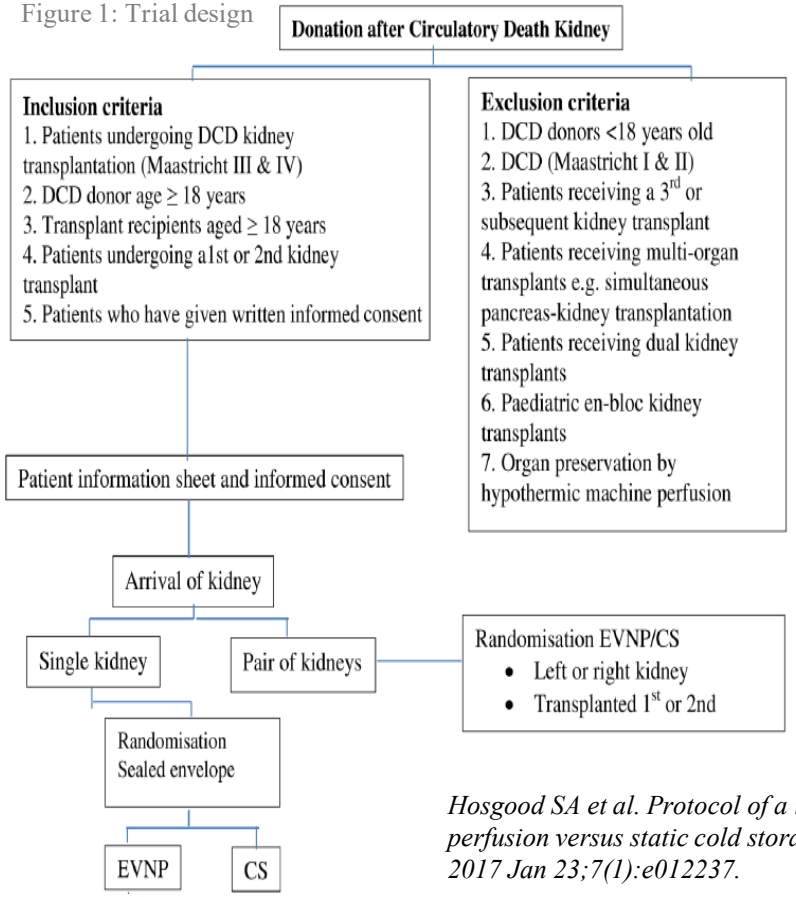


Table 1 Ex vivo normothermic perfusion (EVNP) score

EVNP score	
Macroscopic appearance	**Points**
Excellent perfusion with global and even pink appearance	1 point
Moderate perfusion with some areas of patchy or mottled perfusion	2 points
Poor perfusion with a globally mottled and purple appearance	3 points
Mean renal blood flow (mL/min/100 g) <50 mL/min/100 g	1 point
Mean renal blood flow (mL/min/100 g) >50 mL/min/100 g	0 point
Total urine output (mL) <43mL/hour	1 point
Total urine output (mL) >43mL/hour	0 point

Scores for macroscopic appearance, renal blood flow and urine output will be added to yield an overall assessment score ranging from 1 (the highest quality) to 5 (the lowest quality).

Hosgood SA et al. Protocol of a randomised controlled, open-label trial of ex vivo normothermic perfusion versus static cold storage in donation after circulatory death renal transplantation. BMJ Open. 2017 Jan 23;7(1):e012237.

Ann Surg. 2019 Nov;270(5):906-914.

Transplantation of High-risk Donor Livers After Ex Situ Resuscitation and Assessment Using Combined Hypo- and Normothermic Machine Perfusion: A Prospective Clinical Trial.

van Leeuwen OB1, de Vries Y1, Fujiyoshi M1, Nijsten MWN2, Ubbink R3, Pelgrim GJ3, Werner MJM1, Reyntjens KMEM4, van den Berg AP5, de Boer MT1, de Kleine RHJ1, Lisman T6, de Meijer VE1, Porte RJ1. Department of Surgery, Section of HPB Surgery & Liver Transplantation, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

During the first 2.5 hours of NMP, hepatobiliary viability was assessed, using predefined criteria:

perfusate lactate <1.7 mmol/L,

pH 7.35 to 7.45, bile production >10 mL, and bile pH >7.45

Ann Surg. 2019 Nov;270(5):783-790.

Novel Real-time Prediction of Liver Graft Function During Hypothermic Oxygenated Machine Perfusion Before Liver Transplantation.

Muller X1, Schlegel A1, Kron P1, Eshmuminov D1, Würdinger M1, Meierhofer D2, Clavien PA1, Dutkowski P1. Department of Surgery and Transplantation, University Hospital Zurich, Switzerland.

54 livers during HOPE: fluorometric analysis of released mitochondrial flavin (flavin mononucleotide, FMN) in the machine perfusate.

mitochondrial FMN release in machine perfusates of livers strong correlation with lactate clearance and coagulation factors after transplantation

AUROC of 0.79 [95% confidence interval (CI), 0.62-0.97] for severe allograft dysfunction and for early graft loss (AUROC 0.93, 95% CI, 0.84-1.0).

