Preservatie van donorlevers: hoe de aanpak van levertransplantatie verandert

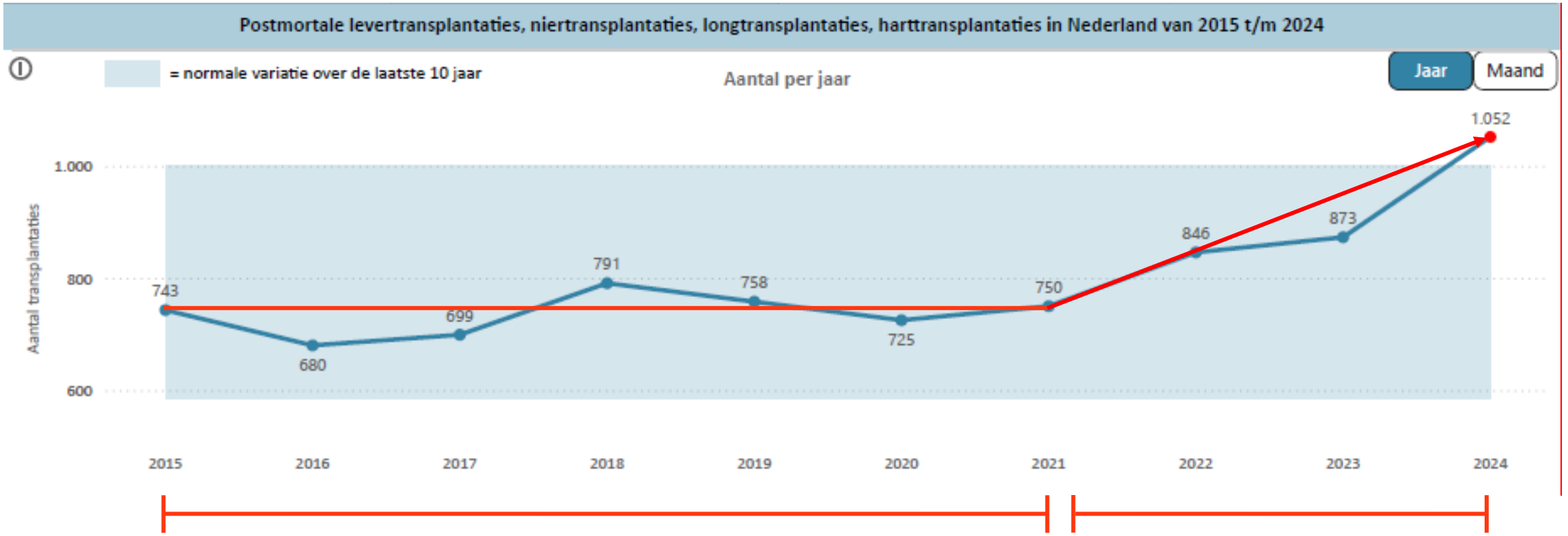
Digestive Disease Days: MDL Update

Jeroen de Jonge
HPB & Transplant Surgeon
Head Liver Perfusion Unit

Erasmus MC Transplant Institute
Rotterdam

17 maart 2026

Orgaantransplantatie in Nederland: goed nieuws



25-30% meer transplantaties in laatste 3-4 jaar: effect van donorwet……of ?

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Desondanks, mortaliteit op en verwijdering van de wachtlijst

*Voor **~15%** van de patiënten komt de LTx te laat*

40 Patiënten overleden of verwijderd van de wachtlijst

95 Donorlevers beschikbaar, maar niet gebruikt

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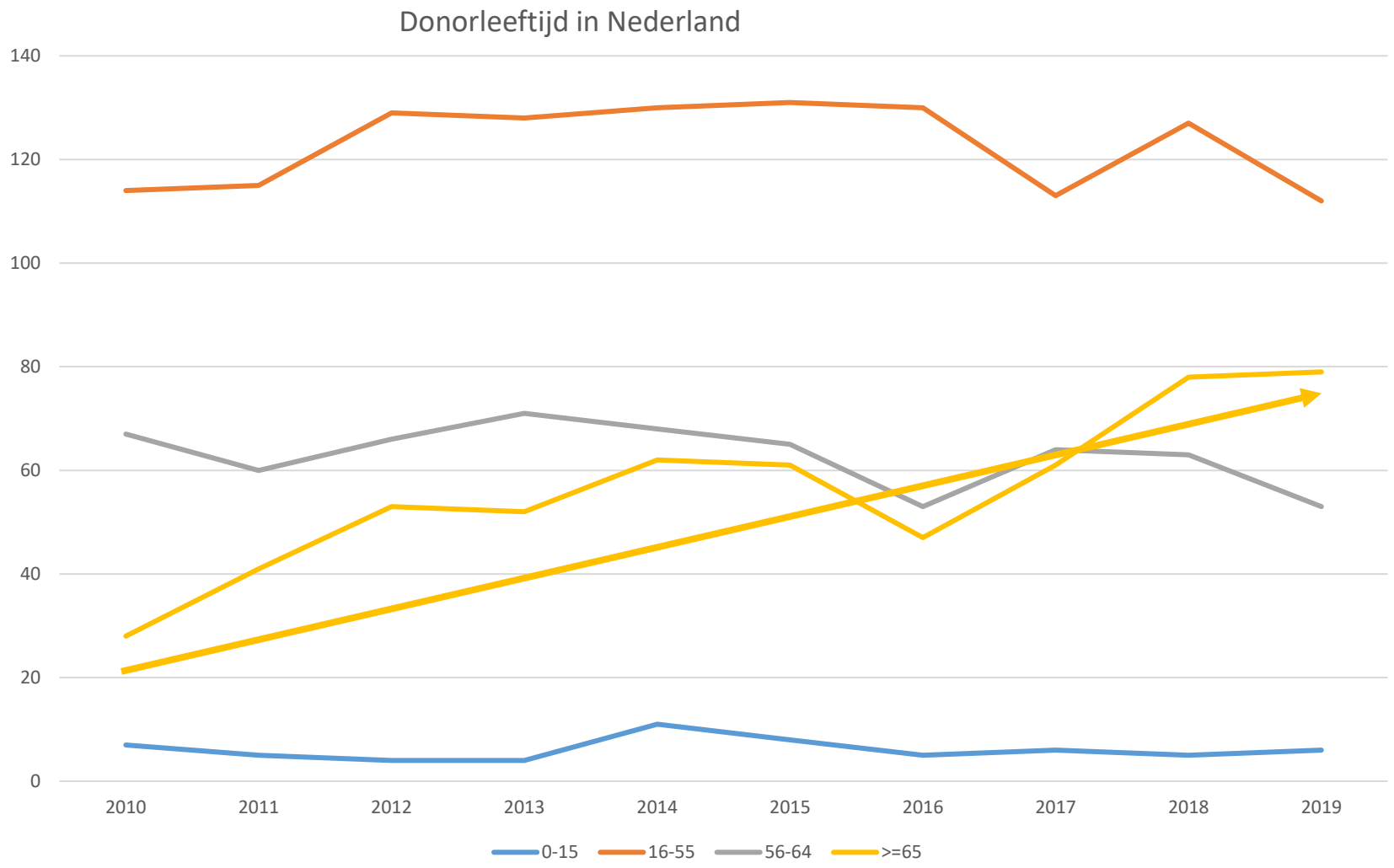
Kwaliteit van donororganen neemt af: vergrijzing



16-55 years old: -2%

> 65 years old: **+182%**

56-64 years old: -21%

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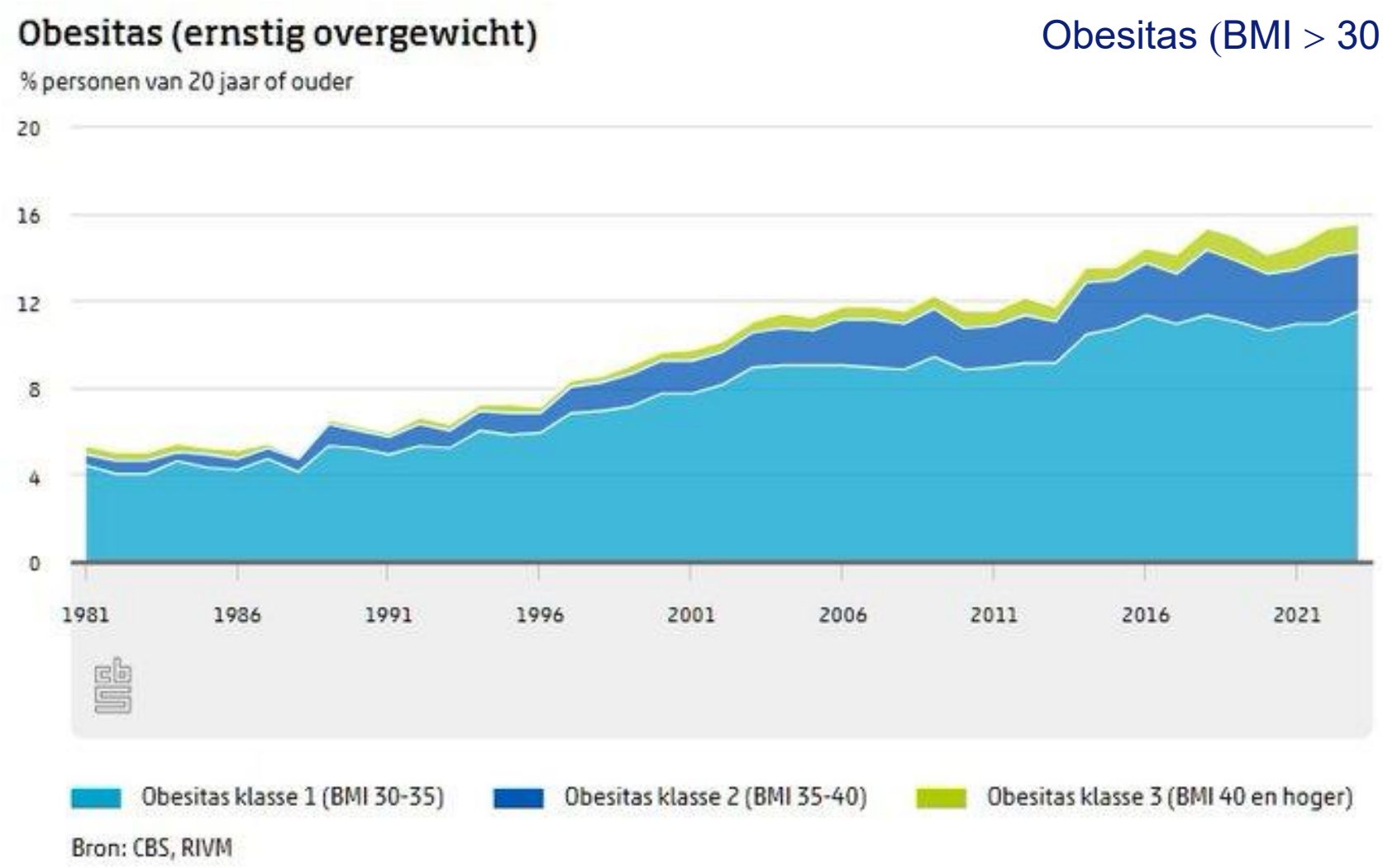
Kwaliteit van donororganen neemt af: obesitas



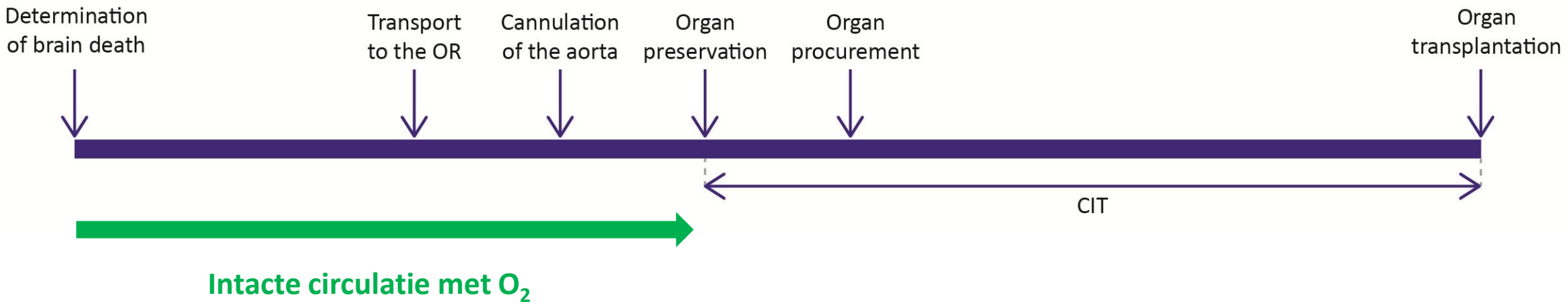
Obesitas (BMI > 30)

