Intraoperative hemoadsorption in heart transplantation patients

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Conflicts of interest

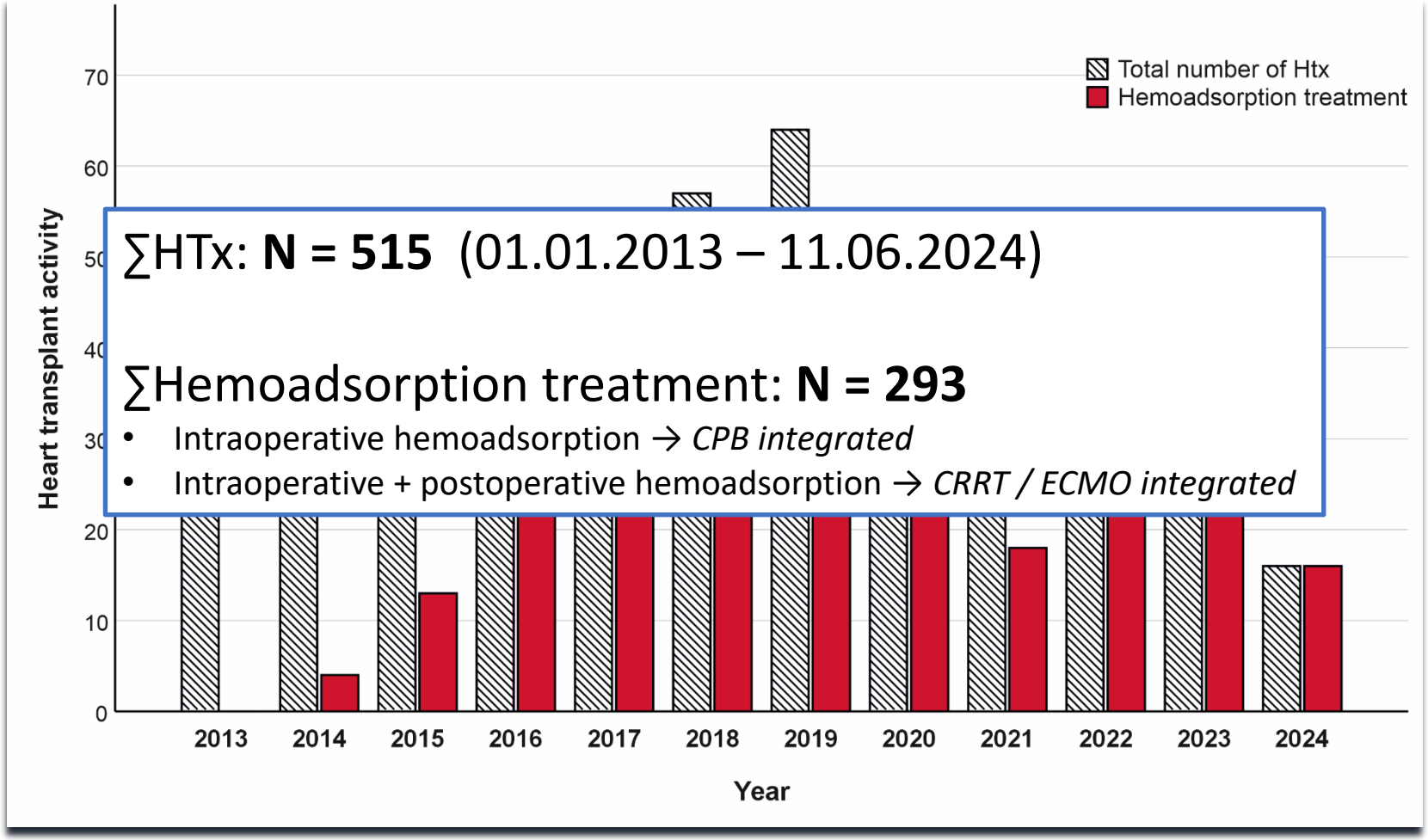
Conflict 1

Speaker reports travel funding and honoraria for lectures from

CytoSorbents Europe GmbH, Berlin, Germany *in the last five years.*

SINGLE CENTRE 10–YEAR CLINICAL EXPERIENCE:

HEMOADSORPTION TREATMENT DURING HEART TRANSPLANTATION – SEMMELWEIS UNIVERSITY BUDAPEST HEART AND VASCULAR CENTRE

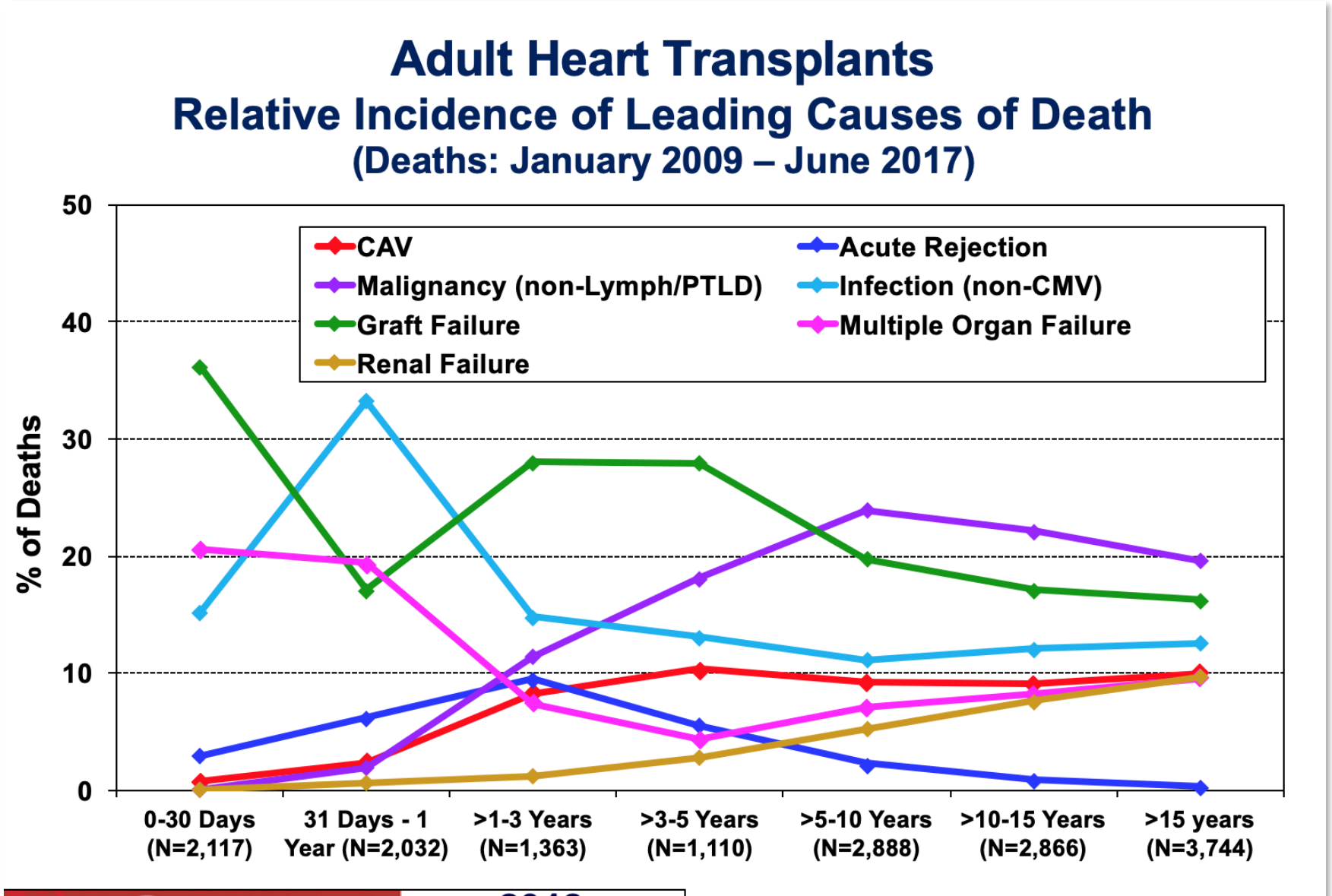


∑HTx: **N = 515** (01.01.2013 – 11.06.2024)

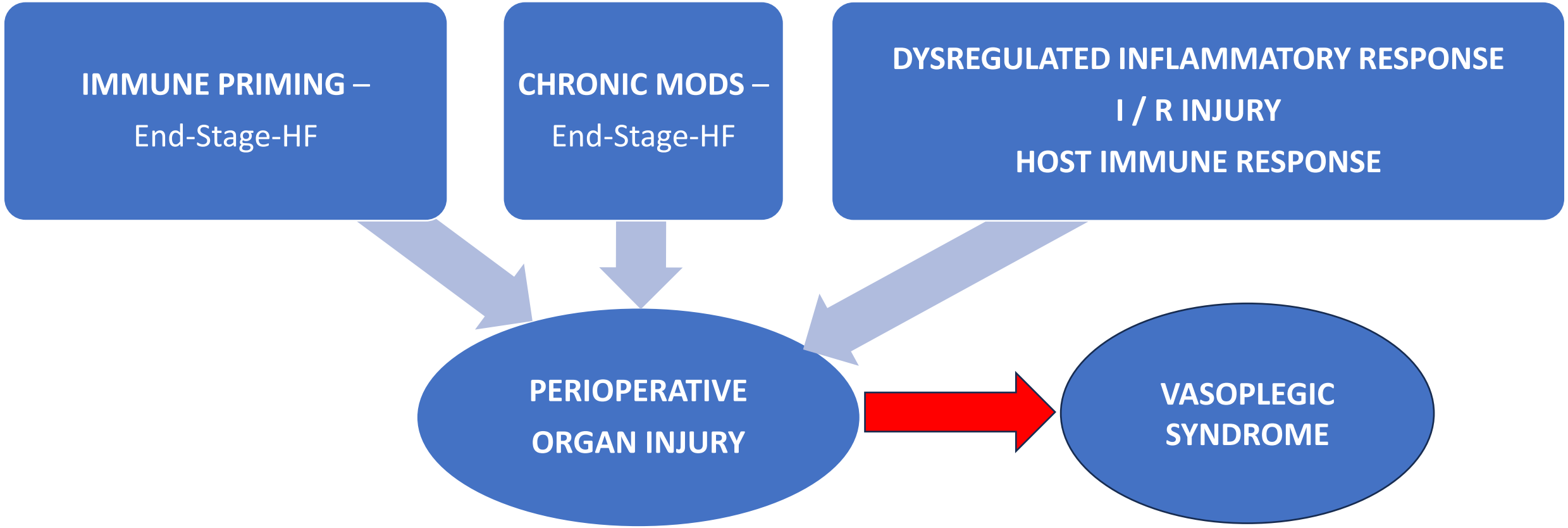
∑Hemoadsorption treatment: **N = 293**

- Intraoperative hemoadsorption → *CPB integrated*
- Intraoperative + postoperative hemoadsorption → *CRRT / ECMO integrated*