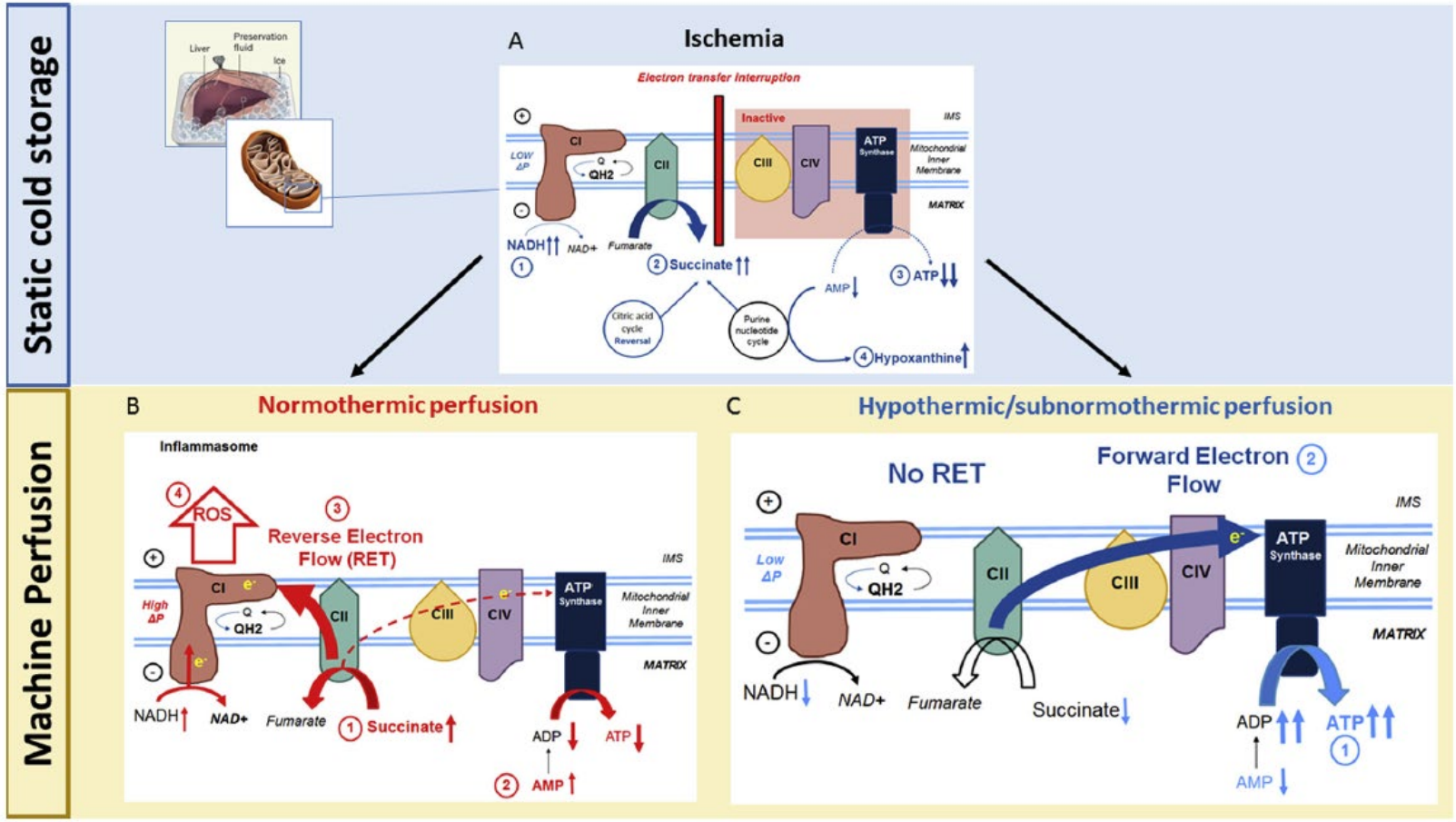
CONCLUSIONS:

Assessment of flavin, a marker of mitochondrial complex I injury, in the perfusate provides a fast prediction of liver graft function and loss during ex situ MP before implantation.

Gastroenterology 2019 ; 156:1542-1547

Continuous or endischemic NMP after ischemia triggers an inflammatory cascade, mostly related to mitochondrial derived reactive oxygen species.

In contrast, hypothermic perfusion techniques mitigate oxidative stress despite high availability of oxygen in the cold, probably owing to changes in mitochondrial electron transfer



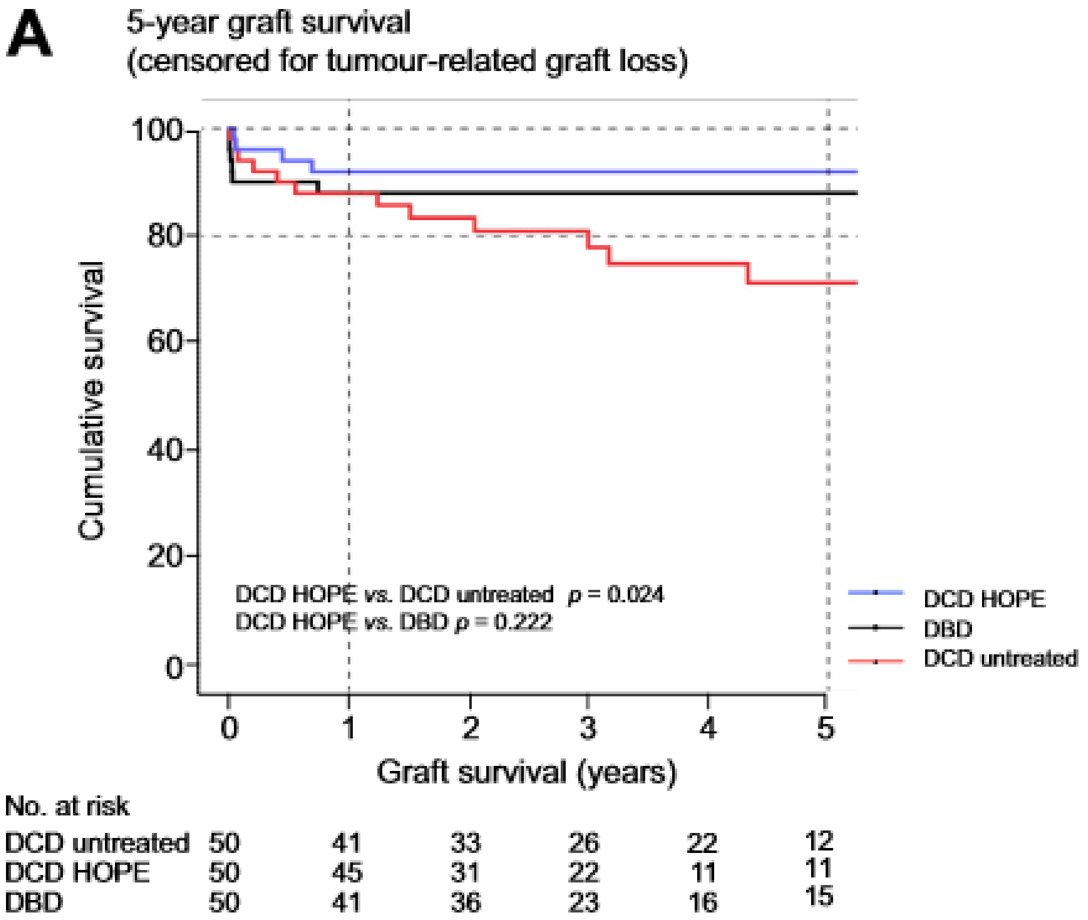
Applications

1) Check graft quality and function (selection)?