NL figures 2025:

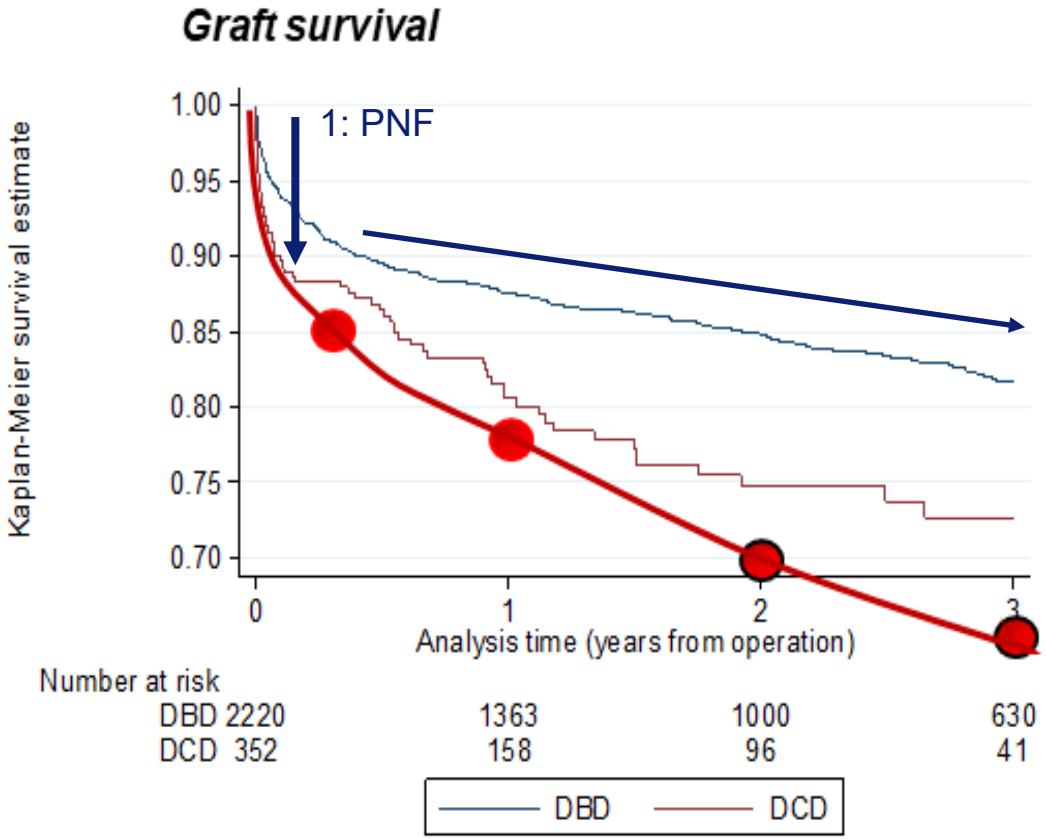
- 51% Overgewicht
- 16% Obesitas (1 op 6)

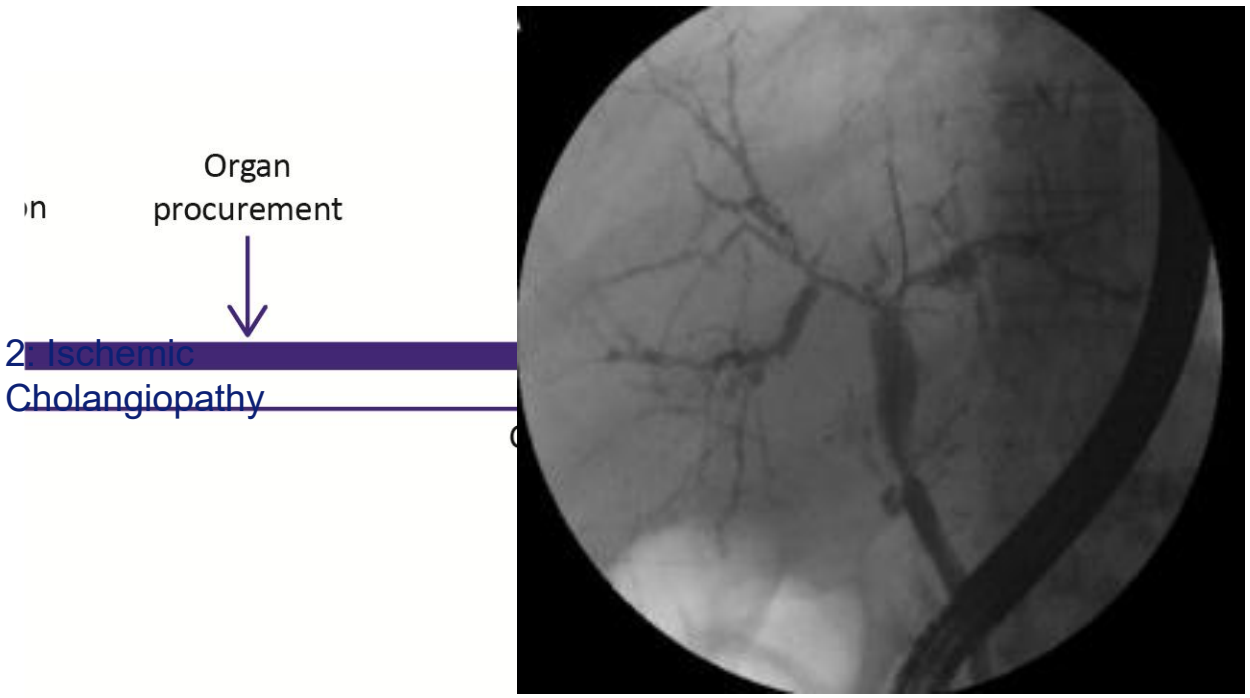
Kwaliteit van donororganen neemt af: toename DCD

- DBD = donation after brain death



Kwaliteit van donororganen neemt af: toename DCD





De Vries. Biochim et Biophys Acta 2018

Intacte circulatie met O_2

Verminderde/geen circulatie weinig/zonder O_2

Callaghan et al BMJ 2013

Dutch National Registry 2000-2020 (N=607)

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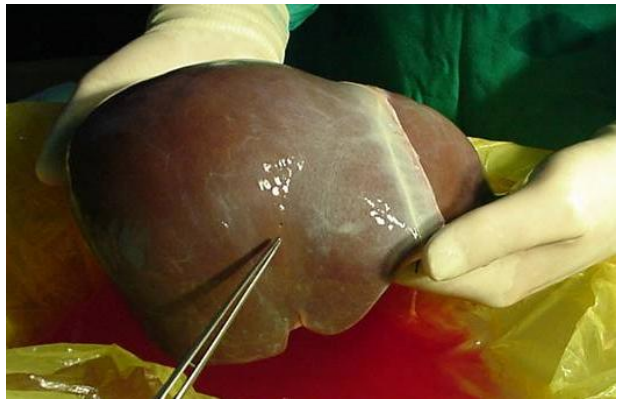
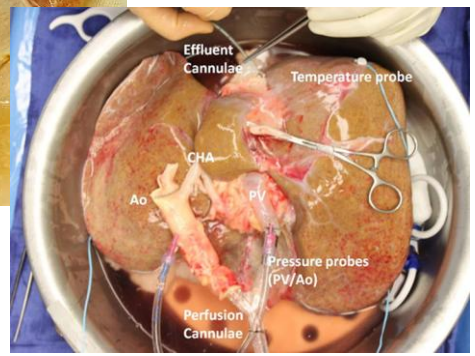
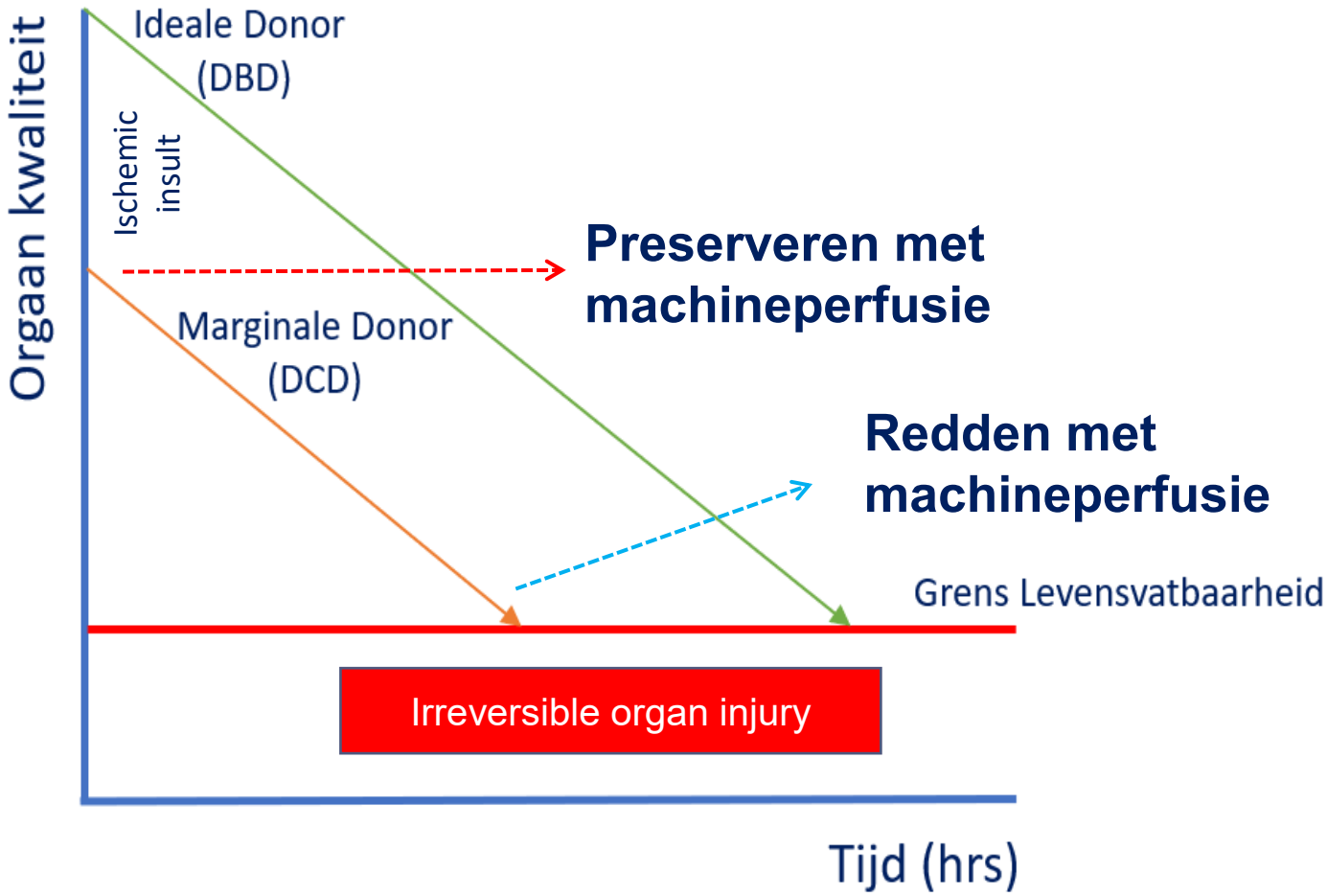
Machineperfusie voor **extended criteria** donorlevers



Van 35 jaar, DBD



Naar 67 jaar, DCD



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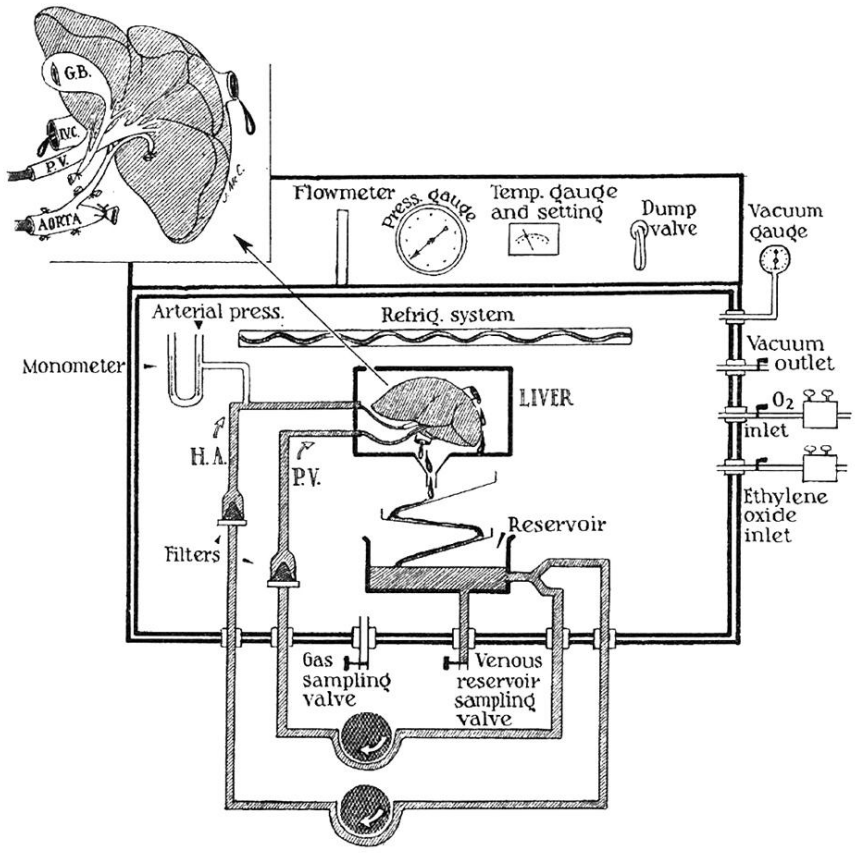
Nieuw……?