HEART TRANSPLANTATION AND MULTIPLE ORGAN FAILURE



HTx AND MULTIPLE ORGAN FAILURE – PATHOPHYSIOLOGY

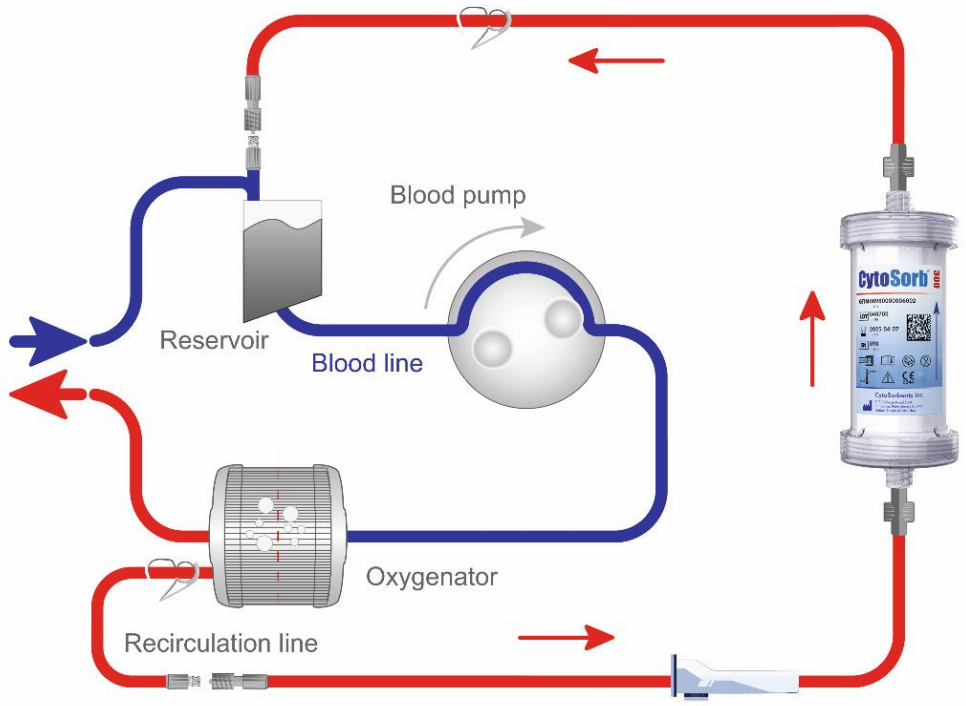


van Vessem ME et al. Eur J Cardiothorac Surg (2017);51(3):532–8.
Omar S et al. Am J Med Sci (2015), 349(1):80-88.
Patarroyo M et al. J Heart Lung Transplant (2012), 31(3):282-287.
Vistnes M et al. Expert Rev. Mol. Diagn. (2010), 10(2): 147–157.
Byrne J et al. European Journal of Cardio-thoracic Surgery (2004), 25(3):327-332.

CONCEPTION AND HYPOTHESIS

INTRAOPERATIVE CPB-INTEGRATED HEMOADSORPTION (CytoSorb™) **BENEFICIALLY AFFECTS:**

- *Severity of hemodynamic instability*
- *Frequency of vasoplegic syndrome*
- *Frequency of postoperative organ dysfunctions*
- *Frequency of immunological adverse events*



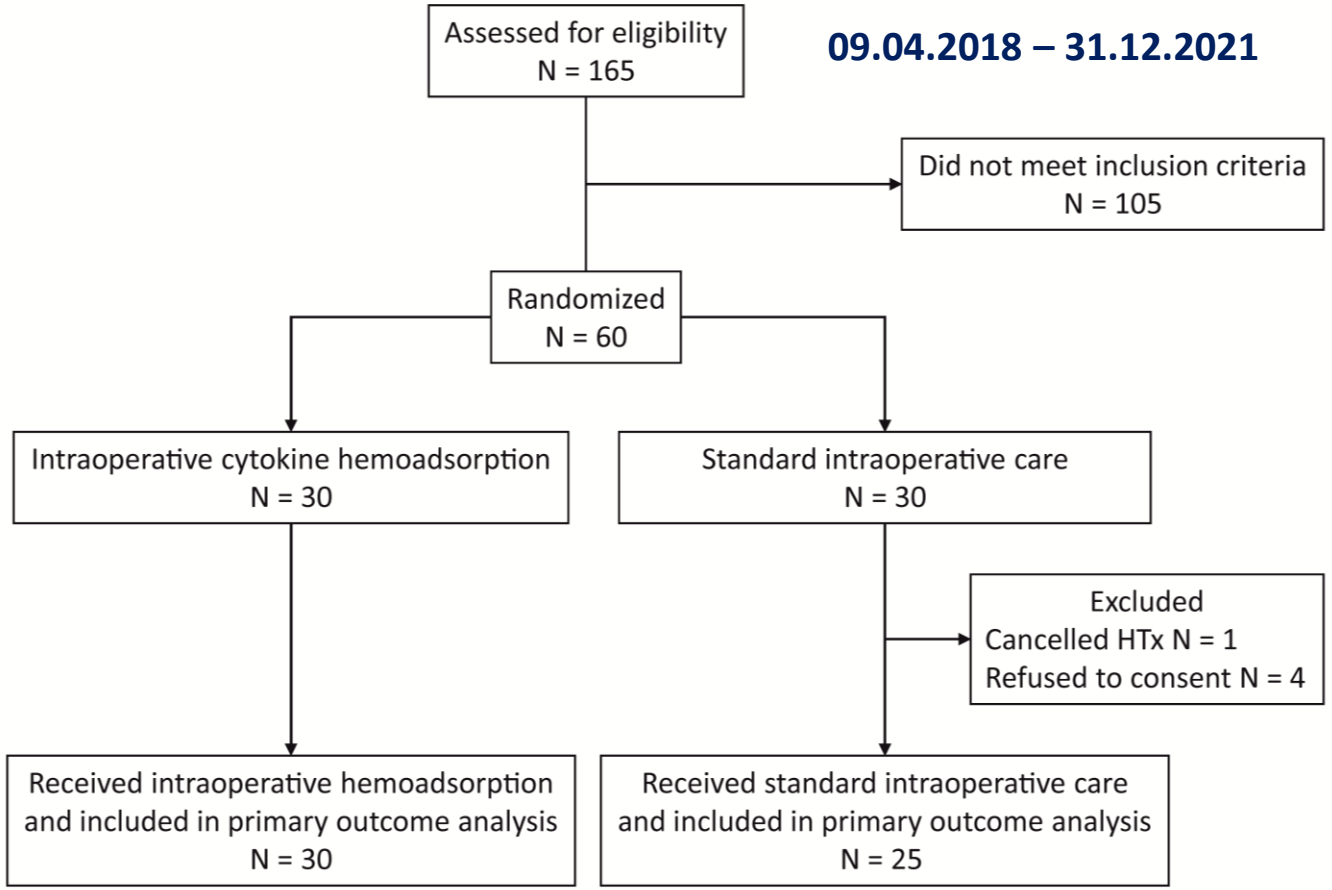
Nemeth E et al. ESC Heart Failure 2024; 11: 772–782

RANDOMIZED CONTROLLED TRIAL – OPEN LABEL, SINGLE CENTER

ClinicalTrials.gov Identifier: ***NCT03145441***

- **INCLUSION CRITERIA**
  - *Age ≥ 18 years*
  - *United Network for Organ Sharing (UNOS) Status 6*

- **EXCLUSION CRITERIA**
  - Age < 18 years
  - Long-standing hospitalization prior to HTx procedure
  - Inotrope dependence prior to HTx procedure
  - Mechanical circulatory support prior to HTx procedure
  - Progressive end-organ failure prior to HTx procedure
  - 'High Urgency status'
  - Retransplantation



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BASELINE CLINICAL CHARACTERISTICS_1

Parameters	Control group N=25	Hemoadsorption group N=30	*P*
Recipient age, year	56 (48-60)	56 (47-61)	0.839
Donor age, year	46 ± 9	41 ± 11	0.355
Body Mass Index, kg/m^2	26.9 ± 4.8	25.4 ± 3.3	0.084
Female sex, n	10 (40.0%)	15 (50.0%)	0.458
Diabetes mellitus, n	6 (24.0%)	5 (16.7%)	0.521
Chronic Kidney Disease, n [a]	10 (40.0%)	13 (43.3%)	0.803
Chronic anemia, n	10 (40.0%)	9 (30.0%)	0.437
ACEI / ARB, n	10 (40.0%)	18 (60.0%)	0.140
ARNI, n	9 (36.0%)	12 (40.0%)	0.761
Amiodarone, n	3 (12.0%)	**11 (36.7%)**	0.061
Pulmonary vascular resistance, Wood unit	2.4 (1.2-3.5)	2.7 (1.9-4.4)	0.257
IMPACT score, point	4 (2.5-5.0)	4 (2.0-7.0)	0.892

Data: median (IQR), mean±SD, n (frequency)
Statistics: Mann-Whitney U test, two–sample *t*–test, qui square test, Fisher's exact test
[a] CKD: estimated Glomerular Filtration Rate < 60 ml/min/1.73 m^2
ACEI: Angiotensin-Converting Enzyme Inhibitor; ARB: Angiotensin II receptor blocker
ARNI, angiotensin receptor–neprilysin inhibitor; IMPACT: Index for Mortality Prediction After Cardiac Transplantation (0-50)

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BASELINE CLINICAL CHARACTERISTICS_2

Parameters	Control group N=25	Hemoadsorption group N=30	*P*
Etiology of end-stage heart failure			
Ischemic cardiomyopathy, n	8 (32.0%)	8 (26.7%)	0.665
Hypertrophic cardiomyopathy, n	1 (4.0%)	3 (10.0%)	0.617
Idiopathic cardiomyopathy, n	12 (48.0%)	15 (50.0%)	0.883
Other, n	4 (16.0%)	4 (13.3%)	1.00
Intraoperative factors			
Aorta cross-clamp time, min	50 (41-79)	72 (43-86)	0.375
CPB time, min	129 (104-169)	133 (116-154)	0.819
Total ischemic time, hour	173 ± 41	152 ± 45	0.484

Data: n (frequency), median (IQR), mean±SD;
Statistics: qui square test, Fisher's exact test, Mann-Whitney U test, two–sample *t*–test
CPB: cardiopulmonary bypass

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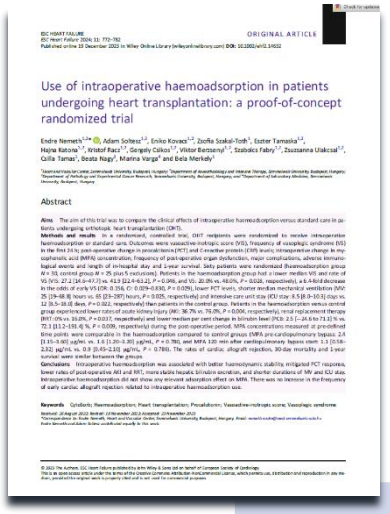
BASELINE CLINICAL CHARACTERISTICS_3