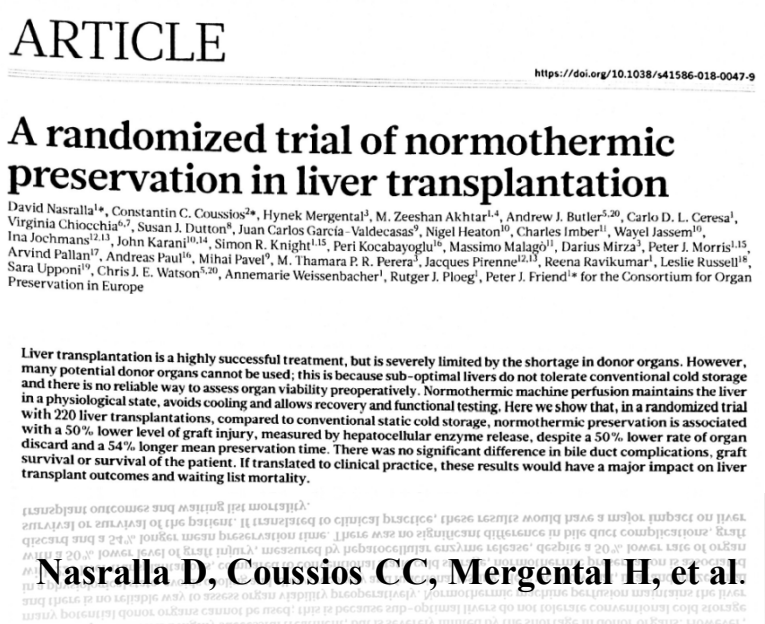
2) Improve graft early and long term (treatment)?

Hypothermic Oxygenated Perfusion

Outcome Parameter	[p v]alue DCD [HOP]E vs. DCD [u]ntreated	p value DCD HOPE vs. DBD
Non-anastomotic strictures	0.09	0.362
Anastomotic strictures:	0.624	0.0538
Treated conservative/ERCP	0.287	0.0905
Treated with hepaticojejunostor[ny]	0.617	1.0
Temporary anastomotic stent	1.0	0.3567
Temporary PTCD	0.715	0.242
Biliary cast	1.0	0.242
Bile leak	1.0	1.0
Arterial complication	0.741	1.0
Primary non-function	0.494	1.0
Total graft loss	0.0198	0.3178



Schlegel A, Muller X, Kalisvaart M, et al. Outcomes of DCD liver transplantation using organs treated by hypothermic oxygenated perfusion before implantation. Journal of Hepatology



ARTICLE

https://doi.org/10.1038/s41586-018-0047-9

A randomized trial of normothermic preservation in liver transplantation

David Nasralla[1*], Constantin C. Coussios[2*], Hynek Mergental[3], M. Zeeshan Akhtar[1,4], Andrew J. Butler[5,20], Carlo D. L. Ceresa[1], Virginia Chiocchia[6,7], Susan J. Dutton[8], Juan Carlos García-Valdecasas[9], Nigel Heaton[10], Charles Imber[11], Wayel Jassem[10], Ina Jochmans[12,13], John Karani[10,14], Simon R. Knight[1,15], Peri Kocabayoglu[16], Massimo Malago[11], Darius Mirza[3], Peter J. Morris[1,15], Arvind Pallan[17], Andreas Paul[16], Mihai Pavel[9], M. Thamara P. R. Perera[3], Jacques Pirenne[12,13], Reena Ravikumar[1], Leslie Russell[18], Sara Upponi[19], Chris J. E. Watson[5,20], Annemarie Weissenbacher[1], Rutger J. Ploeg[1], Peter J. Friend[1*] for the Consortium for Organ Preservation in Europe

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Nasralla D, Coussios CC, Mergental H, et al.

A randomized trial of normothermic preservation in liver transplantation.

Nature. 2018; 557:50-56.

Trial outcomes

	NMP (n = 170)	SCS (n=160)
Peak AST		
DBD	562.2 (427.3-647.9)	880.2 (708.5-1093.5)
Secondary outcomes		
PNF	1 (0.8%)	0 (0%)
EAD	12 (10.1%)	29 (29.9%)

Improve graft early and long term?

Cochrane Library

Cochrane Database of Systematic Reviews

Machine perfusion preservation versus static cold storage for deceased donor kidney transplantation (Review)

All randomised controlled trials (RCTs) and quasi-RCTs comparing HMP/NMP versus SCS for deceased donor kidney transplantation

No studies on NMP, ongoing study

HMP reduces the risk of DGF in kidneys from DCD donors, as well as kidneys from DBD donors