Fokko Belzer “portable” kidney machine



Thomas Starzl liver chamber

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Wel anders: ex-situ liver machine perfusion devices

Organ Recovery systems

- Hypothermic
- Pre-oxygenation

OrganOx living organs for life

- Normothermic
- Oxygenation

XVIVO PERFUSION

- Hypo- or Normothermic (7 – 37° C)
- Controlled Rewarming
- Oxygenation

LIVERASSIST

to BridgeLife Europe

- Hypothermic
- Oxygenation

TransMedics®
Bringing new life to organ transplant™

- Normothermic
- Oxygenation

Jferetica Purification Therapies

- Hypo- or Normothermic (4 – 37° C)
- Controlled Rewarming
- Oxygenation

PerLife®

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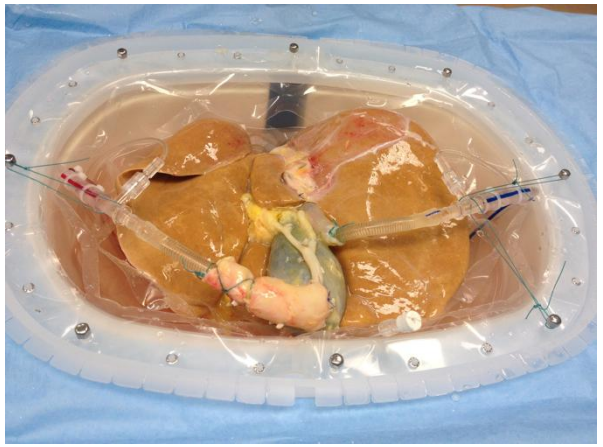
Machineperfusie van de lever: koud of warm ?



Cold

8-12°C

Hypothermic Oxygenated PErfusion (**[D]HOPE**)

Warm

35-37°C

Normothermic Machine Perfusion (**NMP**)

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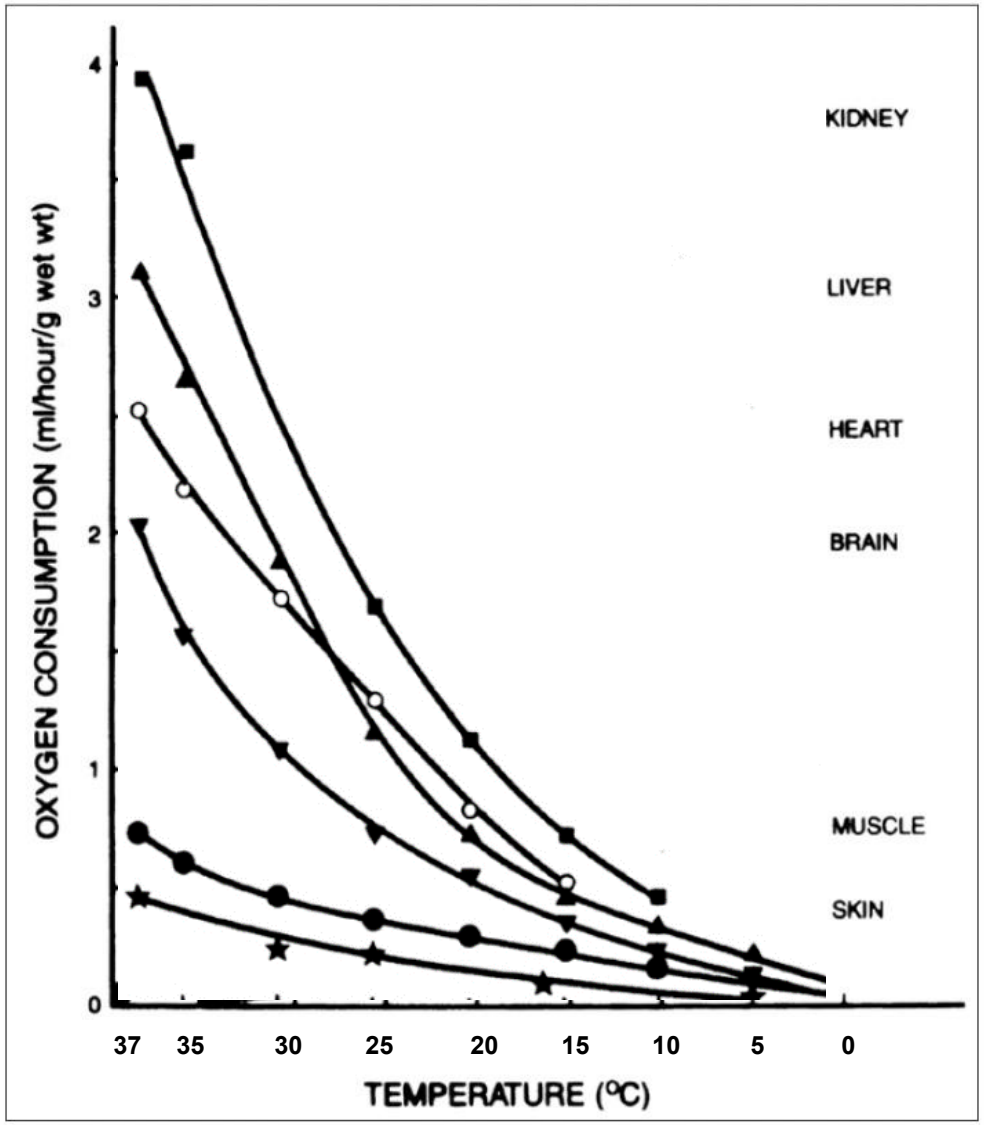
DHOPE: waarom koude perfusie?
Principes van de thermodynamica



Arrhenius equation (1915)

$$k = Ae^{-\frac{E_a}{RT}}$$

- 50% reduction metabolism each 10°C
- remaining **~15% metabolism at 10°C**

  ~5-10% metabolism at 4°C

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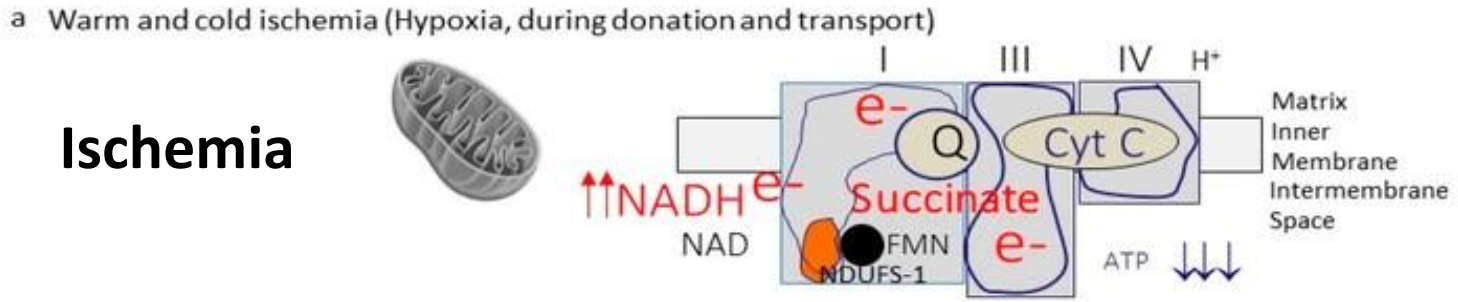
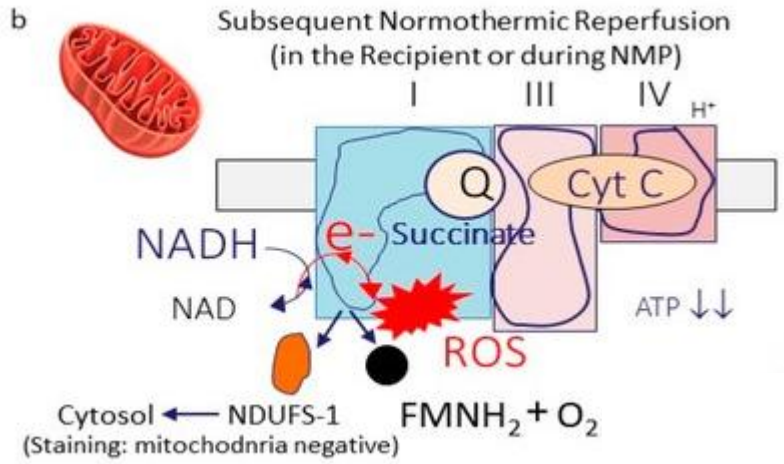
DHOPE: waarom <u>geoxygeneerde</u> perfusie?
dempen van mitochondriale ischemia/reperfusie schade (IRI)

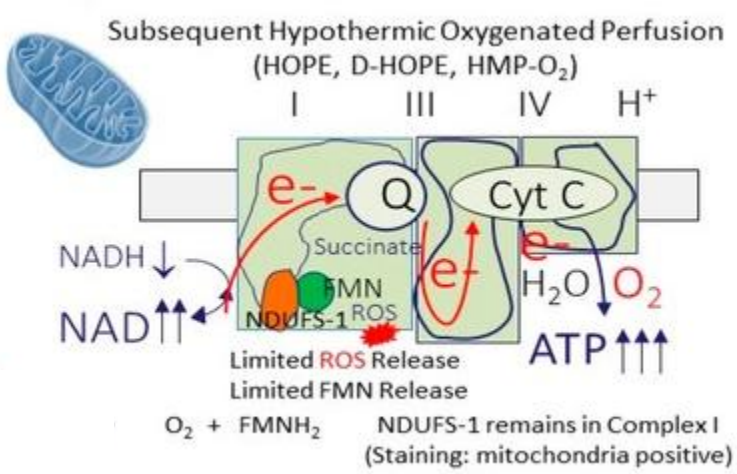


biomedicines

Rebecca Panconesi



Normothermic reperfusion



Hypothermic re-oxygenation

Biomedicines **2021**, *9*, 161. https://doi.org/10.3390/biomedicines9020161

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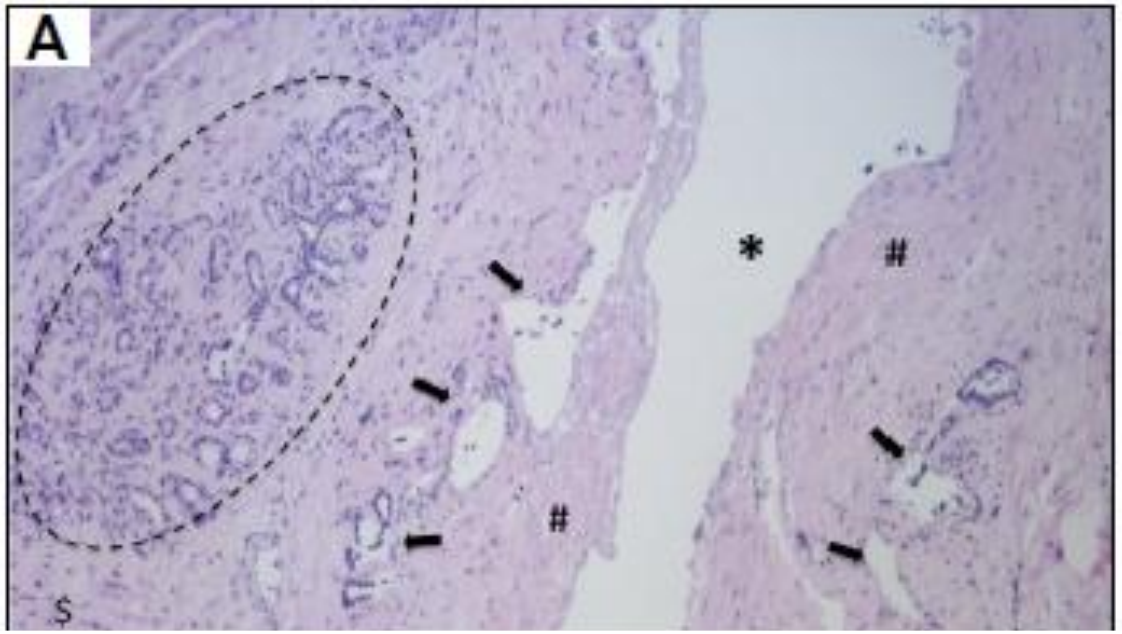
DHOPE gunstig effect op cholangiocyt-schade in DCD levertransplantatie