Parameters	Control group N=25	Hemoadsorption group N=30	*P*
Creatinine, µmol/L	104.0 (82.5-149.5)	105.5 (80.3-132.8)	0.742
eGFR, ml/min/1.73 m^2	64.2 (42.4-73.6)	61.5 (46.9-76.5)	0.813
Hemoglobin, g/dL	13.4 ± 1.9	13.0 ± 1.3	0.068
Bilirubin, µmol/L	9.5 (5.8-16.8)	11.8 (6.3-14.2)	0.919
C-reactive protein, mg/L	3.3 (1.8-7.3)	2.3 (0.9-4.8)	0.151
Procalcitonin, µg/L	0.04 (0.03-0.09)	0.04 (0.02-0.07)	0.463
TNF–α, pg/mL	0.88 (0.07–10.98)	0.25 (0.07–9.29)	0.764
IL-6, pg/mL	**4.6 (2.2-16.1)**	**2.9 (0.01-5.7)**	**0.029**
IL–1β, pg/mL	2.17 (0.43–5.26)	3.55 (0.74–10.09)	0.122
IL–10, pg/mL	6.89 (4.14–13.80)	8.14 (4.49–12.52)	0.600
C3a, ng/mL	163.4 (97.3–272.9)	119.95 (82.13–182.43)	0.166
C4a, ng/mL	693.4 (537.1–1075.2)	554.9 (438.2–715.4)	0.051
Terminal Complement Complex, mAU/mL	2903.2 ± 648.5	2595.7 ± 851.9	0.144
White cell count, G/L	8.2 (6.2-9.7)	8.0 (7.0-9.2)	0.980

Data: median (IQR), mean±SD;
Statistics: Mann-Whitney U test, two–sample *t*–test
eGFR= estimated Glomerular Filtration Rate

Nemeth E et al. ESC Heart Failure 2024; 11: 772–782
Nemeth E et al. RCT secondary analysis – data under publication process



Use of intraoperative haemoadsorption in patients undergoing heart transplantation: a proof-of-concept randomized trial

Abstract

SUMMARY OF THE RCT RESULTS

Hemodynamic stability / severity of vasoplegia

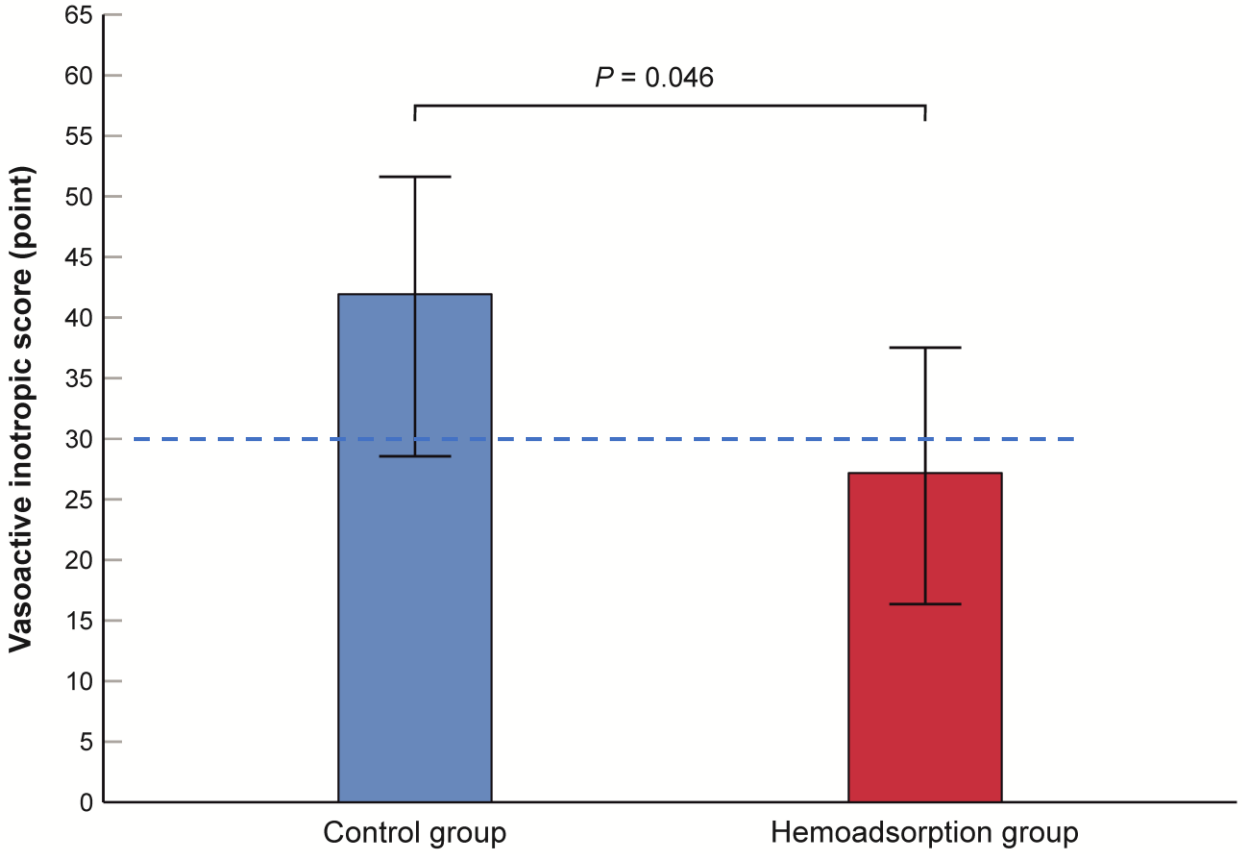
Characteristics of the inflammatory response

Complications / immunological adverse events

HEMODYNAMIC STABILITY
AND
SEVERITY OF VASOPLEGIA

EARLY POSTOPERATIVE HEMODYNAMIC INSTABILITY

Composite Endpoint: **Vasoactive Inotropic Score** → calculated for the first postoperative 24 hours



Vasoactive Inotropic Score =
dopamine dose (µg/kg/min)
+**dobutamine** dose (µg/kg/min)
+100×adrenaline dose (µg/kg/min)
+10×**phosphodiesterase inhibitor** dose (µg/kg/min)
+100×**noradrenaline** dose (µg/kg/min)
+10000×**vasopressin** dose (U/kg/min)

Yamazaki Y et al. J Anesth (2018) 32:167-73

N=55
Data: median;
Error Bars: 95% Confidence Intervals;
Statistics: Mann-Whitney U test

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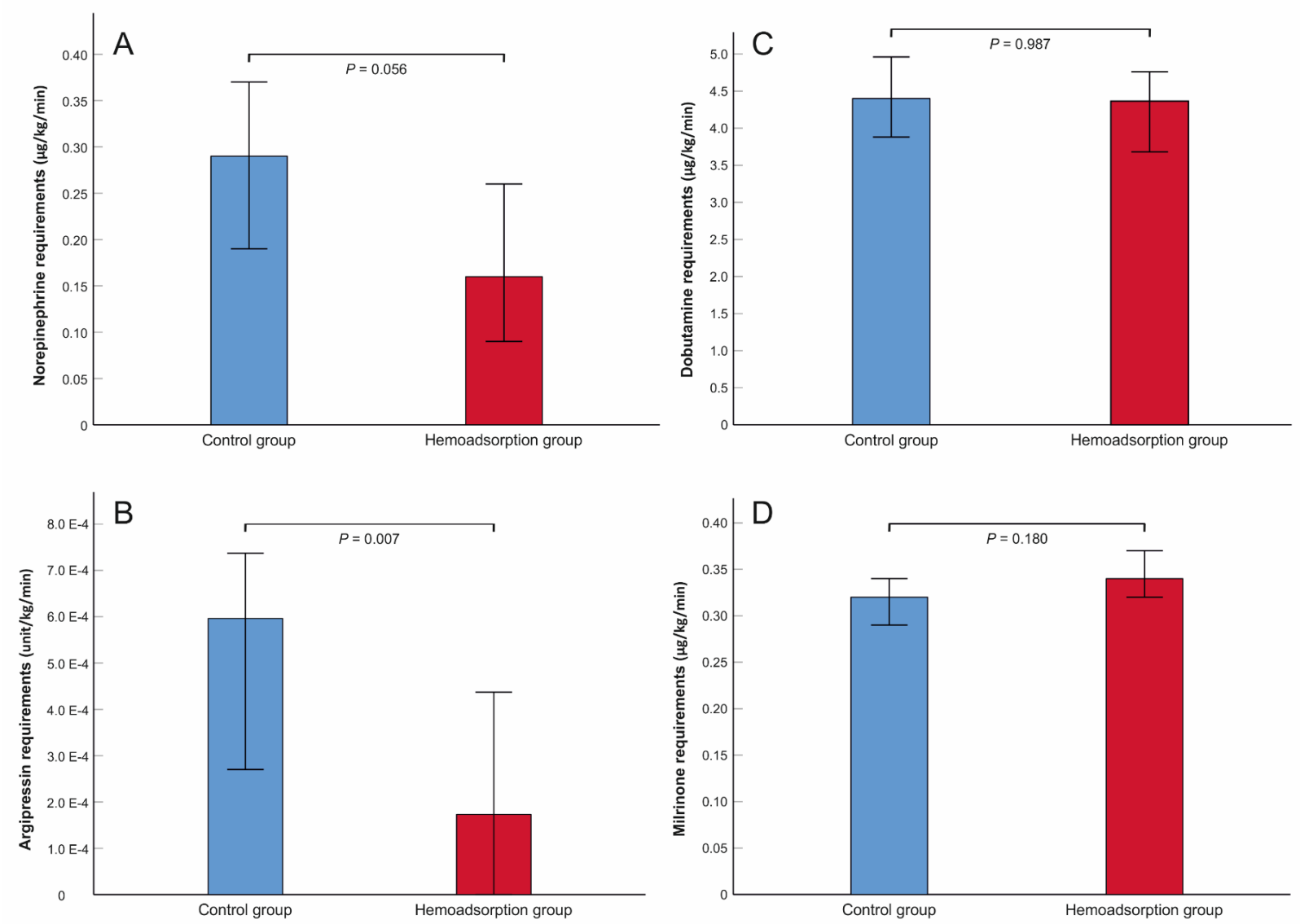
EARLY POSTOPERATIVE HEMODYNAMIC INSTABILITY

NORADRENALINE

DOBUTAMINE



ARGININE VASOPRESSIN

MILRINONE

N=55; Data: median; Error Bars: 95% Confidence Intervals; **Statistics:** Mann-Whitney U test