To prevent one episode of DGF 7 KT DCD and 14 KTD BD

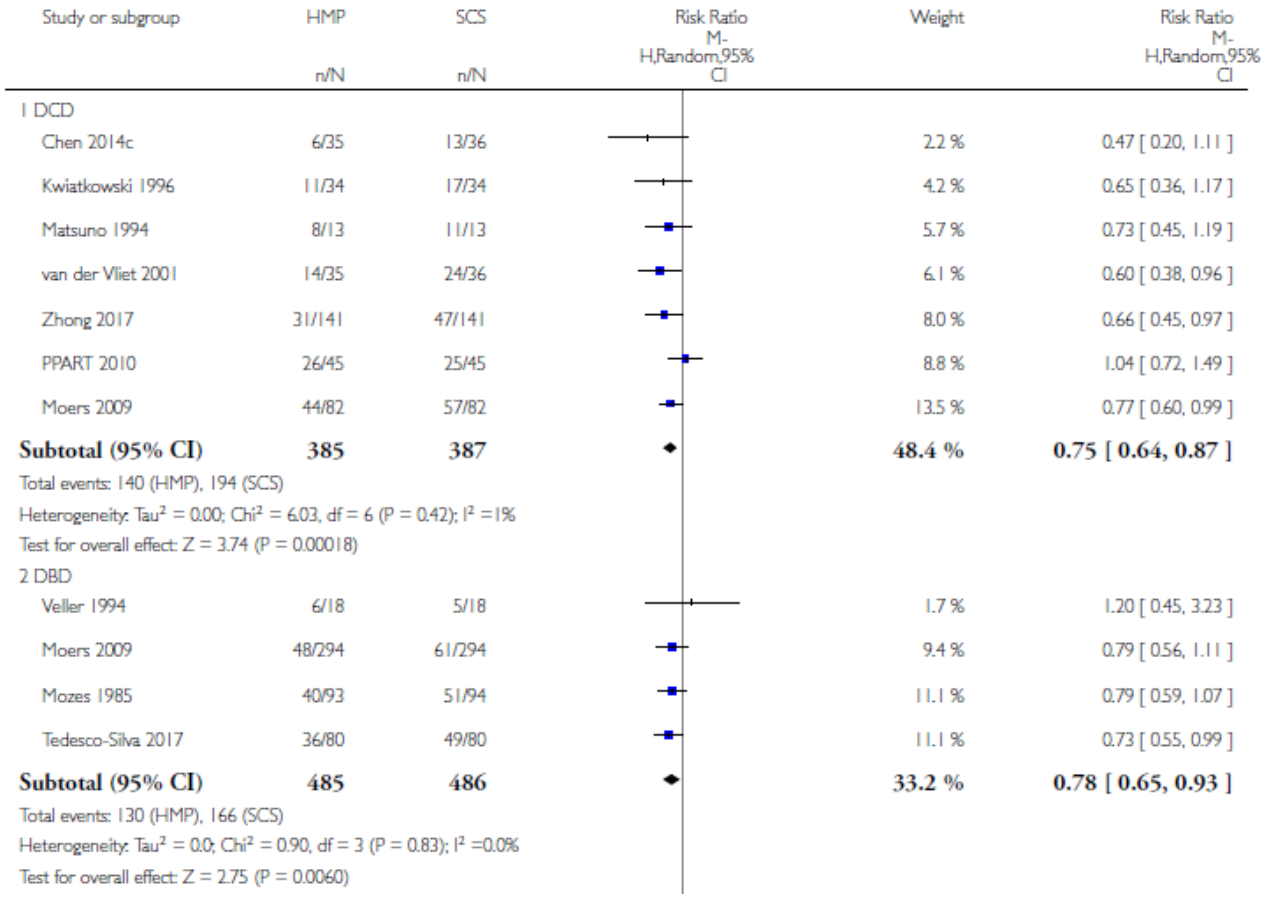
Studies performed in the last decade all used the LifePort (no Oxygen)

The effect of HMP on other outcomes (incidence of acute rejection, patient survival, hospital stay, long-term graft function, duration of DGF) ***remains uncertain***