Injury to peribiliary glands and vascular plexus before liver transplantation predicts formation of non-anastomotic biliary strictures

Op den Dries, J Hepatol 2014



Altijd >50% galweg epitheel verloren in CBD van DCD levers (*)

Necrose van stroma (#)

Celdood in oppervlakkige PBG (↓↓)

Diepe PBG gespaard (---)

Necrose van de diepe PBG and peribiliaire arteriolen voorspelt Ischemische Cholangiopathie

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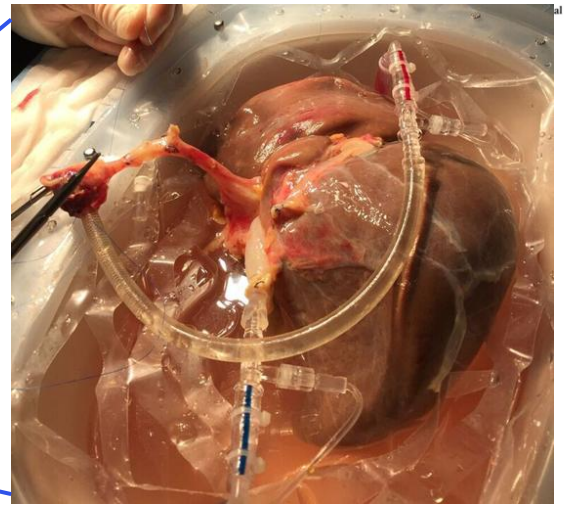
Multicenter RCT DHOPE – DCD



RESEARCH SUMMARY

Hypothermic Machine Perfusion in Liver Transplantation — A Randomized Trial

van Rijn R et al. DOI: 10.1056/NEJMoa2031532

CLINICAL PROBLEM

Livers obtained from donors after circulatory death, rather than after brain death, are increasingly used for transplantation owing to persistent shortage of donor organs, but their use is associated with an increased risk of nonanastomotic biliary strictures. More-advanced preservation methods are needed to reduce the incidence of this major complication.

CLINICAL TRIAL

Design: A randomized, controlled trial of hypothermic oxygenated machine perfusion to prevent nonanastomotic biliary strictures in patients undergoing transplantation of livers obtained from donors after circulatory death.

Intervention: 160 adult patients undergoing liver transplantation were assigned to receive a liver preserved with either hypothermic oxygenated machine perfusion (after static cold preservation during transportation) or conventional static cold storage alone (control). The primary end point was the incidence of nonanastomotic biliary strictures within 6 months after transplantation.

RESULTS

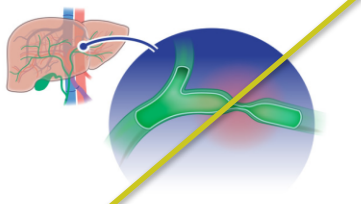
Efficacy: The incidence of symptomatic nonanastomotic biliary strictures was lower in the machine-perfusion group than in the control group.

Safety: The frequency and severity of adverse events were similar in the two patient groups.

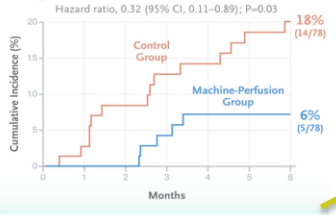
LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- Whether hypothermic machine perfusion is also beneficial in transplantation of livers obtained from brain-dead donors
- Whether prevention of post-transplantation cholangiopathy increases the cost-effectiveness of machine perfusion

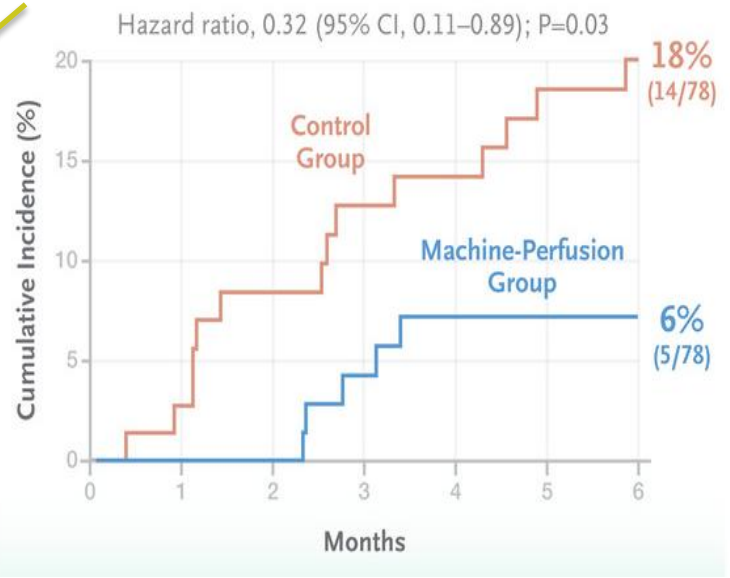


Cumulative Incidence of Symptomatic Nonanastomotic Biliary Strictures



CONCLUSIONS

Hypothermic oxygenated machine perfusion led to a lower risk of nonanastomotic biliary strictures following the transplantation of livers obtained from donors after circulatory death than conventional static cold storage.



Highlights:

- Absolute risk reduction: 12% → **NNT 8**
- Total number of biliary stentings: 5 vs. 22
- PRS 30% vs 46% NS
- EAD 26% vs 40% NS
- AKI dialysis 10% NS
- Re-LT 6 mnd 4 vs 8% NS
- Complications NS
- **NNT 16 needed to prevent 1 re-LTx**

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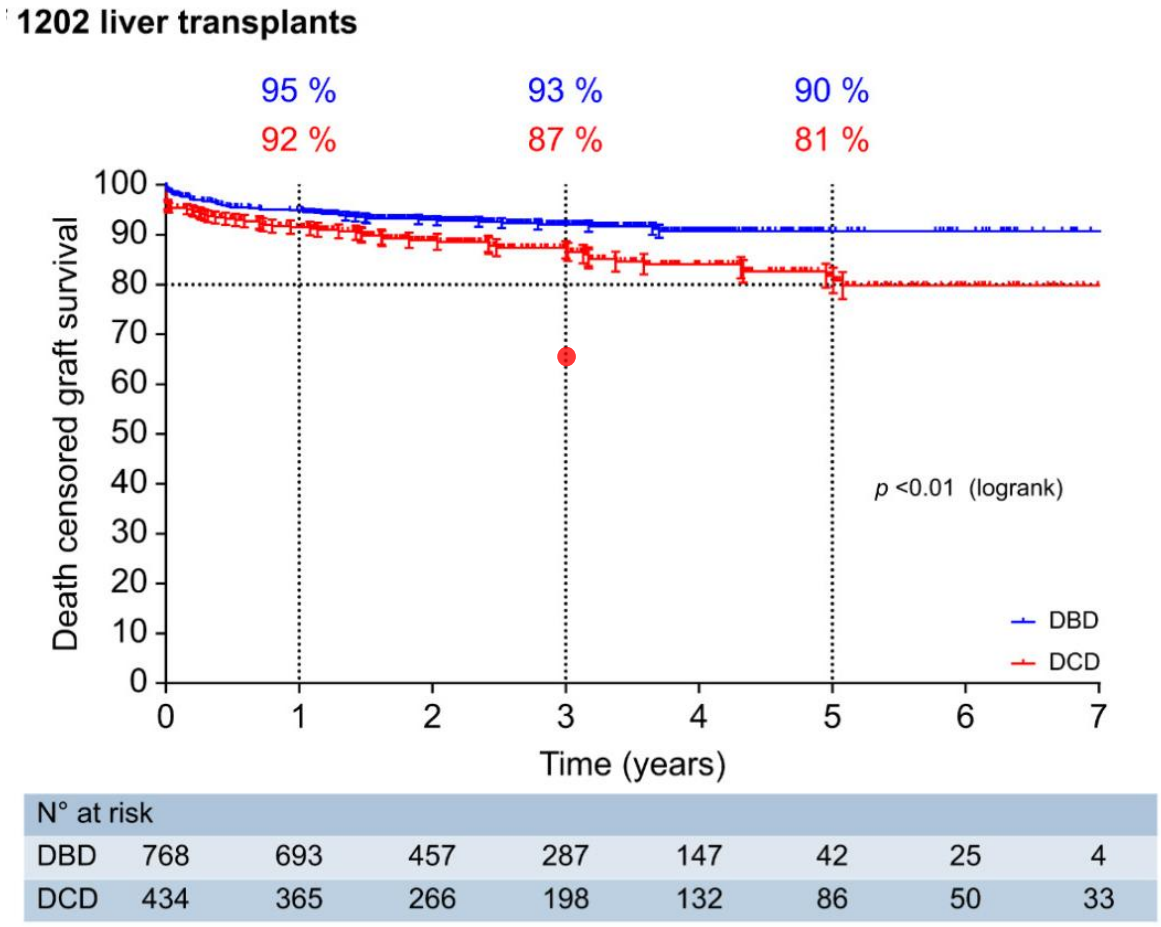
Hypothermic Oxygenated machine perfusion: real-world data

- DBD:
  - 3 year death-censored graft survival: 93%
  - 12 months cumulative incidence NAS: 2.3%
- DCD:
  - 3 year death-censored graft survival: 87%
  - 12 months cumulative incidence NAS: 12,6%



N° at risk								
DBD	768	693	457	287	147	42	25	4
DCD	434	365	266	198	132	86	50	33

Eden, et al. HOPE-REAL Study. Journal of Hepatology 2024

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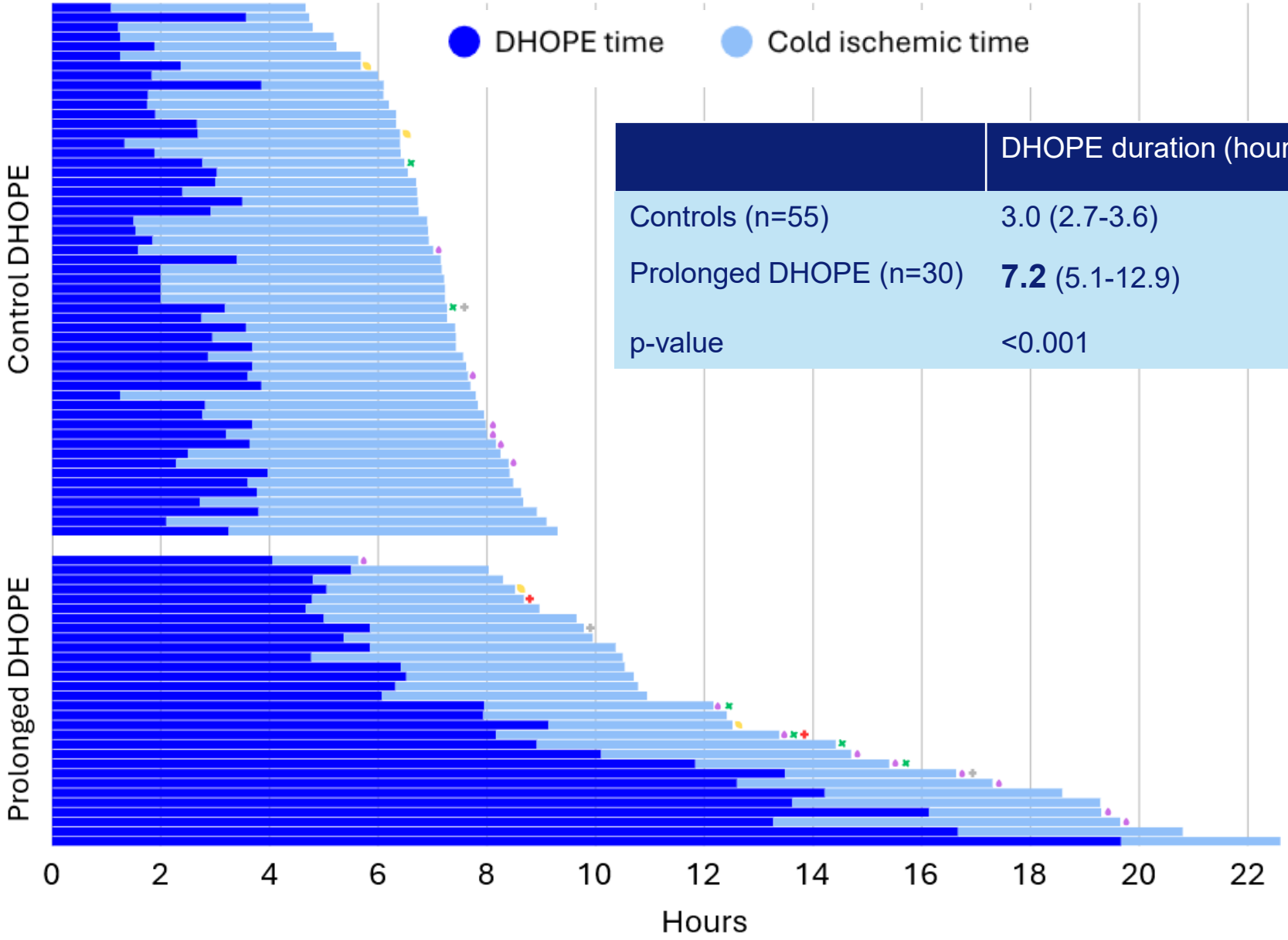
Kunnen we de preservatietijd verlengen met DHOPE?