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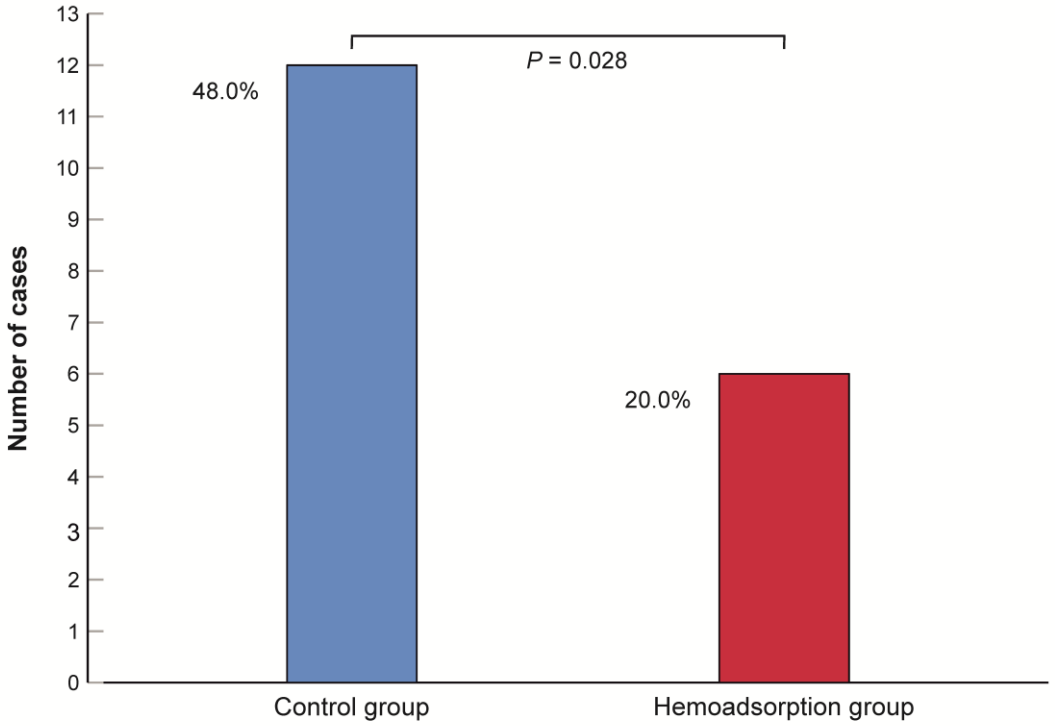
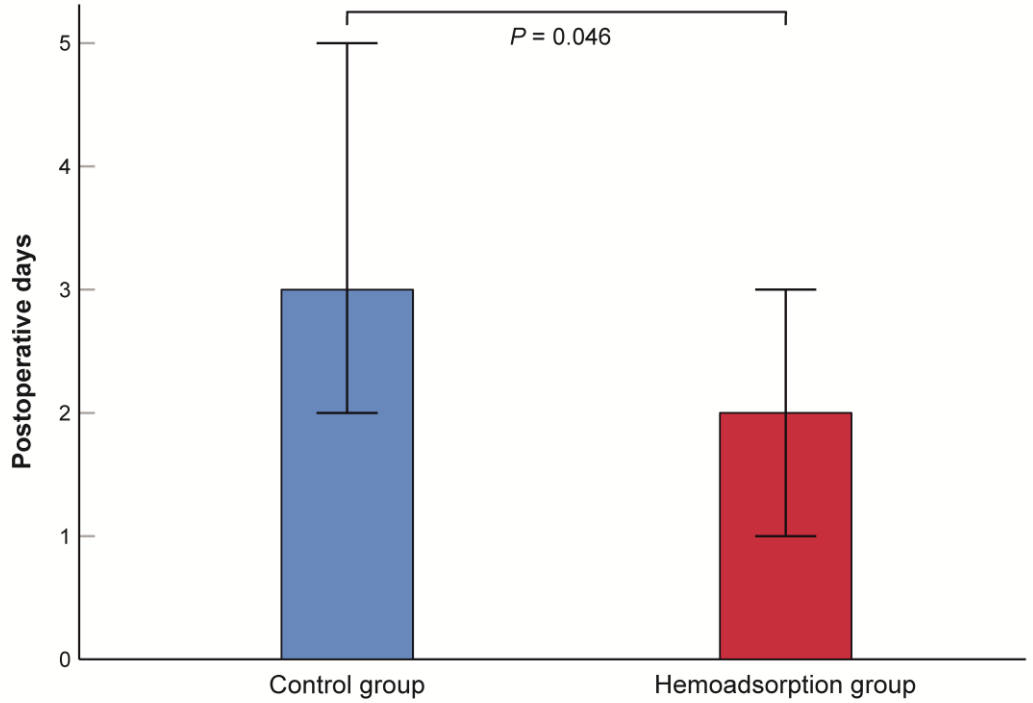
SEVERITY OF VASOPLEGIA

Vasoplegic Syndrome:

- **Noradrenaline reqirements ≥ 0.3 µg/kg/min AND arginine vasopressin reqirements at any dose**



Frequency of Vasoplegic Syndrome



Length of vasopressor support

N=55; Data: number of patients and median; Error Bars: 95% Confidence Intervals
Statistics: qui square test, Fisher's exact test, Mann-Whitney U test

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INDEPENDENT PREDICTORS – EARLY POSTOPERATIVE VASOPLEGIA

Parameters	OR	95% CI	*P*
Intraoperative hemoadsorption	0.156	0.029-0.830	0.029
Preoperative amiodarone therapy	6.315	1.032-38.630	0.046
CPB ≥ 180 minutes	25.776	2.089-318.016	0.011

Multivariable logistic regression, backward elimination likelihood-ratio, N = 55

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Adjusted covariates in the regression model:

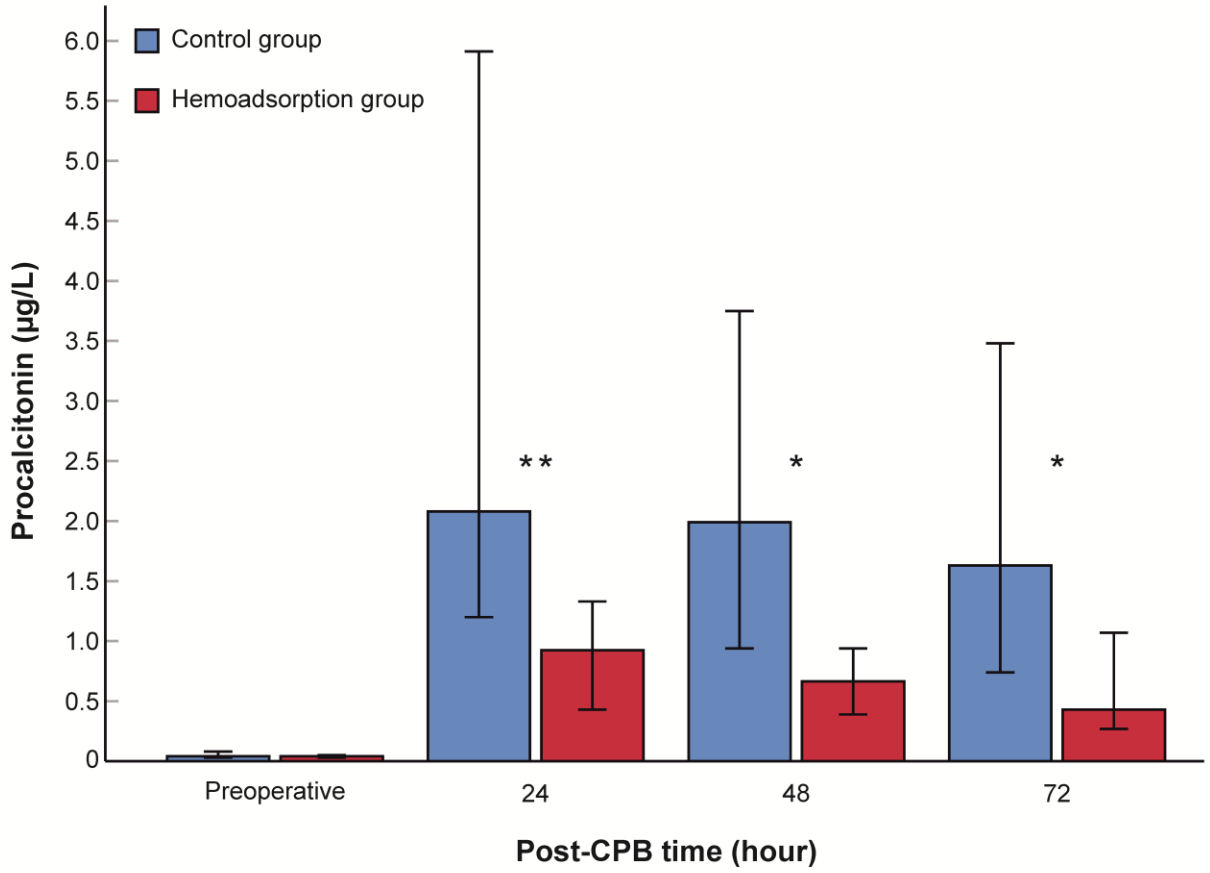
- intraoperative hemoadsorption treatment;
- female sex;
- chronic kidney disease;
- angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker treatment pre-transplant;
- amiodarone treatment pre-transplant;
- preoperative pulmonary vascular resistance > 3.0 Wood units;
- CPB ≥ 180 minutes.