Hypothermic perfusion
Improved DGF for DCD and DBD

DCD

DBD

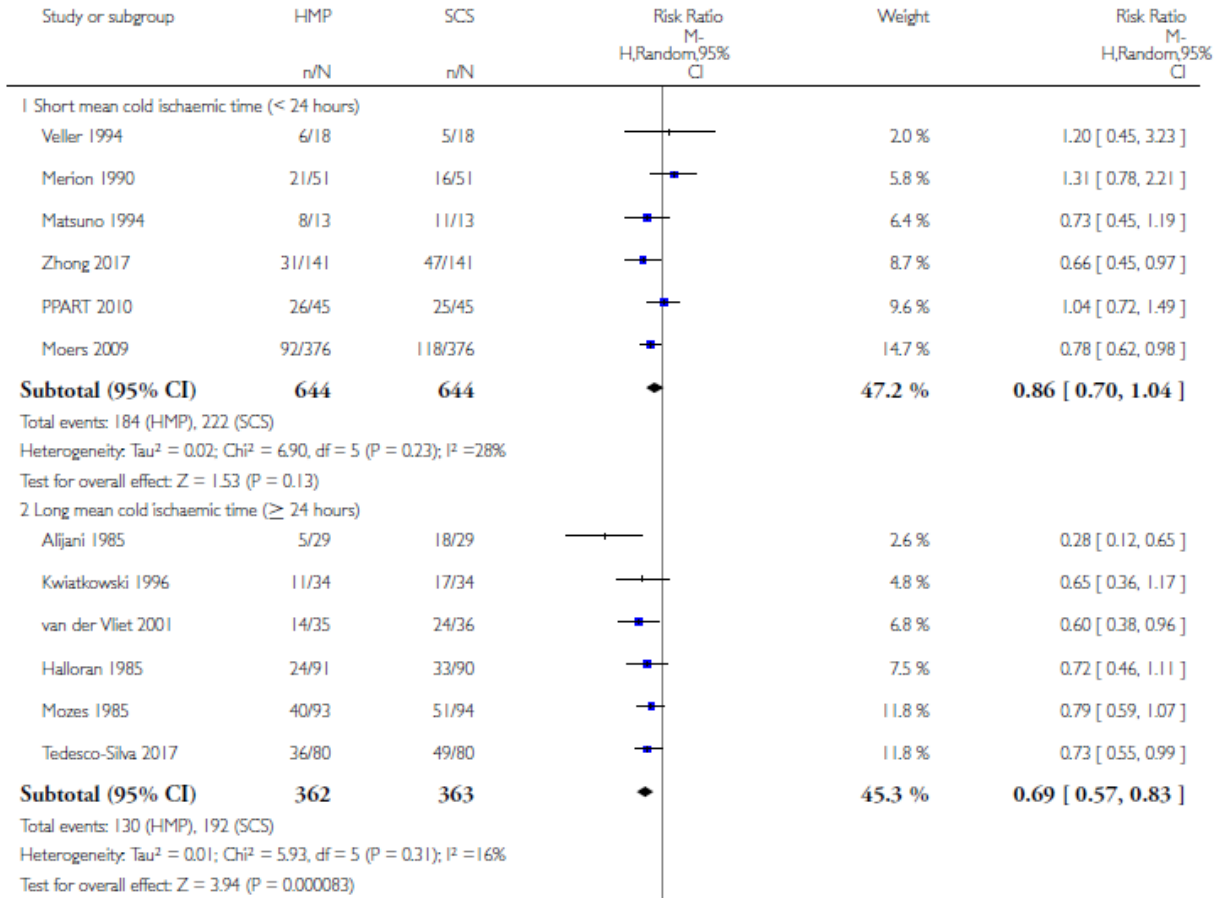


Study or subgroup	HMP n/N	SCS n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 DCD					
Chen 2014c	6/35	13/36		2.2 %	0.47 [0.20, 1.11]
Kwiatkowski 1996	11/34	17/34		4.2 %	0.65 [0.36, 1.17]
Matsuno 1994	8/13	11/13		5.7 %	0.73 [0.45, 1.19]
van der Vliet 2001	14/35	24/36		6.1 %	0.60 [0.38, 0.96]
Zhong 2017	31/141	47/141		8.0 %	0.66 [0.45, 0.97]
PPART 2010	26/45	25/45		8.8 %	1.04 [0.72, 1.49]
Moers 2009	44/82	57/82		13.5 %	0.77 [0.60, 0.99]
Subtotal (95% CI)	**385**	**387**		**48.4 %**	**0.75 [0.64, 0.87]**
Total events: 140 (HMP), 194 (SCS)					
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 6.03$, df = 6 (P = 0.42); $I^2 = 1\%$					
Test for overall effect: Z = 3.74 (P = 0.00018)					
2 DBD					
Veller 1994	6/18	5/18		1.7 %	1.20 [0.45, 3.23]
Moers 2009	48/294	61/294		9.4 %	0.79 [0.56, 1.11]
Mozes 1985	40/93	51/94		11.1 %	0.79 [0.59, 1.07]
Tedesco-Silva 2017	36/80	49/80		11.1 %	0.73 [0.55, 0.99]
Subtotal (95% CI)	**485**	**486**		**33.2 %**	**0.78 [0.65, 0.93]**
Total events: 130 (HMP), 166 (SCS)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.90$, df = 3 (P = 0.83); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.75 (P = 0.0060)					

Hypothermic perfusion and CIT < or >24 hours
Different effect on DGF

CIT< 24 hs
P=n.s.

CIT > 24 hs
P<0.05



Study or subgroup	HMP n/N	SCS n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Short mean cold ischaemic time (< 24 hours)					
Veller 1994	6/18	5/18		2.0 %	1.20 [0.45, 3.23]
Merion 1990	21/51	16/51		5.8 %	1.31 [0.78, 2.21]
Matsuno 1994	8/13	11/13		6.4 %	0.73 [0.45, 1.19]
Zhong 2017	31/141	47/141		8.7 %	0.66 [0.45, 0.97]
PPART 2010	26/45	25/45		9.6 %	1.04 [0.72, 1.49]
Moers 2009	92/376	118/376		14.7 %	0.78 [0.62, 0.98]
Subtotal (95% CI)	**644**	**644**		**47.2 %**	**0.86 [0.70, 1.04]**
Total events: 184 (HMP), 222 (SCS)					
Heterogeneity: Tau² = 0.02; Chi² = 6.90, df = 5 (P = 0.23); I² =28%					
Test for overall effect: Z = 1.53 (P = 0.13)					
2 Long mean cold ischaemic time (≥ 24 hours)					
Alijani 1985	5/29	18/29		2.6 %	0.28 [0.12, 0.65]
Kwiatkowski 1996	11/34	17/34		4.8 %	0.65 [0.36, 1.17]
van der Vliet 2001	14/35	24/36		6.8 %	0.60 [0.38, 0.96]
Halloran 1985	24/91	33/90		7.5 %	0.72 [0.46, 1.11]
Mozes 1985	40/93	51/94		11.8 %	0.79 [0.59, 1.07]
Tedesco-Silva 2017	36/80	49/80		11.8 %	0.73 [0.55, 0.99]
Subtotal (95% CI)	**362**	**363**		**45.3 %**	**0.69 [0.57, 0.83]**
Total events: 130 (HMP), 192 (SCS)					
Heterogeneity: Tau² = 0.01; Chi² = 5.93, df = 5 (P = 0.31); I² =16%					
Test for overall effect: Z = 3.94 (P = 0.000083)					

Received: 16 October 2018 | Revised: 19 February 2019 | Accepted: 6 March 2019
DOI: 10.1111/ctr.13536

ORIGINAL ARTICLE

WILEY Clinical TRANSPLANTATION

Evaluation of outcomes in renal transplantation with hypothermic machine perfusion for the preservation of kidneys from expanded criteria donors

In 2012 French Transplant Health Authority recommended HMP in ECD-DBD

Multivariate analysis of DGF occurrence (logistic regression)

Variable	Level	OR	95% CI	*P*-value
Storage method	CS	1	-	<0.0001
	HMP	0.49	0.40-0.60	
Recipient factors				
BMI	Underweight and normal (<25 kg/m^2)	1	-	
	Overweight (25-29 kg/m^2)	1.27	1.06-1.53	0.0002
	Obese (≥30 kg/m^2)	1.59	1.27-1.98	
Cause of ESRD	Polycystic kidney disease	0.77	0.63-0.95	
	Other	1	-	0.014
Time spent on dialysis	<3 y	1	-	<0.0001
	≥3 y	1.7	1.46-1.98	
Previous transplants	No	1	-	0.003
Donor factors				
eGFR (mL/min)		0.99	0.99-1.00	<0.0001
Gender	Male	1	-	
	Female	0.81	0.71-0.94	0.004
Transplant factors				
Cold ischemia time (h)		1.03	1.02-1.04	<0.0001