	DHOPE duration (hours)	Total preservation time (hours)
Controls (n=55)	3.0 (2.7-3.6)	8.2 (±1.3)
Prolonged DHOPE (n=30)	**7.2** (5.1-12.9)	**14.1** (±4.5)
p-value	<0.001	<0.001

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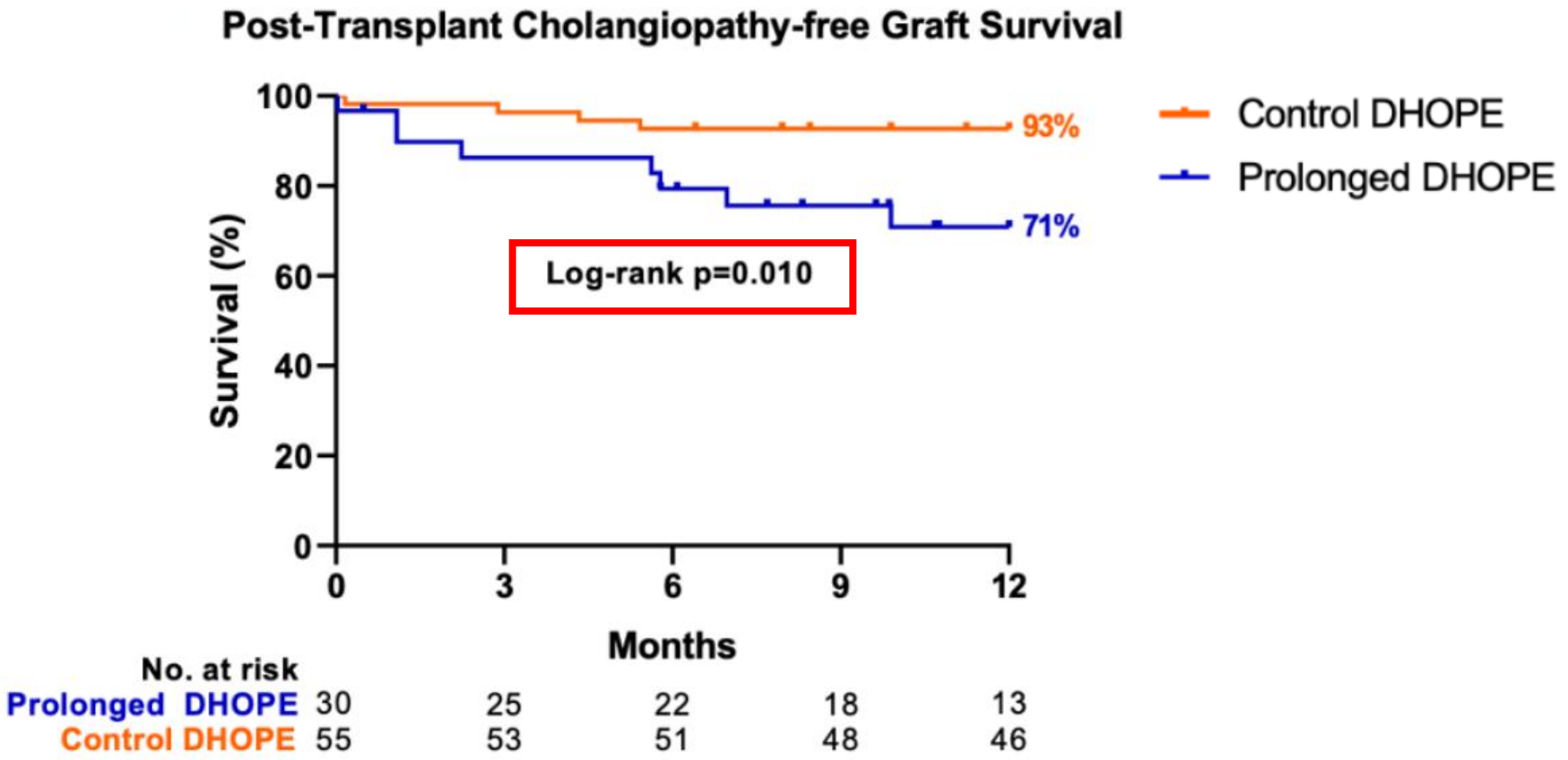
Maar komt bij DCD donorlevers met een prijs:
galwegcomplicatie-vrije graft-survival



Deel 2: Wat als je de donorlever vooraf niet vertrouwt?
DCD, oud, steatose, hoog donorlab, lange stervensfase

Vroeger afwijzen voor de zekerheid,
→ nu mogelijkheid tot functioneel testen buiten het lichaam:

Warm

35-37°C

Normothermic Machine Perfusion (**NMP**)

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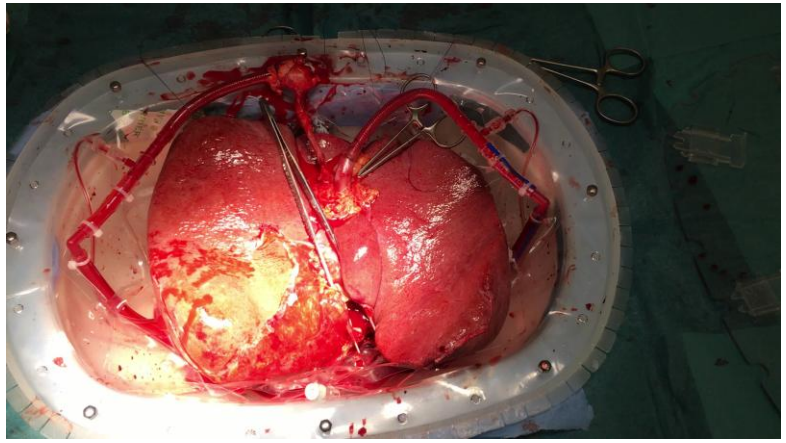
Complexe procedure beschermen, opwarmen & test *DHOPE-COR-NMP*



Hypothermic perfusion (10ºC)

1 hour

DHOPE

Switch

Rewarming (20-37ºC)

1 hour

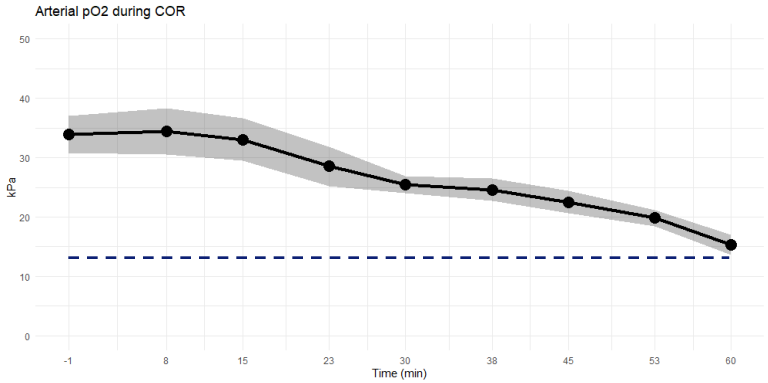
COR

Normothermic perfusion (37ºC)

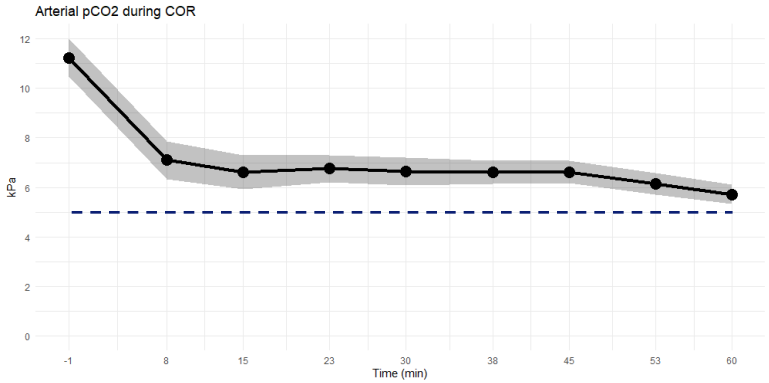
at least 2.5 hours

NMP

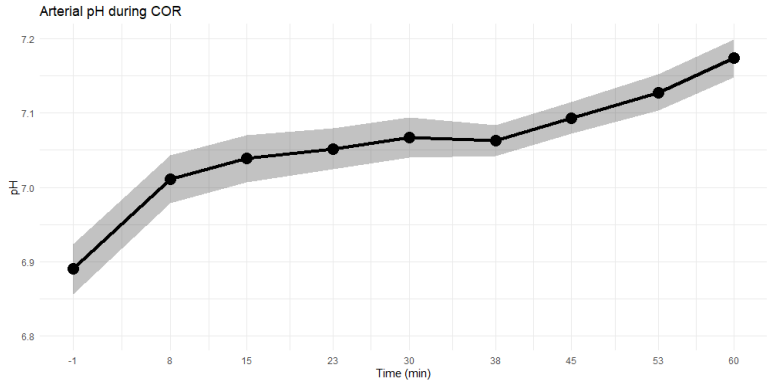
Wat gebeurt er tijdens de opwarming van de donorlever?