OR: odds ratio;
CI: confidence interval;
CPB: cardiopulmonary bypass

6.4-fold decrease in the odds of early vasoplegic syndrome

CHRARACTERISTICS OF THE INFLAMMATORY RESPONSE

INFLAMMATORY RESPONSE – PROCALCITONIN



N=55; Data: median; Error Bars: 95% Confidence Intervals; **Statistics:** Mann-Whitney U test; * *P*<0.05; ** *P*<0.01

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INFLAMMATORY RESPONSE – POST-CPB 24 hours

Parameters	Control group N=25	Hemoadsorption group N=30	*P*
C-reactive protein, mg/L	86.6 (51.3-128.1)	79.9 (30.5-95.1)	0.108
TNF–α, pg/mL	0.07 (0.07-5.77)	0.07 (0.07-1.07)	0.681
IL-6, pg/mL	82.8 (51.6-139.3)	72.3 (48.8-171.0)	0.822
IL–1β, pg/mL	1.06 (0.38-3.68)	4.22 (0.95-7.05)	0.058
IL–10, pg/mL	144.9 (48.2-250.0)	106.7 (56.8-240.4)	0.896
IL–6/IL–10 ratio	0.78 (0.36-1.44)	0.70 (0.34-1.74)	0.801
C3a, ng/mL	140.2 (105.3-225.9)	131.1 (84.0-211.3)	0.286
C4a, ng/mL	509.5 (389.2-750.1)	538.2 (376.4-654.9)	0.815
Terminal Complement Complex, mAU/mL	3008.1 ± 1310.2	2653.6 ± 497.2	0.183
White cell count, G/L	12.7 ± 5.6	12.4 ± 4.7	0.817

Data: median (IQR), mean±SD;
Statistics: Mann-Whitney U test, two–sample *t*–test

Nemeth E et al. RCT secondary analysis – data under publication process

COMPLICATIONS

SECONDARY OUTCOME PARAMETERS

Parameters	Control group N=25	Hemoadsorption group N=30	*P*
Postcardiotomy ECMO, n	3 (12.0%)	0	0.088
Postoperative bleeding, mL	570 (385-1305)	565 (350-1130)	0.543
Reoperation for bleeding/tamponade, n	2 (8.0%)	0	0.202
Postoperative mechanical ventilation, hour	**65 (23-287)**	**25 (19-68.8)**	**0.025**
Acute kidney injury$_{total}$, n[a]	**19 (76.0%)**	**11 (36.7%)**	**0.004**
Postoperative renal replacement therapy, n	**4 (16.0%)**	**0**	**0.037**
Per cent change in bilirubin, %	**72.1 (11.2–191.4)**	**2.5 (-24.6–71.1)**	**0.009**
Early Sepsis, n[b]	1 (4.0%)	0	0.455
Length-of-Intensive Care Unit-stay, day	**12 (8.5-18.0)**	**8.5 (8.0-10.3)**	**0.022**
Length-of-hospital stay, day	28 (24-38.5)	25 (22-34.3)	0.232
30-day mortality, n	2 (8.0%)	0	0.202

[a] AKI classification: KDIGO creatinine–based definition criteria for the first postoperative 5 days
[b] Early sepsis: screened for the first postoperative 5 days

Data: n (frequency), median (IQR);
Statistics: qui square test, Fisher's exact test, Mann-Whitney U test

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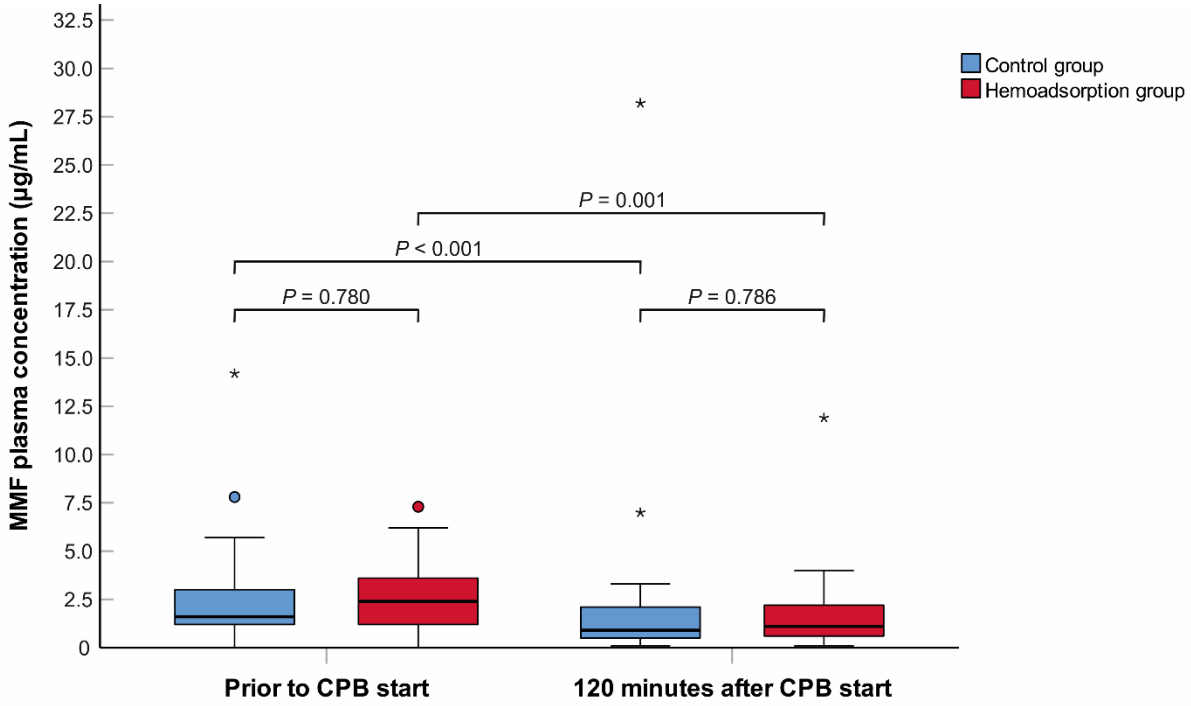
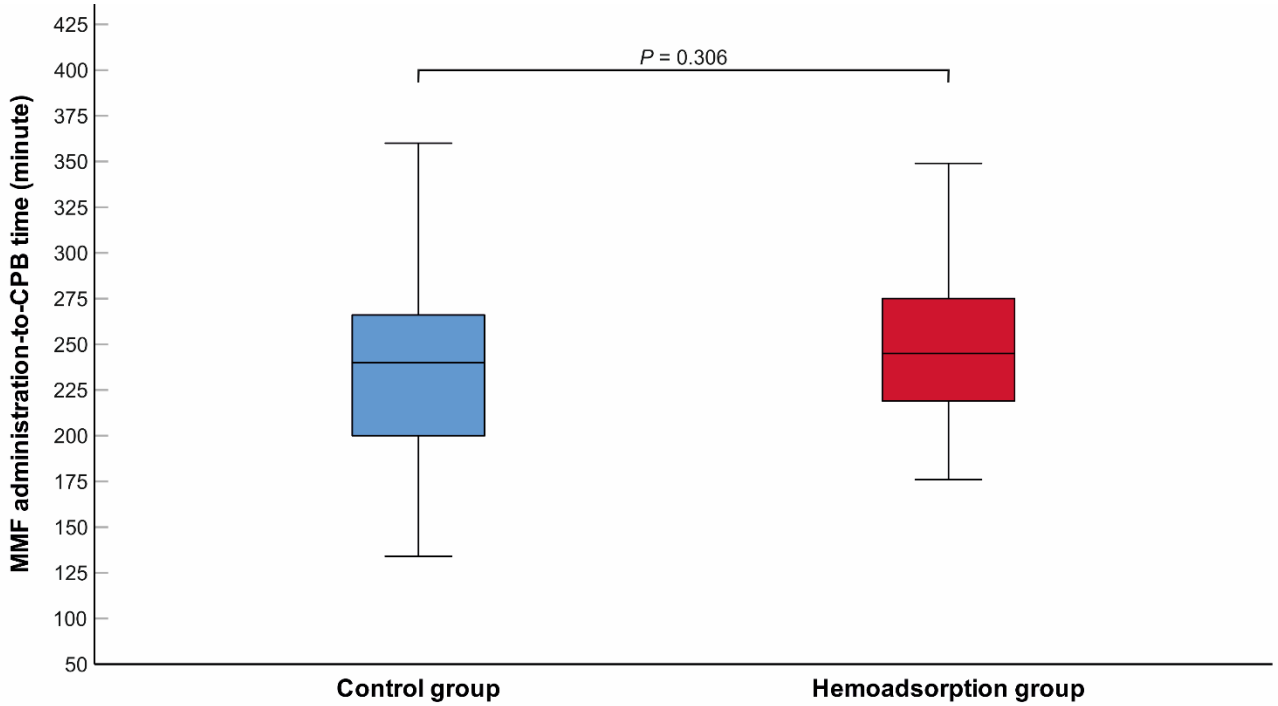
IMMUNOLOGICAL ADVERSE EVENTS

INTRAOPERATIVE CHANGE OF MYCOPHENOLATE MOFETIL





N=55; **Statistics:** Mann-Whitney U test; Wilcoxon signed ranks test; two-sample *t*-test
Filled circle: outlier
Asterisk: extreme value

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Check for updates

OPEN ACCESS

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Pharmacokinetics of immunosuppressive agents during hemoperfusion in a sheep model

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Key findings

Negligible clearance was observed in the measurements before and after the adsorber for PRED and BAS. For all other substances, a saturable adsorption sub-model with linear decrease of adsorption efficiency over the adsorbed amount best described the results. The maximum absolute adsorption amounts implied an adsorption rate of less than 5% of the daily administered doses for all tested substances.

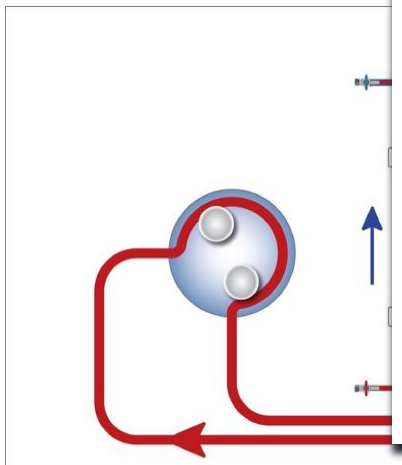
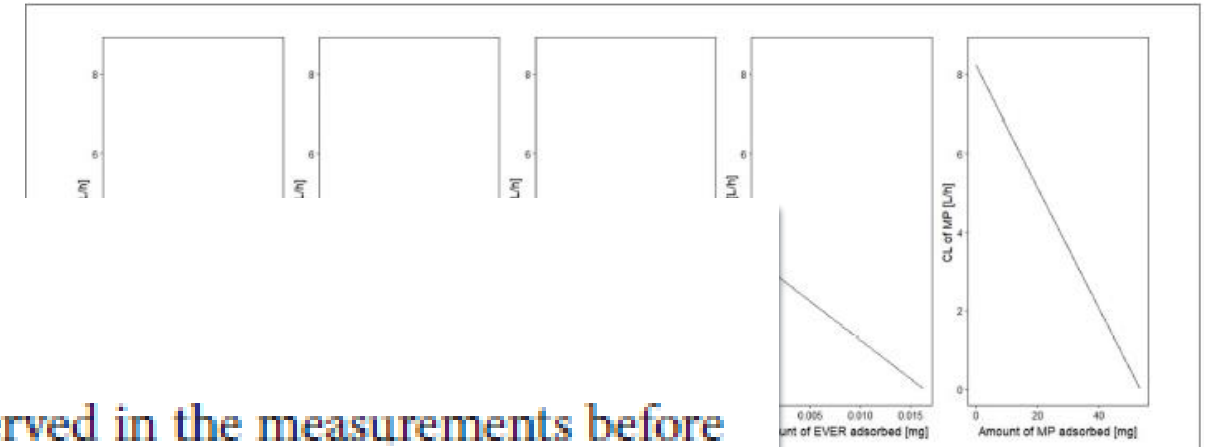


FIGURE 1
Extracorporeal circulation with hemoadsorber.



nce indicated saturation of the adsorption kinetics
e mofetil; EVER, everolimus; MP, methylprednisolone.