Decreasing CIT is a priority in the new French national transplant plan (2017-2021);

the objective is 15 hours in 2018 for DBD kidney transplants and

below 12 hours for DCD with HMP

Received: 16 October 2018 | Revised: 19 February 2019 | Accepted: 6 March 2019
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WILEY Clinical TRANSPLANTATION

Evaluation of outcomes in renal transplantation with hypothermic machine perfusion for the preservation of kidneys from expanded criteria donors

	Overall study cohort					
	HMP group (n = 801)		CS group (n = 3515)		Missing data	*P value*
Kidney Donor Risk Index (Rao, mean, 95%CI)	2.25	2.22-2.29	2.20	2.18-2.21	0%	0.009
Kidney Donor Profile Index						
<85%	135	17%	750	21%	0%	0.005
≥85%	666	83%	2765	79%		
Antidiuretic hormone						
No	226	32%	1132	36%	11%	0.025
Yes	483	68%	1983	64%		
Transplant characteristics						
Cold ischemic time (h, mean, 95%CI)	16.9	16.5-17.3	17.4	17.2-17.6	1%	0.05

Report CNT

2000-2015

38% KTs > 15

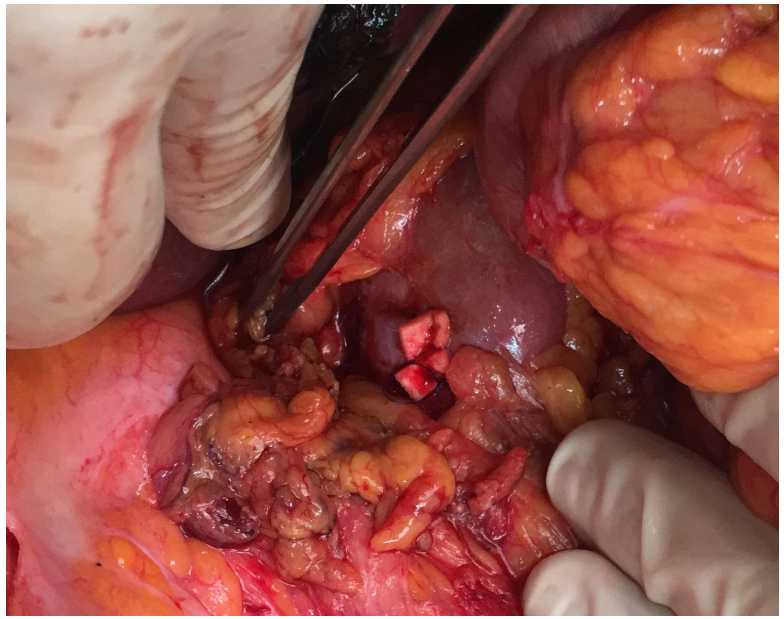
CIT hs

§§ sono esclusi i trapianti combinati e rene doppio ?