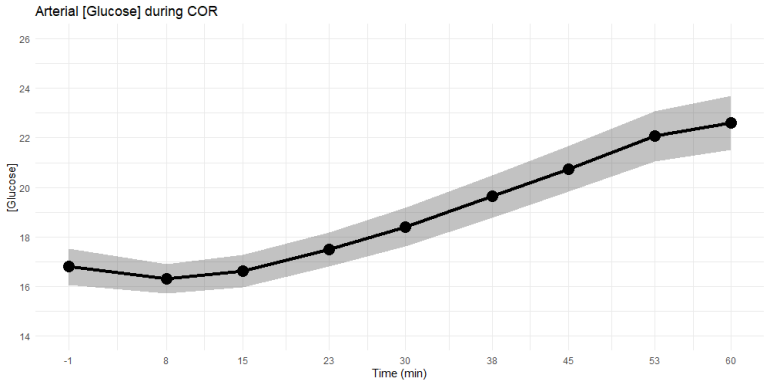
PO2



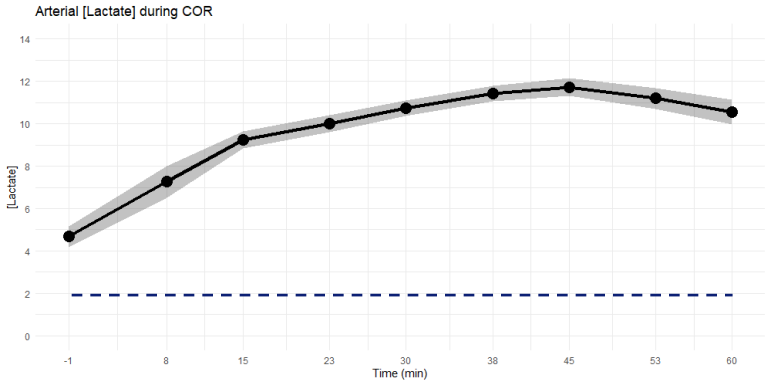
PCO2



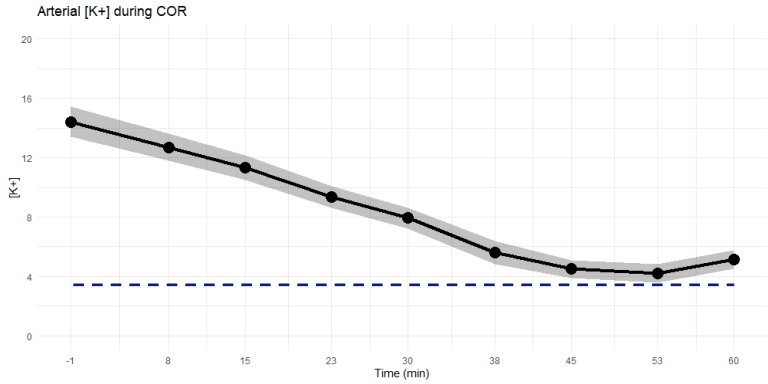
pH



Glucose



Lactate



K^+

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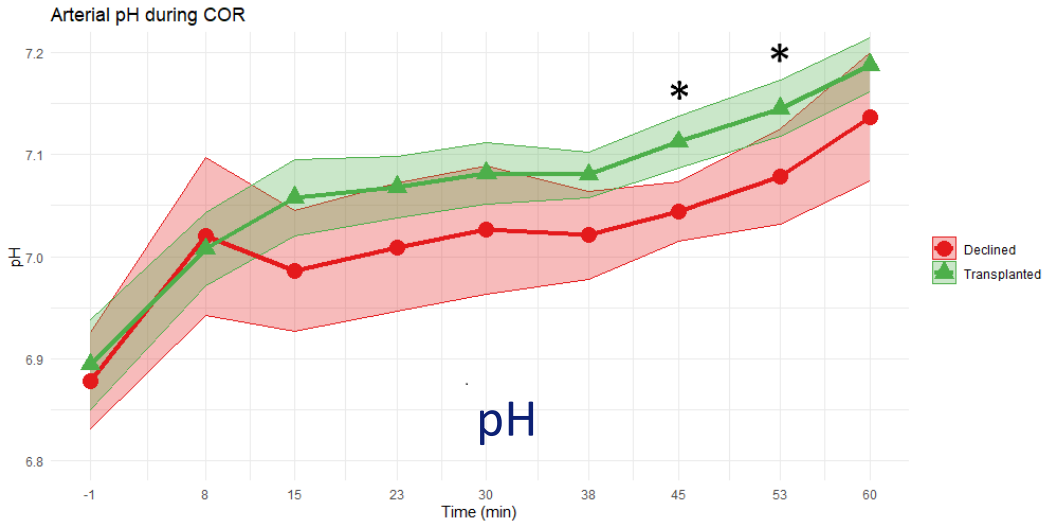
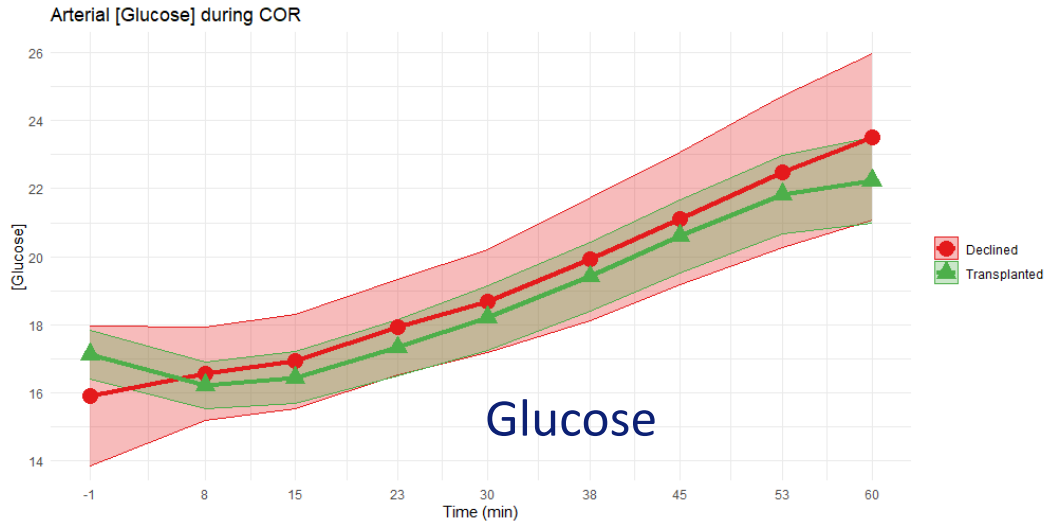
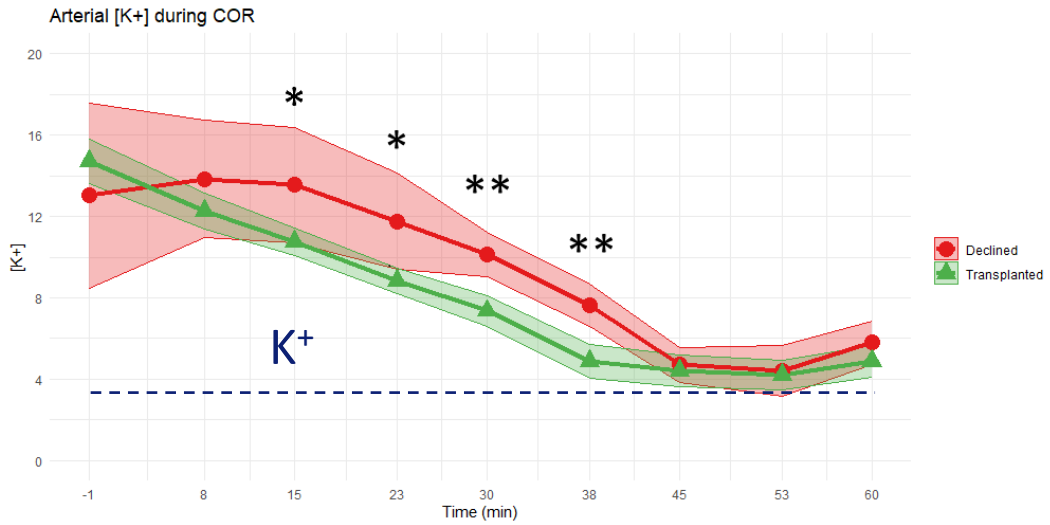
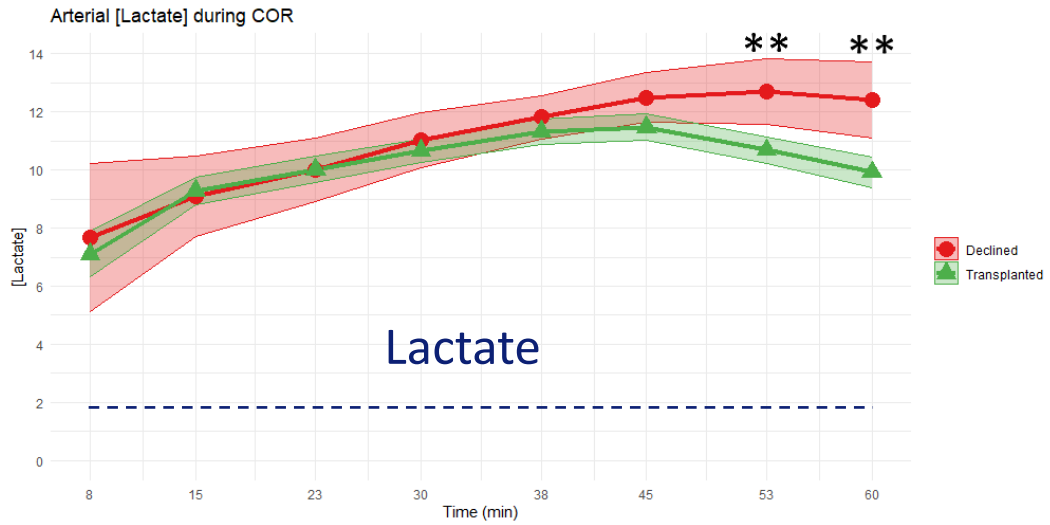
Verschillen in wel / niet getransplanteerde levers









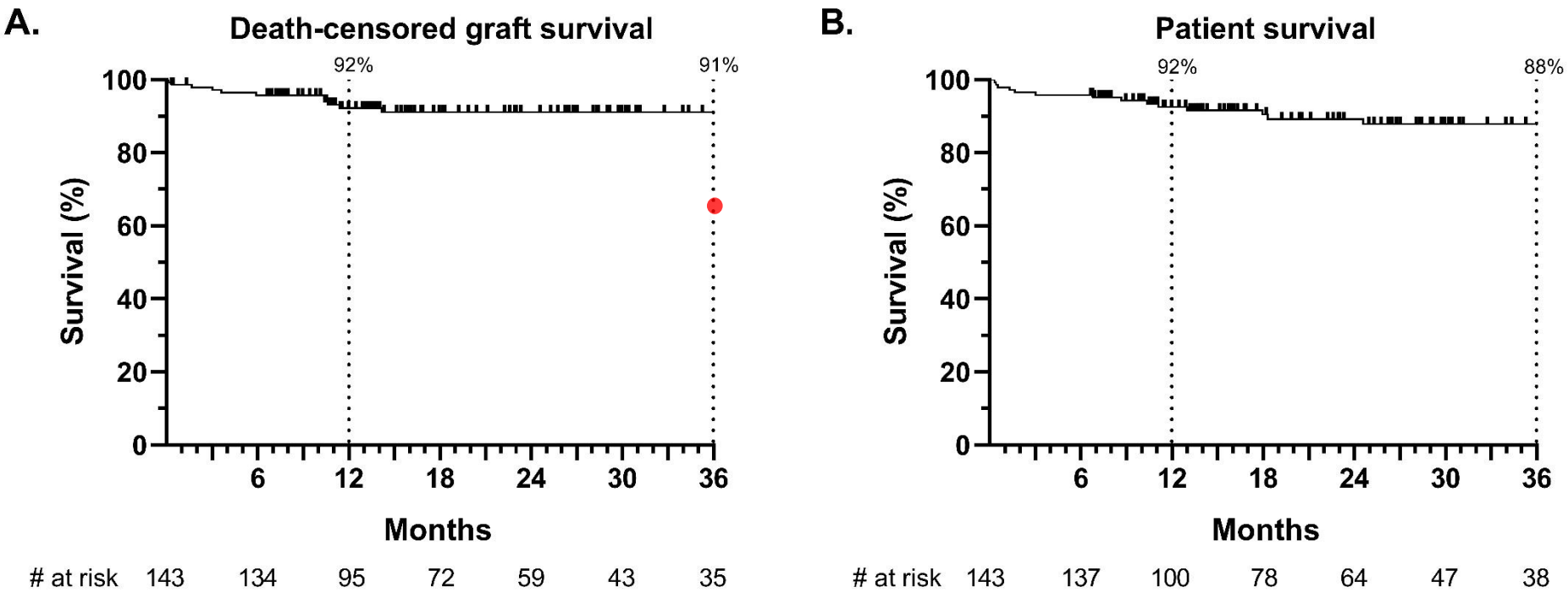
Functionele levertest: hepatocyt en cholangiocyt criteria

Beslismoment na 2,5 uur warme perfusie op 37° C

	Parameter	Green zone	Orange zone	Red zone
Hepatocytes	Bile production (ml)	≥ 10[a]	5 to 10	< 5
	Perfusate lactate (mmol/L)	< 1.7	1.7 to 4.0	> 4.0
	Perfusate pH	7.35–7.45	7.25 to 7.35	< 7.25
Cholangiocytes	Bile pH	> 7.45	7.40 to 7.45	< 7.40
	ΔpH	> 0.10	0.05 to 0.10	< 0.05
	ΔHCO_3^- (mmol/L)	> 5.0	3.0 to 5.0	< 3.0
	ΔGlucose (mmol/L)	< −5.0	−3.0 to −5.0	> −3.0