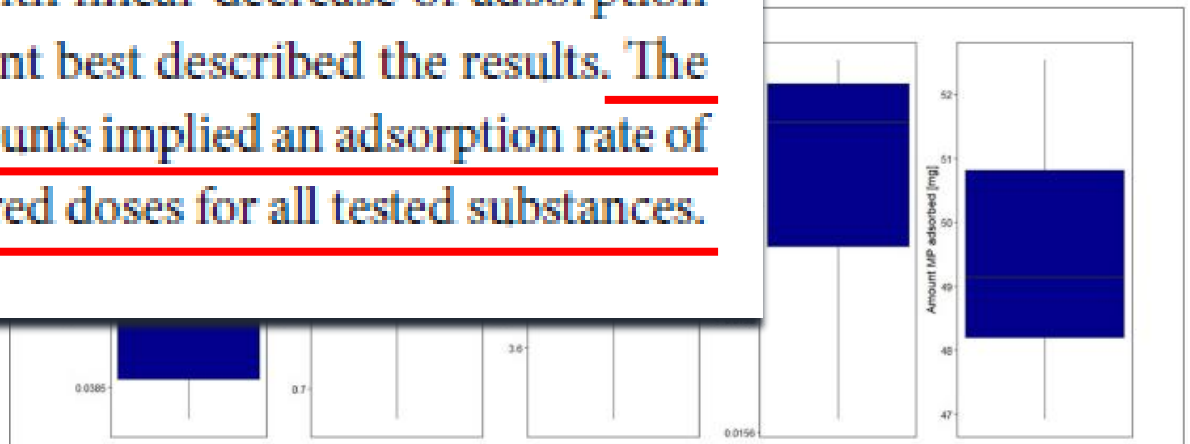


FIGURE 5
Boxplot of the total estimated adsorbed amount for the investigated drugs by hemoperfusion. Lower and upper box boundaries: 25th and 75th percentiles, respectively; line inside box: median; lower and upper error lines: 10th and 90th percentiles, respectively; TAC, tacrolimus; MMF, mycophenolate mofetil; EVER, everolimus; MP, methylprednisolone.

Leber B et al. Front Med (2023) 10:1258661.

EARLY ALLOGRAFT REJECTION – 1 MONTH SCREENING

Endomyocardial biopsy	Control group N=25	Hemoadsorption group N=30	*P*
Cellular rejection			
Week 1, n	**0**	**0**	
Week 2, n	5 (20.0%)	5 (16.7%)	1.00
Week 3, n	5 (20.0%)	5 (16.7%)	1.00
Week 4, n	6 (24.0%)	10 (33.3%)	0.448
Antibody-mediated rejection			
Week 1, n	**1** (4.0%)	**0**	0.455
Week 2, n	1 (4.0%)	2 (6.7%)	1.00
Week 3, n	1 (4.0%)	3 (10.0%)	0.617
Week 4, n	2 (8.0%)	1 (3.3%)	0.585
35/36 (**97.2%**) registered cellular and 11/11 (100%) registered antibody mediated rejection confirmed as **grade I** (ISHLT)			
1/36 (**2.8%**) registered cellular rejection confirmed as **grade II** (ISHLT) → Control Group, week 4			

Data: n (frequency); **Statistics:** qui square test, Fisher's exact test

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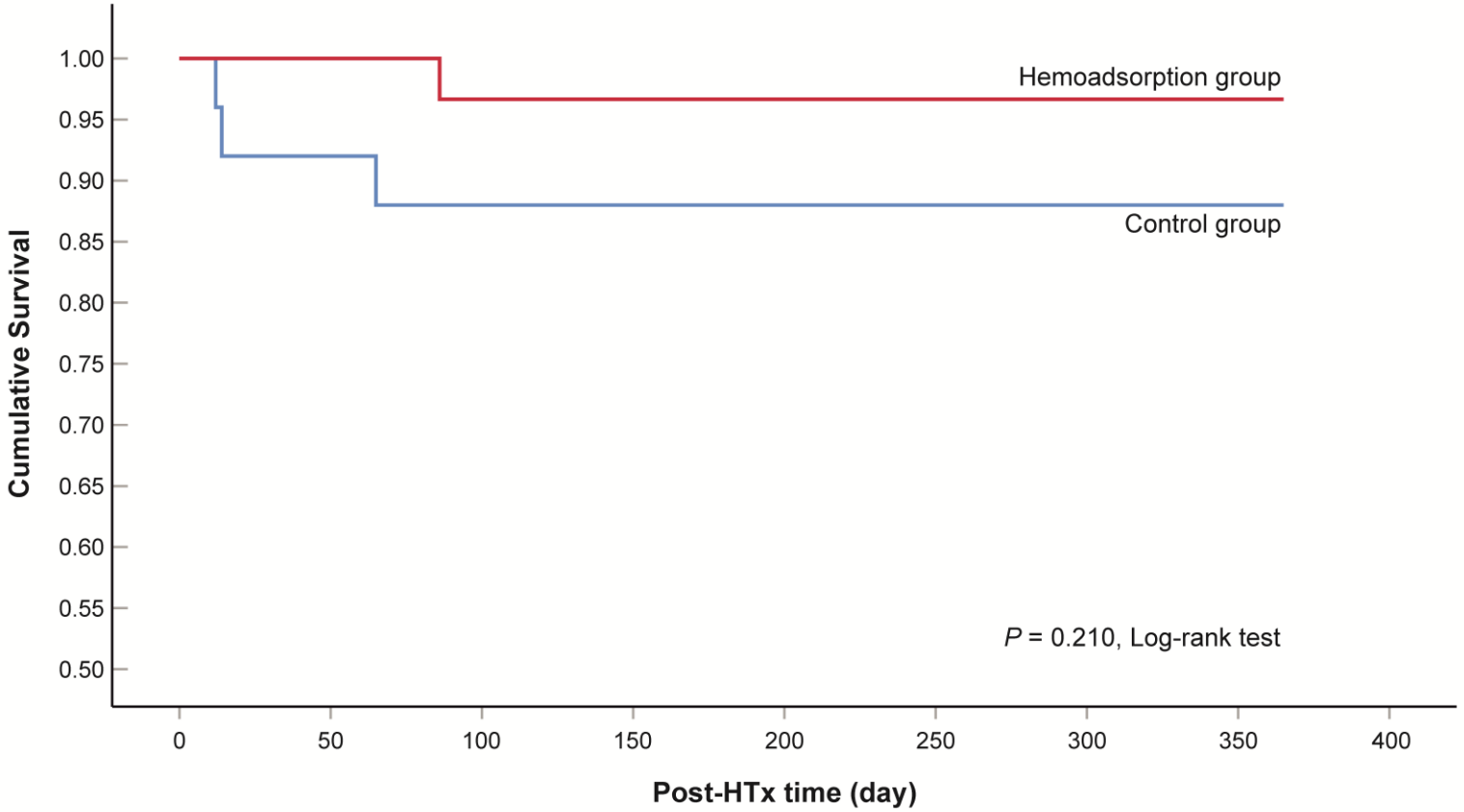
1-YEAR SURVIVAL



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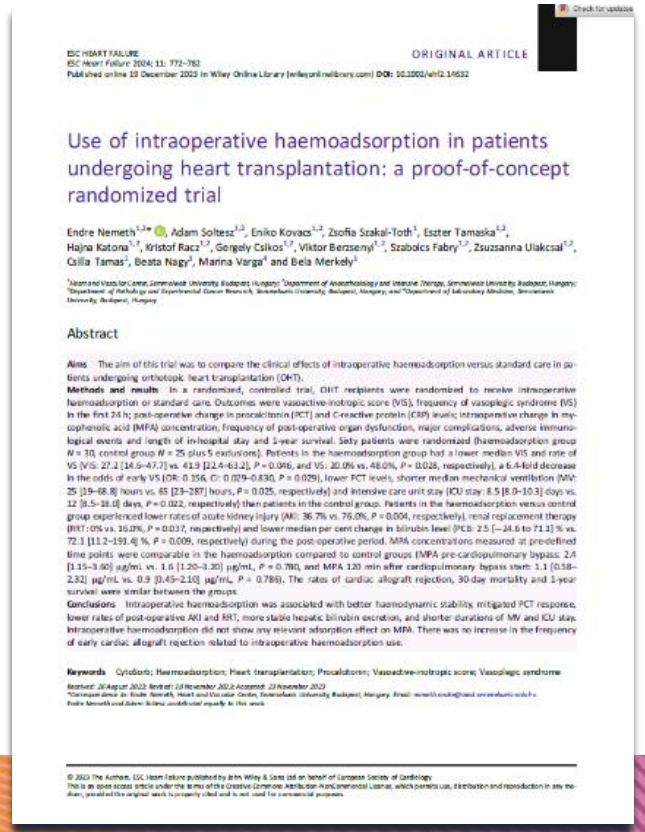
Number at risk:

Hemoadsorption Group:	30	30	29	29	29	28	28	27
Control Group:	25	22	21	21	21	21	21	21

DISCUSSION AND CONCLUSIONS:

FIRST RANDOMIZED CONTROLLED TRIAL IN HEART TRANSPLANTATION

TO TEST THE EFFECT OF INTRAOPERATIVE-PROACTIVE HEMOADSORPTION TREATMENT ON THE OUTCOME OF PATIENTS



ESC HEART FAILURE
ESC Heart Failure 2024; 11: 772–782
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ORIGINAL ARTICLE

Use of intraoperative haemoadsorption in patients undergoing heart transplantation: a proof-of-concept randomized trial

Endre Nemeth[1,2]*, Adam Soltesz[1,2], Eniko Kovacs[1,2], Zsofia Szakal-Toth[1], Eszter Tamaska[1,2], Hajna Katona[1,2], Kristof Racz[1,2], Gergely Csikos[1,2], Viktor Berzsenyi[1,2], Szabolcs Fabry[1,2], Zsuzsanna Ulakcsai[1,2], Csilla Tamas[3], Beata Nagy[4], Marina Varga[4] and Bela Merkely[1]

Abstract

Aims The aim of this trial was to compare the clinical effects of intraoperative haemoadsorption versus standard care in patients undergoing orthotopic heart transplantation (OHT).