CASE-MIX #

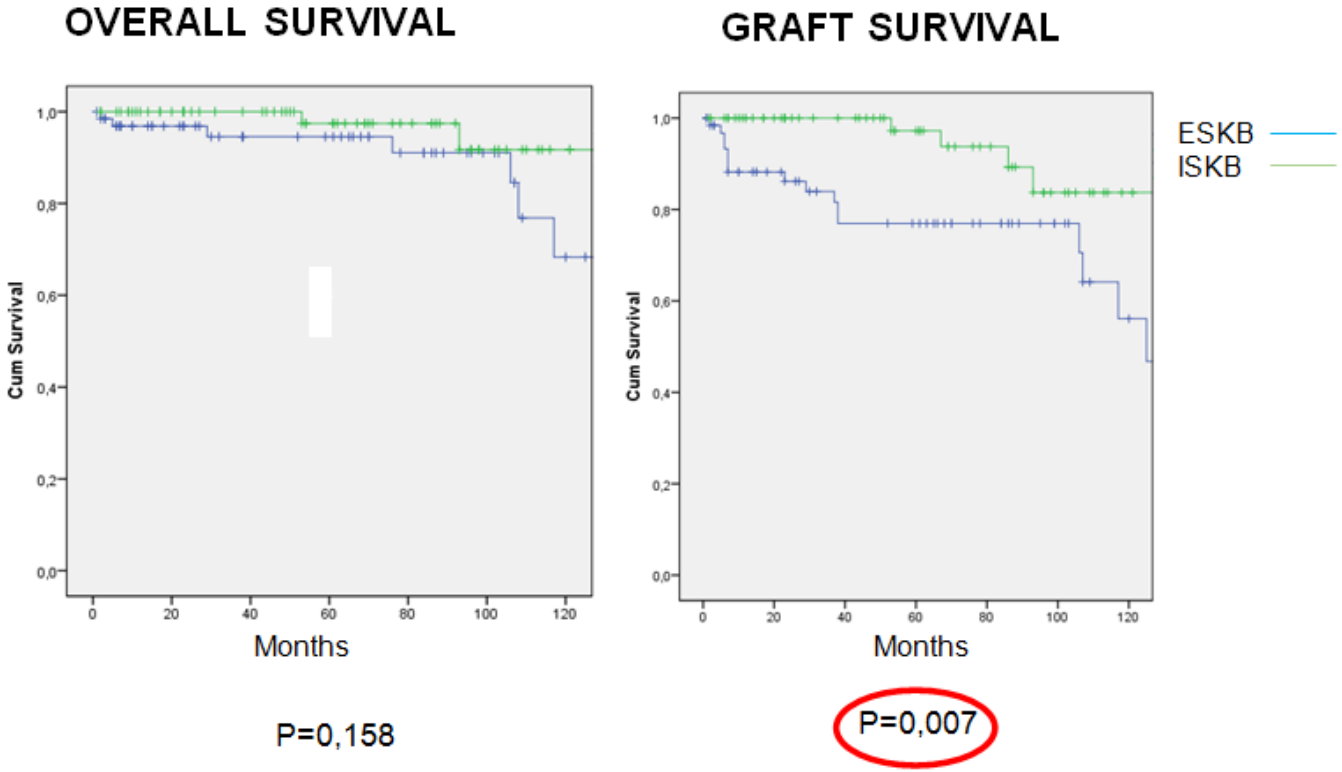
Centro Trapianti	Casi Adulti 2000-15 §§ N° casi	Adulti Donatore età > 60 N° casi	Ricevente età > 50 N° casi	casi complessi N° casi	Combinati N° casi	Rene Doppio N° casi	Ischemia > 900 min. N° casi	Casi Pediatrici §§ N° casi	Combinati Adulti e Pediatrici N° casi	2015 Indice Soddisfacimento della Lista****	2001-2016 Attività Vivente N° casi
AN - A.O. TORRETTE - UMBERTO I	374	116	217	83	10	0	130	0	10	16,4 %	2
AQ - OSPEDALE CIVILE S.SALVATORE	459	100	222	82	0	0	61	0	0	7,3 %	16
BA - AZIENDA OSPEDALE POLICLINICO	808	174	347	121	0	60	135	10	0	8,6 %	100
BG - OSPEDALI RIUNITI - BERGAMO	500	92	213	148	31	72	287	7	42	16,2 %	23
BO - S.ORSOLA-MALPIGHI	956	344	514	329	65	75	394	5	67	11,3 %	112
BS - OSPEDAL.CIVILI BRESCIA	780	225	436	246	0	1	377	5	0	14,1 %	
CA - A. O. G.BROTZU	494	92	234	149	32	24	203	2	32	20,1 %	38
CS - A. O DI COSENZA	173	27	76	17	0	1	25	0	0	13,1 %	
CT - POL. UNIVERSITARIO	526	133	238	37	13	45	213	4	13	12 %	109
FI - AZIENDA OSPEDALIERA CAREGGI	621	253	344	127	0	1	490	0	0	12,1 %	33
GE - AZ.OSP.S.MARTINO	622	167	328	287	28	89	325	192	31	14,5 %	92
LE - A.O. VITO FAZZI	41	4	17	3	0	0	27	0	0		
MI - IRCCS S. RAFFAELE	310	106	179	108	145	30	59	0	145	17,2 %	45
MI - MAGGIORE POLICLINICO	710	174	321	200	15	4	243	162	16	17,8 %	145
MI - OSPEDALE CA GRANDA-NIGUARDA	854	203	453	282	77	45	324	4	78	15,9 %	166
MO - POLICLINICO - MO	384	141	186	128	31	44	169	2	31	11 %	57
NA - U.S. FEDERICO II	587	56	215	116	0	5	18	0	0	10,3 %	
NO - OSP. MAGGIORE DELLA CARITA'	931	371	524	312	0	55	717	0	0	14,7 %	82
PA - ISMETT	174	60	101	50	30	24	16	12	32	10,6 %	167
PA - OSP CIV.BENFRATELLI - M.ASCOLI	613	159	310	153	0	1	328	1	0	19,6 %	22
PA - POLICLINICO UN.(P. GIACCONE)	63	10	28	11	1	0	24	0	1		4
PD - AO - PEDIATRICO	43	2	0	14	0	0	15	207	5	16,8 %	
PD - AZIENDA OSPEDALIERA DI PADOVA	764	277	385	226	150	234	272	0	150	16,8 %	386
PG - AZIENDA OSPEDALIERA DI PERUGIA	284	89	160	53	0	0	0	0	0	6,8 %	
PI - AZIENDA OSPEDALIERA PISANA	389	134	187	126	197	103	137	0	197	10,6 %	333
PR - OSPEDALI RIUNITI - (OSP.MAGGIORE)	640	226	315	240	38	44	249	2	38	7,6 %	83
PV - S. MATTEO	426	118	221	128	2	0	131	0	2	12,3 %	26
RC - AZ.OSP.BIANCHI M MORELLI	209	31	66	27	0	0	29	0	0	12,4 %	29
RM - AZ.OSP.SAN CAMILLO-FORLANINI	256	73	128	47	18	36	18	0	18	15,3 %	27
RM - AZ. OSP. UNIV. POLICLINICO TOR VERGATA	498	104	245	219	10	17	99	0	10	15,1 %	17
RM - AZIENDA POLICLINICO UMBERTO I	539	165	243	45	27	3	153	4	27	11,3 %	95
RM - OSPEDALE PED. BAMBINO GESU	32	0	0	6	0	0	24	174	10	18,5 %	46
RM - POLICLINICO A. GEMELLI E C.I.C.	461	111	207	110	0	18	133	1	0	13,5 %	78
SA - OORR S.GIOVANNI DI DIO E RUGGI D'ARAGONA	259	30	111	37	2	0	19	2	2	9,8 %	
SI - SPEDALI RIUNITI (POL. LE SCOTTE)	640	250	350	209	1	80	278	0	1	14,1 %	77
SS - S.S. ANNUNZIATA SASSARI	163	27	74	38	0	0	34	1	0		
TO - A. O. S.GIOVANNI B. DI TORINO	1469	641	878	619	88	93	858	3	94	14,7 %	117
TO - OSPEDALE REGINA MARGHERITA	4	0	0	1	0	0	1	68	2	14,7 %	
TV - OSPEDALE CA FONCELLO	686	195	335	100	1	55	256	0	1	19,9 %	37
UD - A.O. S.MARIA DELLA MISERICORDIA	600	176	329	239	25	16	290	1	25	19,7 %	20
VA - OSPEDALE. FONDAZIONE MACCHI	655	220	391	146	4	22	126	1	4	20,7 %	23
VI - OSPEDALE DI VICENZA	420	107	184	79	0	34	105	0	0	13,4 %	88
VR - AZIENDA OSPEDALIERA DI VERONA	763	255	395	217	5	132	314	7	5	17,1 %	133
ITALIA	**21180**	**6238**	**10707**	**5915**	**1046**	**1463**	**8106**	**877**	**1089**	**13,7 %**	**2828**

Pre -transplant in situ kidney biopsy to reduce cold ischemia time and improve transplant outcome: a single center retrospective analysis