Van Leeuwen et al. Am J Transplant 2022

Results UMCG + Erasmus MC using the DHOPE-COR-NMP protocol



- 70% tested livers transplanted (143 / 205)
- 0% PNF
- 3,5% HAT

- 5% ischemische cholangiopathie
- 35% stenose op galweg anastomose

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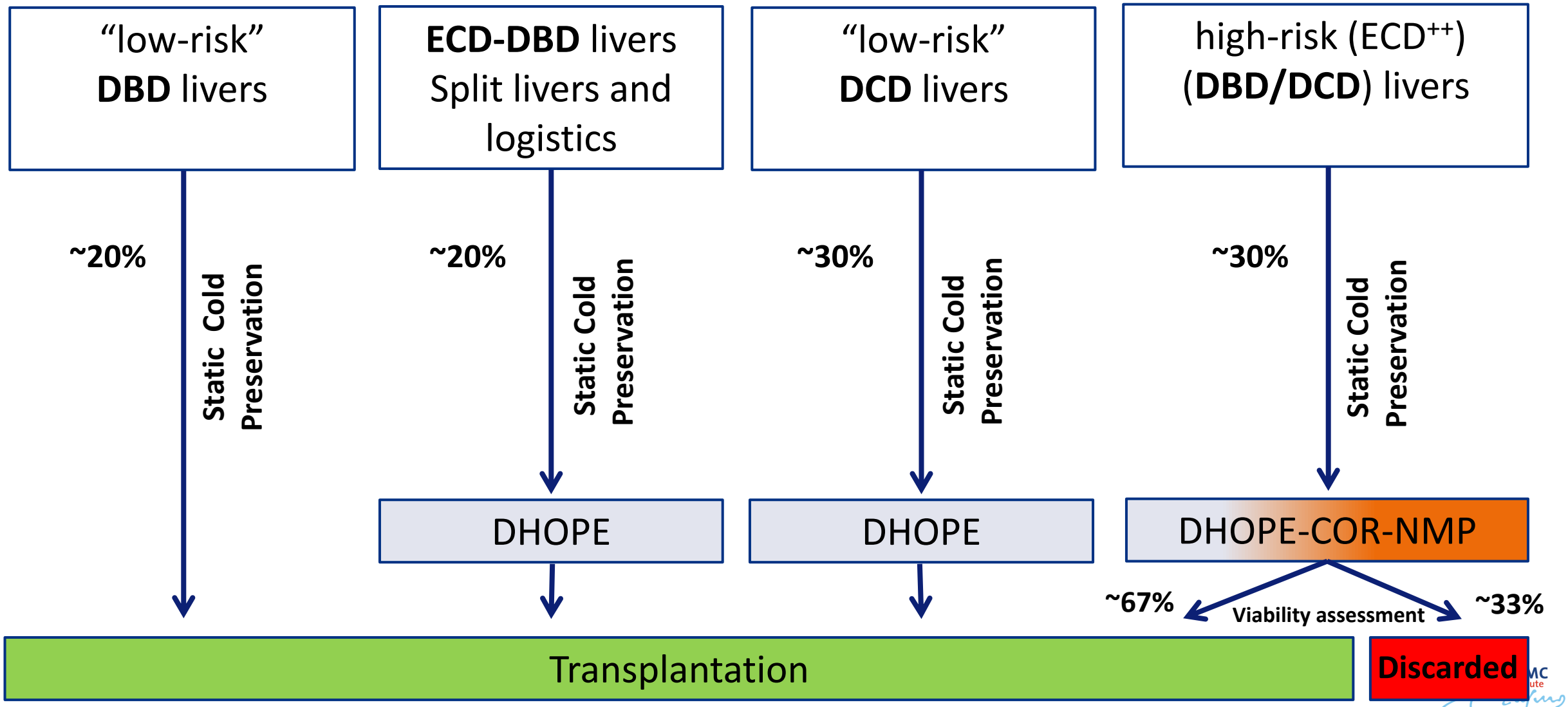
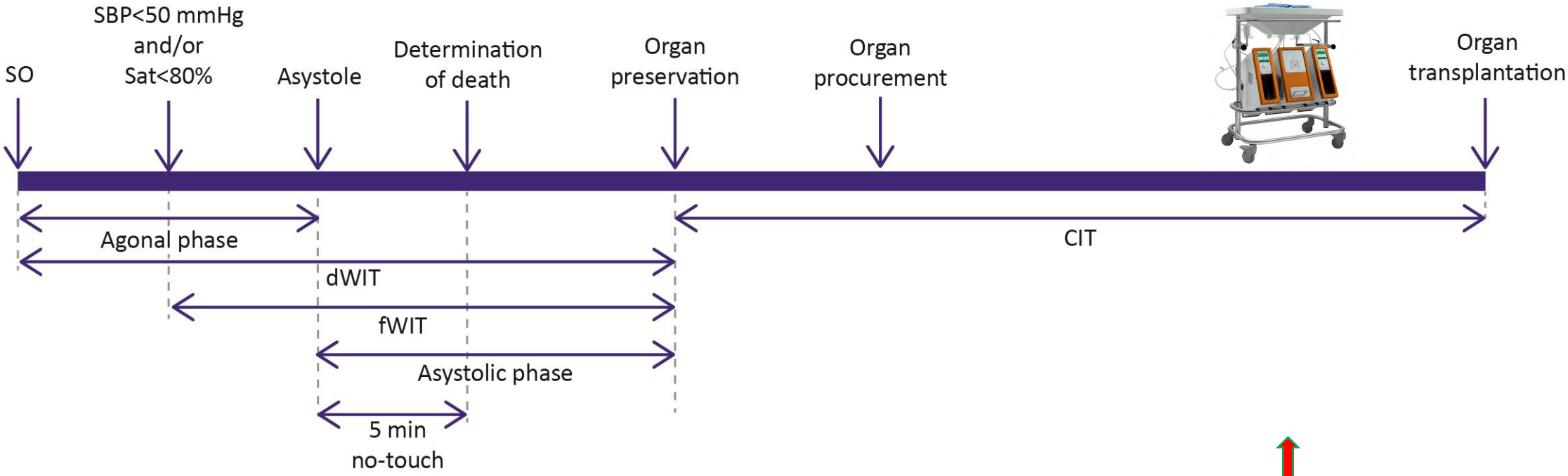
Ex situ Liver Machine Perfusion in NL



Kan het ook anders ?



Re-oxygenatie
in-situ

Re-oxygenatie
ex-situ

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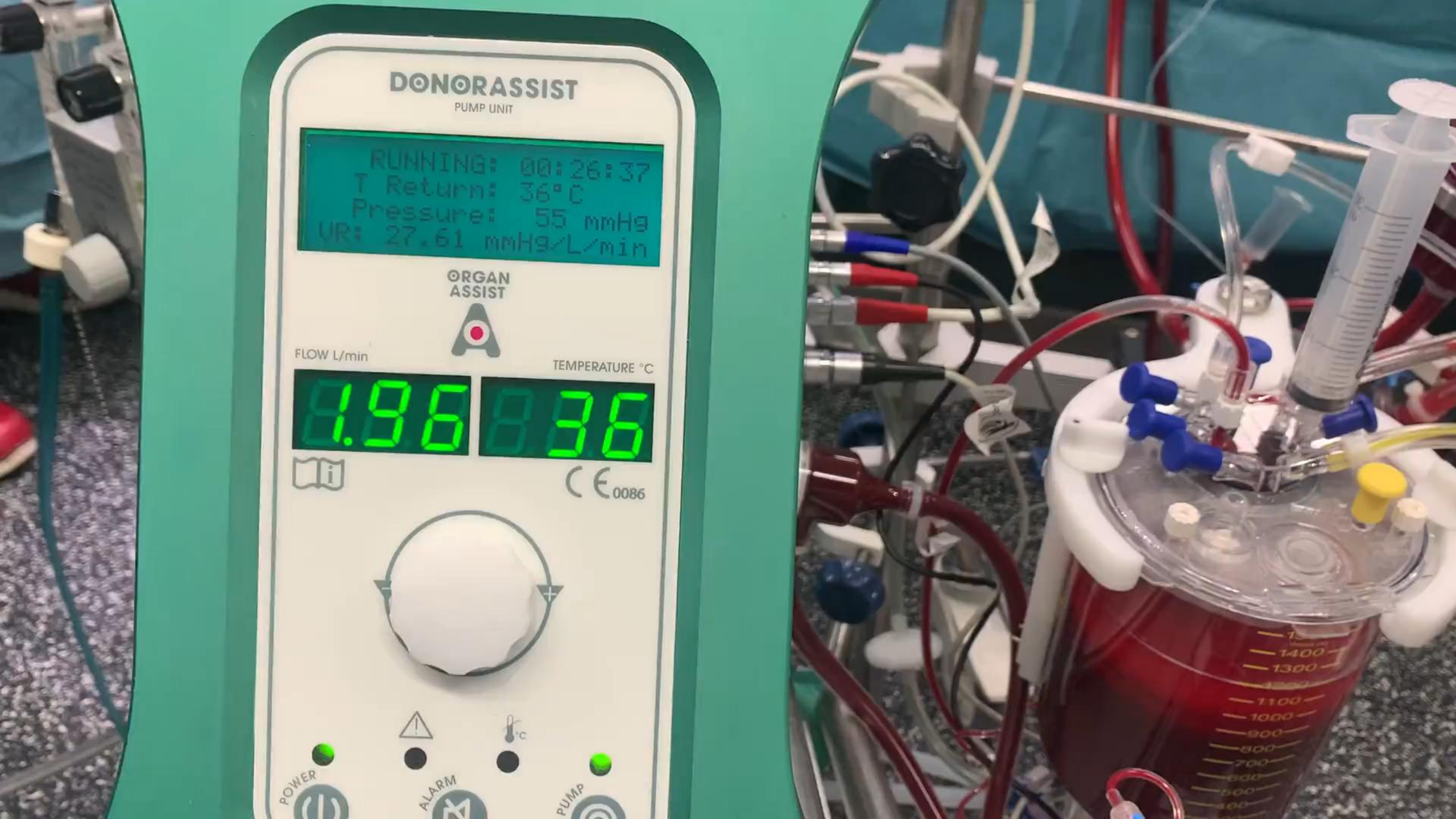
abdominale

Normotherme

Regionale

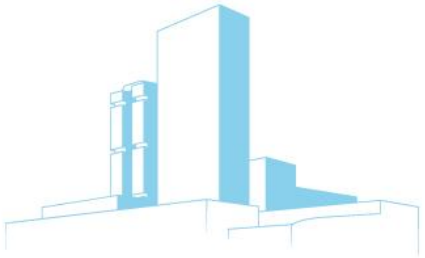
Perfusie (aNRP)

= ECMO tijdens donorprocedure


DONORASSIST
PUMP UNIT
RUNNING: 00:26:37
T Return: 36°C
Pressure: 55 mmHg
VR: 27.61 mmHg/L/min
ORGAN ASSIST
FLOW L/min
TEMPERATURE °C
1.96
36
0086
POWER
ALARM
PUMP