Methods and results In a randomized, controlled trial, OHT recipients were randomized to receive intraoperative haemoadsorption or standard care. Outcomes were vasoactive-inotropic score (VIS), frequency of vasoplegic syndrome (VS) in the first 24 h; post-operative change in procalcitonin (PCT) and C-reactive protein (CRP) levels; intraoperative change in mycophenolic acid (MPA) concentration; frequency of post-operative organ dysfunction, major complications, adverse immunological events and length of in-hospital stay and 1-year survival. Sixty patients were randomized (haemoadsorption group $N = 30$, control group $N = 25$ plus 5 exclusions). Patients in the haemoadsorption group had a lower median VIS and rate of VS (VIS: 27.2 [14.6–47.7] vs. 41.9 [22.4–63.2], $P = 0.046$, and VS: 20.0% vs. 48.0%, $P = 0.028$, respectively), a 6.4-fold decrease in the odds of early VS (OR: 0.156, CI: 0.029–0.830, $P = 0.029$), lower PCT levels, shorter median mechanical ventilation (MV: 25 [19–68.8] hours vs. 65 [23–287] hours, $P = 0.025$, respectively) and intensive care unit stay (ICU stay: 8.5 [8.0–10.3] days vs. 12 [8.5–18.0] days, $P = 0.022$, respectively) than patients in the control group. Patients in the haemoadsorption versus control group experienced lower rates of acute kidney injury (AKI: 36.7% vs. 76.0%, $P = 0.004$, respectively), renal replacement therapy (RRT: 0% vs. 16.0%, $P = 0.037$, respectively) and lower median per cent change in bilirubin level (PCB: 2.5 [−24.6 to 71.1] % vs. 72.1 [11.2–191.4] %, $P = 0.009$, respectively) during the post-operative period. MPA concentrations measured at pre-defined time points were comparable in the haemoadsorption compared to control groups (MPA pre-cardiopulmonary bypass: 2.4 [1.15–3.60] μg/mL vs. 1.6 [1.20–3.20] μg/mL, $P = 0.780$, and MPA 120 min after cardiopulmonary bypass start: 1.1 [0.58–2.32] μg/mL vs. 0.9 [0.45–2.10] μg/mL, $P = 0.786$). The rates of cardiac allograft rejection, 30-day mortality and 1-year survival were similar between the groups.

Conclusions Intraoperative haemoadsorption was associated with better haemodynamic stability, mitigated PCT response, lower rates of post-operative AKI and RRT, more stable hepatic bilirubin excretion, and shorter durations of MV and ICU stay. Intraoperative haemoadsorption did not show any relevant adsorption effect on MPA. There was no increase in the frequency of early cardiac allograft rejection related to intraoperative haemoadsorption use.

Keywords CytoSorb; Haemoadsorption; Heart transplantation; Procalcitonin; Vasoactive-inotropic score; Vasoplegic syndrome

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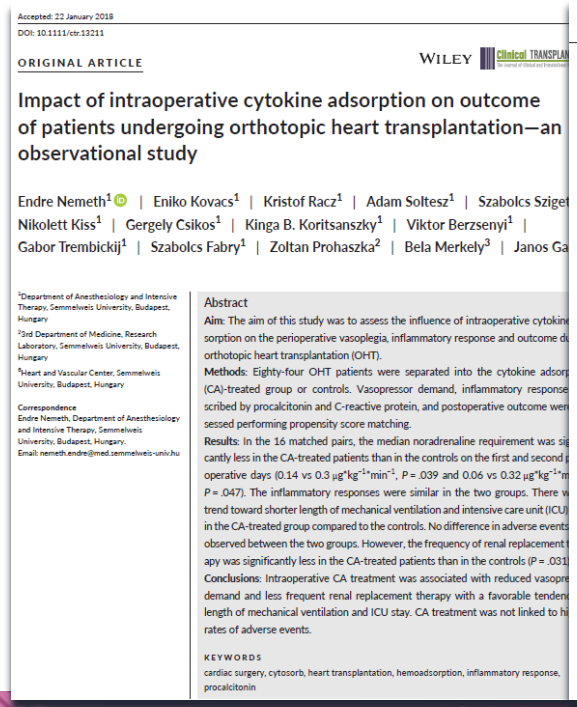

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ORIGINAL ARTICLE

WILEY Clinical TRANSPLANTATION

Impact of intraoperative cytokine adsorption on outcome of patients undergoing orthotopic heart transplantation—an observational study

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Abstract

Aim: The aim of this study was to assess the influence of intraoperative cytokine sorption on the perioperative vasoplegia, inflammatory response and outcome d orthotopic heart transplantation (OHT).

Methods: Eighty-four OHT patients were separated into the cytokine adsorp (CA)-treated group or controls. Vasopressor demand, inflammatory response scribed by procalcitonin and C-reactive protein, and postoperative outcome wer sessed performing propensity score matching.

Results: In the 16 matched pairs, the median noradrenaline requirement was sig cantly less in the CA-treated patients than in the controls on the first and second p operative days (0.14 vs 0.3 μg*kg^{-1}*min^{-1}, $P = .039$ and 0.06 vs 0.32 μg*kg^{-1}*m $P = .047$). The inflammatory responses were similar in the two groups. There w trend toward shorter length of mechanical ventilation and intensive care unit (ICU) in the CA-treated group compared to the controls. No difference in adverse events observed between the two groups. However, the frequency of renal replacement t apy was significantly less in the CA-treated patients than in the controls ($P = .031$

Conclusions: Intraoperative CA treatment was associated with reduced vasopre demand and less frequent renal replacement therapy with a favorable tenden length of mechanical ventilation and ICU stay. CA treatment was not linked to h rates of adverse events.

KEYWORDS
cardiac surgery, cytosorb, heart transplantation, hemoadsorption, inflammatory response, procalcitonin

(856)

Extracorporeal Cytokine Hemoadsorption During Or
Transplantation: A Comparative Study

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Purpose: Increasingly used extracorporeal hem
(Cytosorb®, CytoSorbents Europe GmbH) promote
uncontrolled immune responses in patients with ele
inflammatory cytokines due to septic shock or hyper
diac surgery. In patients undergoing orthotopic h
(OHT) chronic hypoperfusion syndrome, cardiopulmo
contact to the allograft may add up to the developmen
tory environment. This retrospective single center
effect of Cytosorb-therapy (CS) on vasopressor de
complications and overall outcome in patients undergo
Methods: 175 consecutive adult patients have undergo
from 2010 and 2022 separated into three groups based
(47.4%) patients before the use of CS (2010 - 2017),
treated with CS (2017 - 2020) and 41 (23.4%) patie
change of the perioperative protocol abandoning CS filte
Results: The groups showed no significant differences re
acteristics, preoperative laboratory values, postoperative
postoperative lactate levels or total ischemic time of the
no significant differences in primary graft failures (befo
no CS 2.4%, respectively; p=0.53). 30-day-survival rate
induction of CS, 98.0% with CS and 95.1% in patients w
(p=0.52). However, a significant increase in gastrointestin
ing subsequent surgical intervention was observed within
CS: 12.0%, CS 21.6%, no CS 2.6 %, respectively; p=0.02
Conclusion: This study showed no perioperative
patients undergoing OHT regarding vasopressor den
lactate levels and 30-day survival rates. However, w
cant increase in gastrointestinal ischemic events n
intervention within the CS group, which have not beer
ing the CS filter. Further investigations are necessary t
anisms behind this observation.

(350)

Evaluation of Immunosuppressant Drug Tolerability and Infections in Lung Transplant Recipients with Short Telomere Syndrome

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Purpose: Short telomere syndrome (STs) and associations with myelodysplasia has become increasingly appreciated in lung diseases such as pulmonary fibrosis and COPD. Post lung transplant associated outcomes have not been well elucidated. The aim of this study is to evaluate the tolerability of immunosuppression drugs and the incidence of major infections in lung transplant recipients (LTRs) with STs.
Methods: A retrospective 1: 1 matched cohort was conducted on adult LTRs. Patients with short telomere syndrome were matched to a control cohort based on age (5 year age band: +/- 2.5 years) and sex. Multi-organ LTRs, retransplants, and patients that died within 90 days were excluded.

(351)

Utility of Intraoperative Cytokine Hemoadsorption Therapy During Cardiac Transplantation

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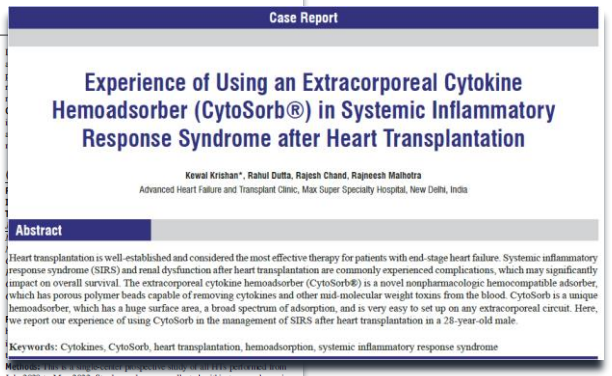
Abstracts

Purpose: CYTOSORB is an approved extracorporeal hemadsorption (HA) device that has shown beneficial effects in reducing the impact of cytokine storm and other inflammatory mediators in patients undergoing complex cardiac surgeries. However till date there is lack of randomised data to demonstrate similar effects in patients undergoing cardiac transplantation. We aimed to study the influence of Intraoperative Cytokine HA therapy using CYTOSORB on perioperative inflammatory response, vasoplegia, blood loss and overall morbidity and mortality during orthotropic cardiac transplantation.
Methods: In this single-centre randomised control trial, 19 patients undergoing Cardiac Transplantation were included. In the Treatment arm (n=12), intra-operative CYTOSORB was utilized as the cytokine HA filter on cardio pulmonary bypass (CPB). In the Control arm (n=7), routine cardiac transplant surgery was performed without CYTOSORB. Primary outcome was level of inflammatory response as measured by procalcitonin (PCT), C-Reactive protein (CRP) and Interleukin 6 (IL-6) measured at the time of anaesthesia induction (0), 24, 48 & 72 hours post-CPB initiation. Secondary outcomes were peri-operative inotropic & vasopressor demand, usage of mechanical circulatory support, blood loss, rate of re-exploration and mortality.
Results: PCT and IL-6 levels were lower (33% & 27.5%) in the Treatment arm. There was no significant difference in the CRP levels in both arms. An approximately 20% reduction in the surgical re-exploration rates was noted in in the Treatment arm. Vasopressor demand was 50% lower in the Treatment arm.The requirement for Mechanical Circulatory Support (MCS) was lower in the Treatment arm (14% & 25%). No difference in inotrope demand was noted in both the arms. There was also no difference in blood transfusions requirement, ICU length of stay and peri-operative mortality in both the arms. There were no increase in adverse events related to the use of CYTOSORB therapy.
Conclusion: Intra-operative HA therapy using CYTOSORB during cardiac transplantation was associated with lower peri-operative inflammatory mediators, lower vasoplegia and lower requirement for MCS and surgical re-exploration. CYTOSORB therapy was not associated with any significant adverse events.