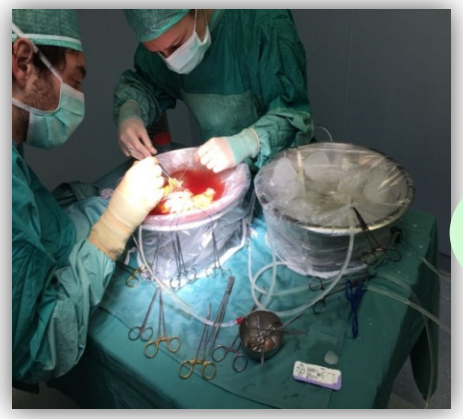
		ESKB (115)	ISKB (207)	p value
Recipient features	Age y; median (IQR)	71 (65-75)	64 (60-69)	**0,000**
	Male gender; n (%)	67 (58,3)	137 (66,2)	0,157
	BMI; median (IQR)	24,5 (22,6- 26,9)	25 (23-27,5)	0,417
	Diabetes; n (%)	1(0,9%)	26(12,6)	0,000
	CV disease; n (%)	88 (76,5)	153 (73,9)	0,654
	Diagnosis; n(%)			
	Diabetic nephropathy	1(0,9)	9(4,3)	
	Chronic glomerulosclerosis	23(20)	29(14)	
	Chronic glomerulonephritis	13(11,3)	39(18,8)	
	Hypertensive nephropathy	15(13)	34(16,4)	
	Renal polycystosis	30(26,1)	47(22,7)	
	Interstitial nephritis	8 (7)	4(1,9)	
	Berger's disease	14(12,2)	10(4,8)	
	Others	11(9,6)	35 (16.9)	
Donor features	Age y; median (IQR)	69 (65-73)	70 (64-75)	0,314
	Male gender; n (%)	63 (54,8)	102 (49,3)	0,343
	BMI; median (IQR)	25,7 (23,9-27,7)	25,7 (23,4-27,7)	0,667
	KDPI%; median (IQR)	95 (87-98)	95 (87-99)	0,475
Karpinski score; median (IQR)		3 (2- 4)	3 (2-4)	0,714
0-4 n(%)		108 (93,9%)	193 (93,2%)	0,814
> 4 n (%)		7 (6,1%)	14 (6,8%)	
Dual kidney tranplant n (%)		22 (19,1)	55 (26,5)	0,134
Cold ischemia time min; median (IQR)		840 (720-960)	730 (635-900)	**0,000**
DGF; n(%)		49 (42,6)	84 (40,6)	0,723

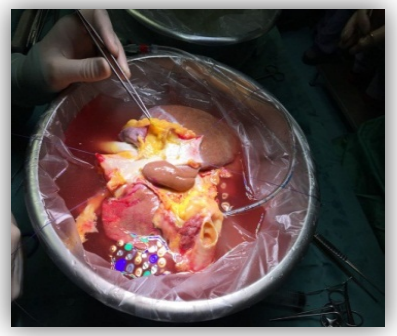
		ESKB (66)	ISKB (66)	p value
Recipient features	Age y; median (IQR)	67(62- 72)	68 (61- 71)	0,855
	Male gender; n (%)	41 (62,1)	44 (66,)	0,716
	BMI; median (IQR)	24,3 (22,7- 27,2)	25,2 (22,9- 27,5)	0,560
	Diabetes; n (%)	1 (1,5)	1(1,5)	1
	CV disease; n (%)	53 (80)	55 (83,3)	0,822
	Diagnosis; n (%)			
	Diabetic nephropathy	0 (0)	1 (1,5)	
	Chronic glomerulosclerosis	12 (18,2)	8 (12,1)	
	Chronic glomerulonephritis	8 (12,1)	12 (18,2)	
	Hypertensive nephropathy	8 (12,1)	10 (15,2)	
	Renal polycystosis	18 (25,7)	20 (27)	
	Interstitial nephritis	2 (3)	1 (1,5)	
	Berger's disease	10 (15,2)	3 (4,5)	
	Others	8 (12,1)	14 (22,1)	
Donor features	Age y; median (IQR)	66 (63-71)	68(63-75)	0,098
	Male gender; n (%)	35 (53)	28 (42,4)	0,296
	BMI; median (IQR)	26 (24- 28)	26 (23-28)	0,709
	KDPI %; median (IQR)	94(85-97)	95(85-98)	0,352
Karpinski score; median (IQR)		3 (2-4)	3 (2-4)	1
0-4 n(%)		62 (93,9)	63 (95,5)	1
> 4 n (%)		4 (6,1)	3 (4,5)	
Dual kidney tranplant; n (%)		11 (16,7)	9 (13,6)	0,809
Cold ischemia time min; median (IQR)		900 (720-1020)	660 (540-780)	**0,000**
DGF; n (%)		35(53)	13 (19,7)	**0,000**

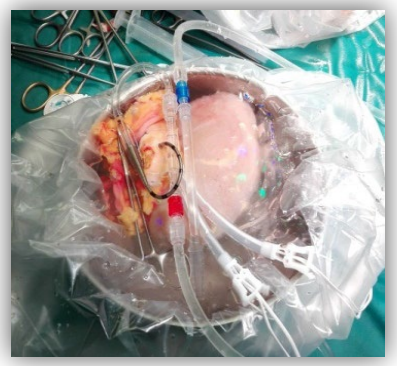


HYPOTHERMIC OXYGENATED PERFUSION WITHOUT INCREASING CIT: POSSIBLE ?

Following surgical back-table procedure, standard HOPE continues until the transplant







Principal Results

First Italian Interventional Clinical Trial

ID: NCT03031067

	HOPE	SCS	p value
Graft dysfunction (EAD and DGF)	9.5 %	33 %	0.05
Primary non-function	L- 0% K-0%	L-3.3% K- 0%	
Aspartate aminotransferase levels at 7 days	L- 344 (166-1032) U/L	L- 637 (124-2001) U/L	0.007
Aspartate aminotransferase levels at 30 days	L- 19.30±12.47 U/L	L- 31.82±22.76 U/L	0.026
Grafts survival at 30 days	L- 100% K- 100%	L- 93.4% K- 96.4%	

Conclusions: objective machine perfusion

1) Check graft quality and function (selection)
2) Improve graft early and long term (treatment)

Do not forget the other strategies: biopsy selection, low CIT…