Erasmus MC Transplantatie Instituut 2025

Erasmus MC
Transplantatie Instituut

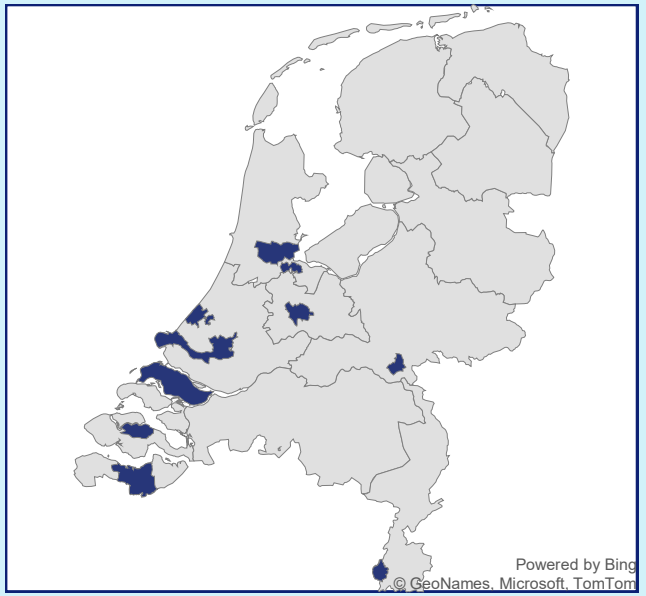


14 aNRP
Perfusions

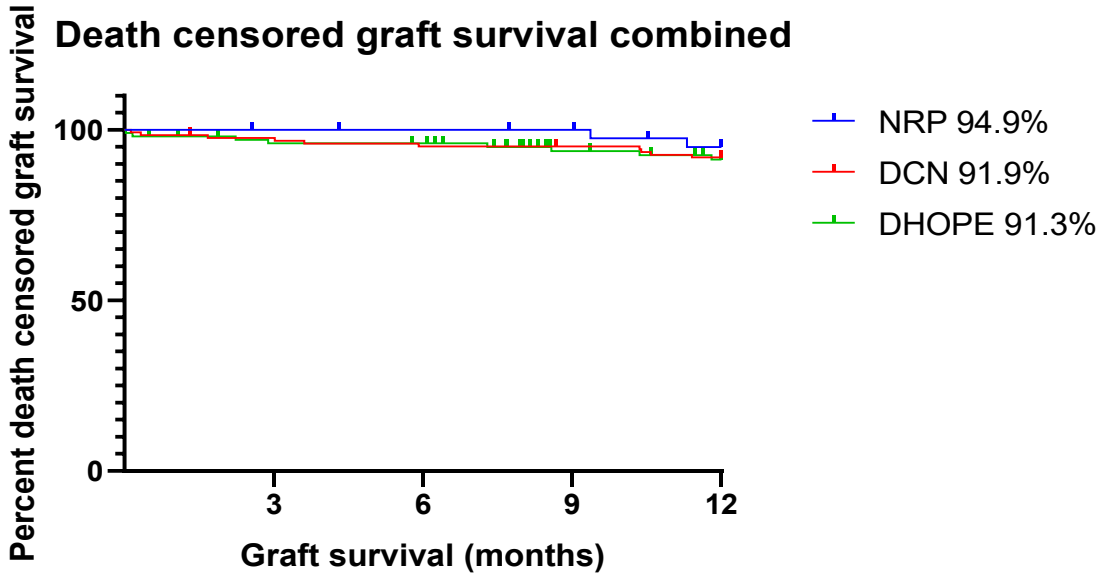
2
LUMC

3
UMCG

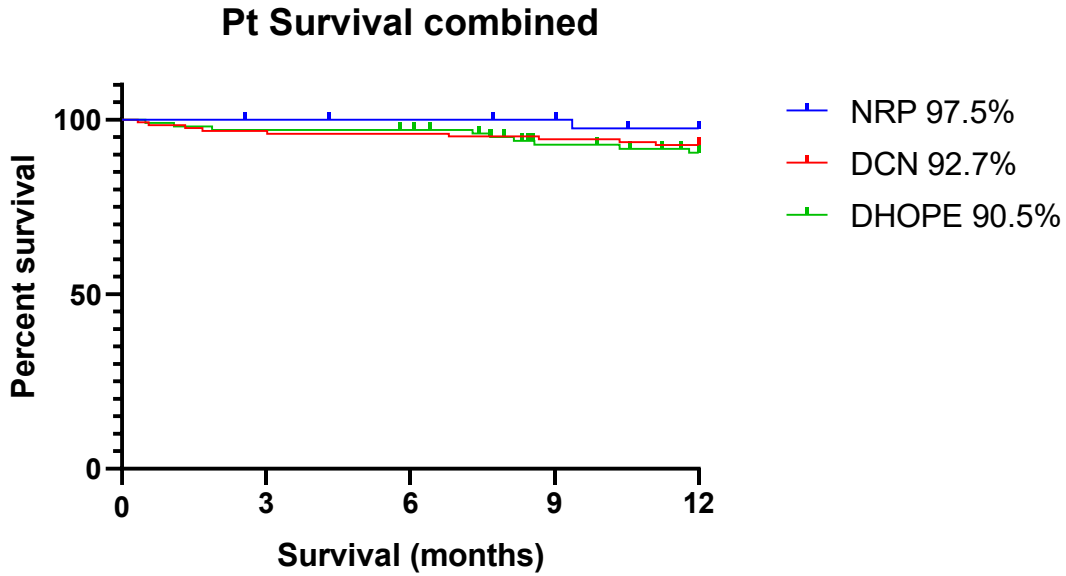
9
Erasmus MC



Uitkomsten aNRP vergeleken met ex-situ perfusie
data UMCG en Erasmus MC



NRP	44	44	43	42	37
DCN	124	121	118	117	112
DHOPE	101	95	94	80	73



NRP	44	44	43	42	38
DCN	124	121	120	118	115
DHOPE	101	99	98	84	77

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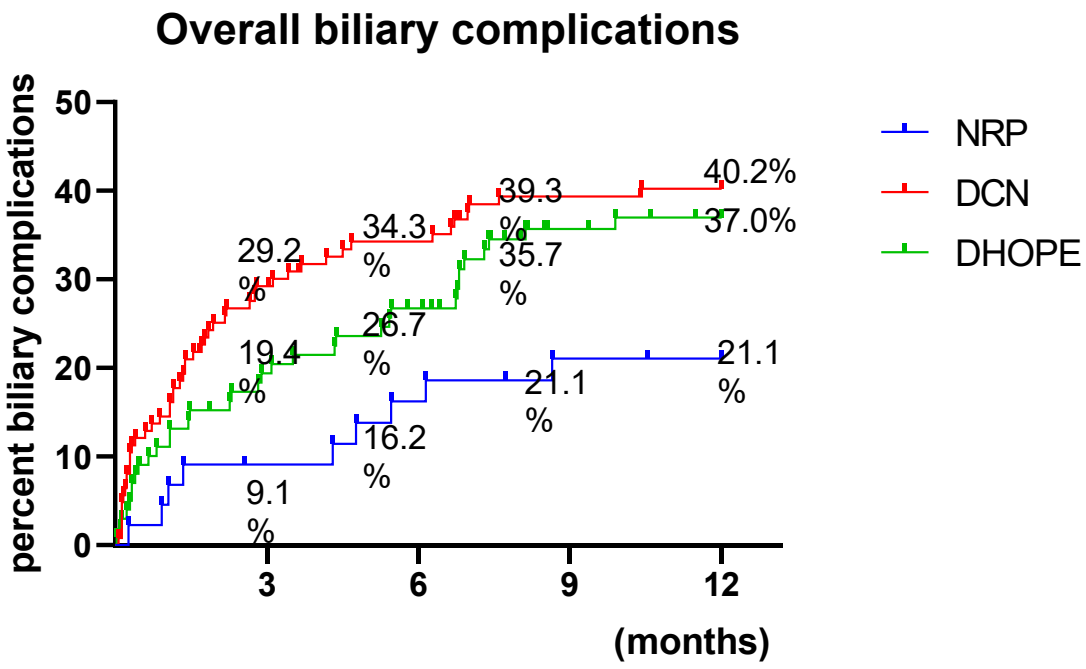
Verschil in galwegcomplicaties aNRP vergeleken met ex-situ perfusie?

data UMCG en Erasmus MC



NRP	44	40	36	33	31
DCN	124	87	79	72	69
DHOPE	101	78	70	52	47

2026 coming soon:
Nation-wide Randomized Clinical Trial:

“In situ versus ex Situ orgaan Preservatle: een geRandomiseerde studiE”

INSPIRE

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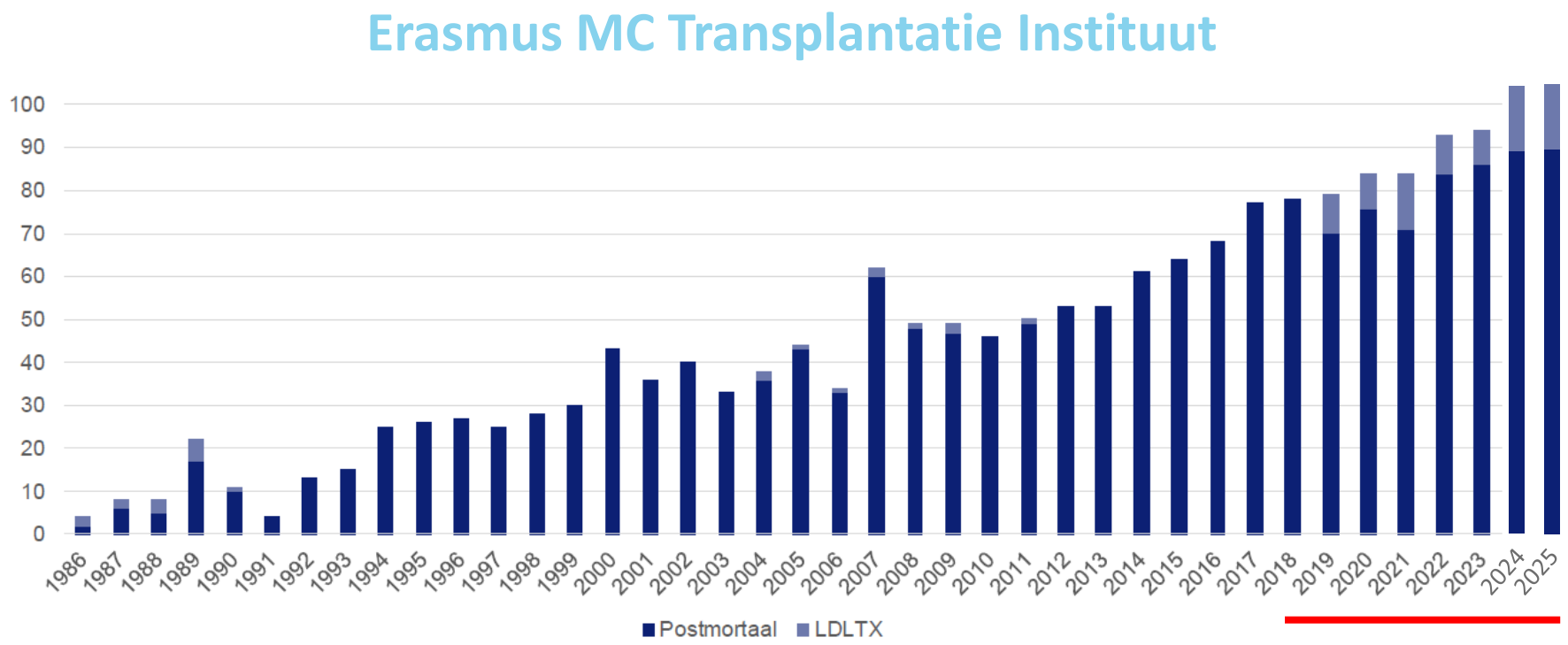
Levertransplantatie na machineperfusie



15% groei post-mortale programma door machineperfusie

	2018	2019	2020	2021	2022	2023	2024	2025
LTx after machine perfusion	11/78 (14%)	11/70 (16%)	19/75 (25%)	30/71 (42%)	48/84 (57%)	61/86 (71%)	78/93 (84%)	68/95 (72%)

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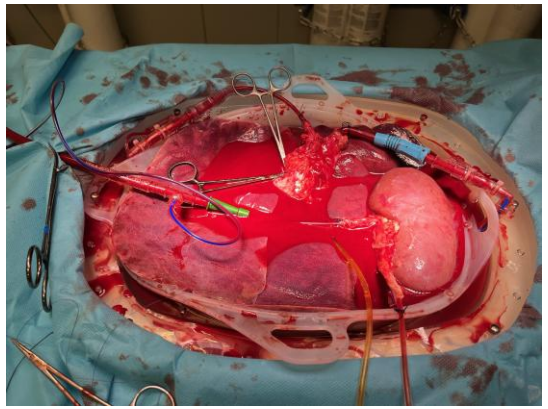
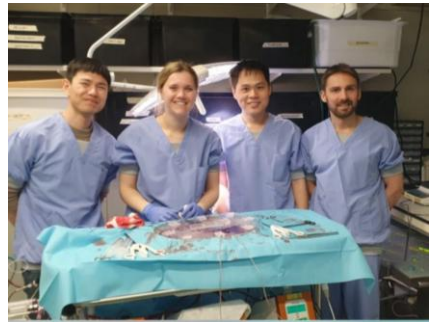
Toekomst van leverperfusie in 5-10 jaar

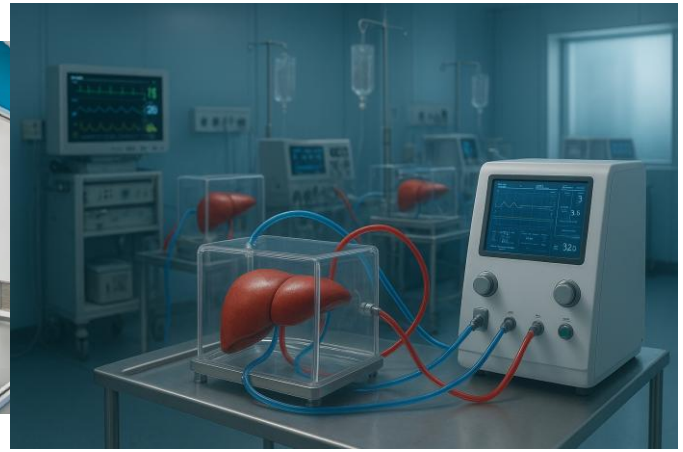
Paralelle perfusies

Liver-split on pump



Gecombineerde lever – nier perfusies





Organ Hub (“Lever IC”)

Regeneratieve geneeskunde met:

- Cellen
- Medicijnen

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Samenvattend

- Meer donorlevers beschikbaar door de nieuwe donorwet,
- Helaas meer slechte donorlevers beschikbaar door de donorwet

- Koude geoxygeneerde leverperfusie beschermt tegen galwegschade
- Koude geoxygeneerde leverperfusie helpt een beetje in de logistiek

- Gecombineerde koude + warme perfusie kan ECD levers testen met 70% gebruik
- aNRP doet hetzelfde, maar lijkt beschermend tegen galwegcomplicaties

- Een Nederlandse RCT gaat het definitieve antwoord binnen 5 jaar geven

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Orgaanperfusie specialisten Erasmus MC Transplantatie Instituut

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Dank voor uw aandacht!

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