Case Report

Experience of Using an Extracorporeal Cytokine Hemoadsorber (CytoSorb®) in Systemic Inflammatory Response Syndrome after Heart Transplantation

Kewal Krishan*, Rahul Dutta, Rajesh Chand, Rajneesh Malhotra
Advanced Heart Failure and Transplant Clinic, Max Super Specialty Hospital, New Delhi, India

Abstract

Heart transplantation is well-established and considered the most effective therapy for patients with end-stage heart failure. Systemic inflammatory response syndrome (SIRS) and renal dysfunction after heart transplantation are commonly experienced complications, which may significantly impact on overall survival. The extracorporeal cytokine hemoadsorber (CytoSorb®) is a novel nonpharmacologic hemocompatible adsorber, which has porous polymer beads capable of removing cytokines and other mid-molecular weight toxins from the blood. CytoSorb is a unique hemoadsorber, which has a huge surface area, a broad spectrum of adsorption, and is very easy to set up on any extracorporeal circuit. Here, we report our experience of using CytoSorb in the management of SIRS after heart transplantation in a 28-year-old male.

Keywords: Cytokines, CytoSorb, heart transplantation, hemoadsorption, systemic inflammatory response syndrome

DISCUSSION AND CONCLUSIONS:

1) The intraoperative hemoadsorption treatment showed clear association with

   - **Decreased severity of post-CPB vasoplegia**
   - **Reduced risk for developing early vasoplegic syndrome**

2) Postoperative hemodynamic effects of the hemoadsorption treatment were independent of the early interleukin and complement changes, but showed link to PCT peak

   - **Relationship with less severe endothelial and / or vasoregulatory dysfunction?**

3) The intraoperative hemoadsorption treatment was associated with:

   - Lower rates of early postoperative organ dysfunction → AKI and RRT; hepatic dysfunction
   - Shorter period of postoperative mechanical ventilation and ICU stay
   - **Less vasopressor need / more stable hemodynamics?**

DISCUSSION AND CONCLUSIONS :

Intraoperative **hemoadsorption treatment was NOT associated** with:

1) Early sepsis
2) Clinically relevant adsorption of MMF
3) Early graft rejection
4) 30-day mortality
5) 1-year mortality

THANK YOU FOR YOUR ATTENTION!

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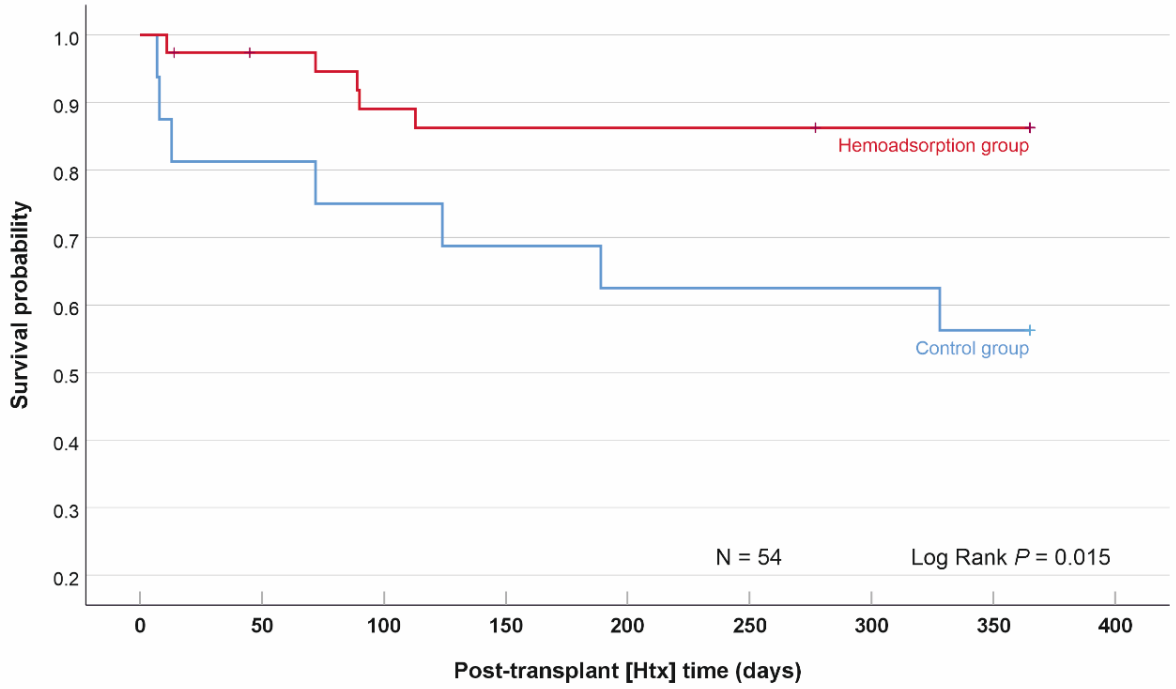
Heart transplantation with prior mechanical circulatory support
Time period: 01.01.2013 – 11.06.2024



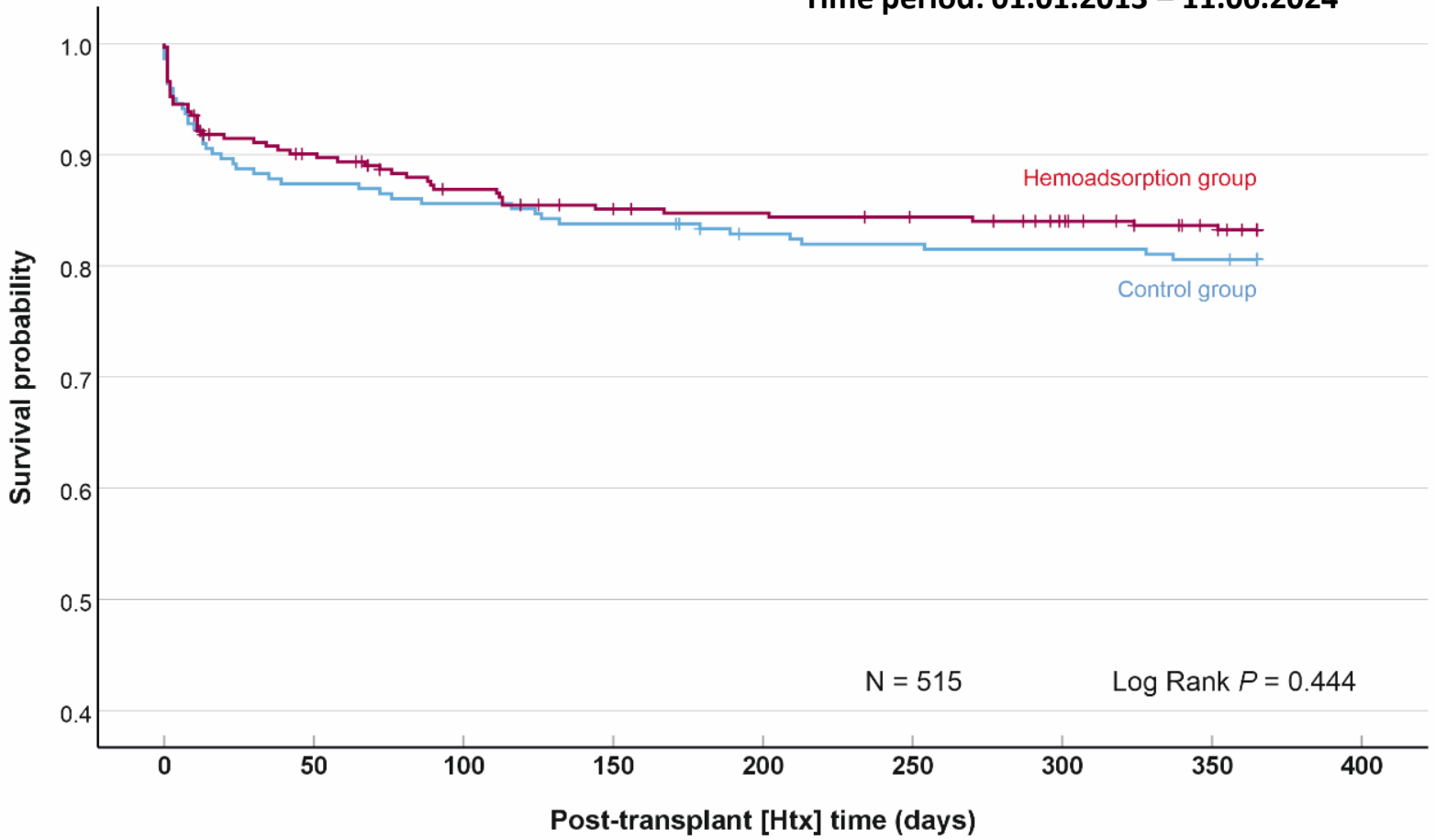
Number at risk:

Control group:	16	11	10	9
Hemoadsorption group:	38	32	31	29

Nemeth E Unpublished data

	Control group (N=16)	Hemoadsorption group (N=38)	*P*-value
Recipient age, year	46 ± 11	43 ± 14	0.383
Female sex, n	4 (25%)	7 (18.4%)	0.714
BMI, kg/m^2	27.7 ± 5.9	25.8 ± 4.2	0.213
HF etiology iDCM, n	4 (25%)	11 (28.9%)	1.00
HU status, n	14 (87.5%)	32 (84.2%)	1.00
MV pre-HTx, n	2 (12.5%)	10 (26.3%	0.474
IMPACT score	10.6 ± 2.6	11.1 ± 4.0	0.349
CPB time, min	205 (194-225)	190 (144-212)	0.043
Total ischemic time, min	234 (143-262)	215 (174-248)	0.736
Pre-HTx temporary MCS			
IABP, n	2 (12.5%)	0	0.084
VA-ECMO, n	1 (6.3%)	2 (5.3%)	1.00
Paracorporeal LVAD, n	1 (6.3%)	2 (5.3%)	1.00
Paracorporeal RVAD, n	0	1 (2.6%)	1.00
Paracorporeal BiVAD, n	7 (43.8%)	16 (42.1%)	1.00
Pre-HTx durable LVAD, n	5 (31.3%)	17 (44.7%)	0.357

Time period: 01.01.2013 – 11.06.2024



Number at risk:

Control group:	**222**	**190**	**180**	**176**
Hemoadsorption group:	**293**	**244**	**232**	**221**

Nemeth E Unpublished data

Supplementary Material

Table S1. *Applied immunosuppression protocol of orthotopic heart transplantation during the perioperative period and the first month postoperatively.*

Time	Agent	Dose	Route of administration
60 minutes prior to surgery (premedication)			
	MMF	1.5 g	oral
Induction of anaesthesia			
	MP	500 mg	Intravenous
30 minutes after the aortic declamp (on–CPB)			
	MP	500 mg	Intravenous
Postoperative day 0			
	MP	125 mg	Intravenous
	ATG	1.5 mg/kg	Intravenous
	MMF	1.5 g	Intravenous
Postoperative day 1 – 2			
	MP	125 mg	Intravenous
	ATG	1.5 mg/kg	Intravenous
	MMF	2 x 1.5 g	Intravenous / oral
Postoperative day 3 – 4			
	MP	16 mg	oral
	MMF	2 x 1.5 g	oral
Postoperative day 5 – 9			
	MP	16 mg	oral
	MMF	2 x 1.5 g	oral