

X Reunión. Estado del Arte en
INSUFICIENCIA CARDIACA

PRÁCTICA CLÍNICA Y MODELOS ORGANIZATIVOS

Sede: Hotel Meliá María Pita, A Coruña

A CORUÑA 27-28 SEPTIEMBRE 2024



X Meeting. State of the Art in
HEART FAILURE

CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: Hotel Meliá María Pita, A Coruña

#ACoruñaHF2024

A CORUÑA 27-28 SEPTEMBER 2024

Primary graft dysfunction after heart transplantation.

What is new?

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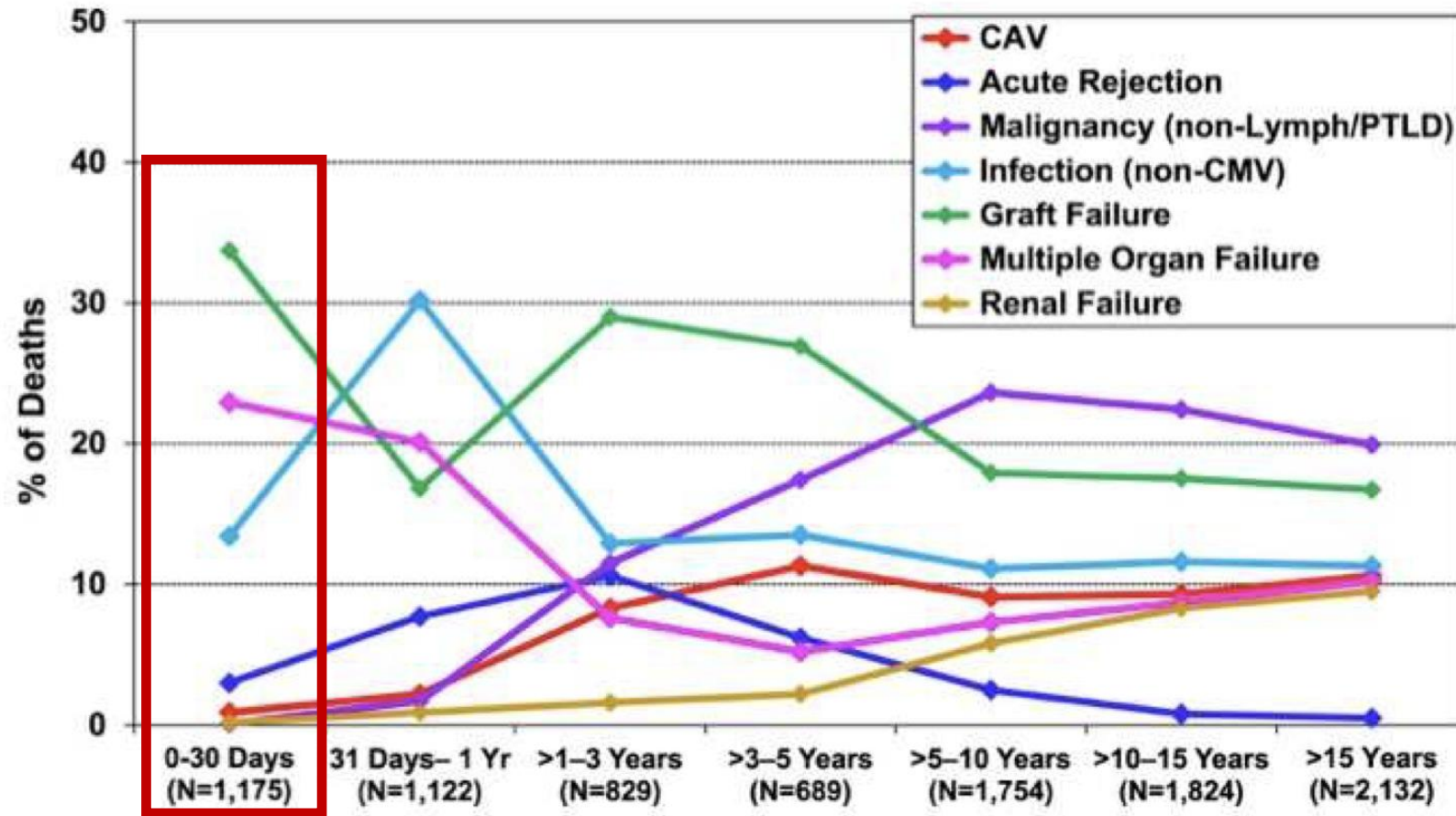
Outline

- What is PGD and why is it important?
- What are the risk factors and prediction models for PGD?
- What are the best managements strategies?

- New insights in PGD: the role of the International PGD Consortium
 - Current results
 - Projects in the pipeline

- Take home messages and future directions

Post HT mortality



Primary graft dysfunction

K Khush, JHLT 2019, 38: 1056-1066

Primary Graft Dysfunction

- **Incidence: 10% after HT**
- **Mortality :50% (1st cause in the 1st month postHT)**
- **Definition: 2014 consensus (42 participating centers)**
 - Primary
 - Secondary (PH, rejection, surgical complications)

ISHLT CONSENSUS

Report from a consensus conference on primary graft dysfunction after cardiac transplantation

Jon Kobashigawa, MD,^a Andreas Zuckermann, MD,^b Peter Macdonald, MD, PhD,^c Pascal Leprince, MD, PhD,^d Fardad Esmailian, MD,^a Minh Luu, MBBS,^a Donna Mancini, MD,^e Jignesh Patel, MD, PhD,^a Rabia Razi, MD, MPH,^a Hermann Reichenspurner, MD, PhD,^f Stuart Russell, MD,^g Javier Segovia, MD, PhD,^h Nicolas Smedira, MD,ⁱ Josef Stehlik, MD, MPH,^j Florian Wagner, MD, PhD^f and on behalf of the Consensus Conference participants

PGD: severity

Table 6 Definition of Severity Scale for Primary Graft Dysfunction (PGD)

1. PGD-Left ventricle (PGD-LV):	<i>Mild PGD-LV: One of the following criteria must be met:</i>	LVEF \leq 40% by echocardiography, or Hemodynamics with RAP $>$ 15 mm Hg, PCWP $>$ 20 mm Hg, CI $<$ 2.0 L/min/m ² (lasting more than 1 hour) requiring low-dose inotropes
	<i>Moderate PGD-LV: Must meet one criterion from I and another criterion from II:</i>	I. <i>One</i> criteria from the following: Left ventricular ejection fraction \leq 40%, or Hemodynamic compromise with RAP $>$ 15 mm Hg, PCWP $>$ 20 mm Hg, CI $<$ 2.0 L/min/m ² , hypotension with MAP $<$ 70 mm Hg (lasting more than 1 hour) II. <i>One</i> criteria from the following: i. High-dose inotropes—Inotrope score $>$ 10 ^a or ii. Newly placed IABP (regardless of inotropes)
	<i>Severe PGD-LV</i>	Dependence on left or biventricular mechanical support including ECMO, LVAD, BiVAD, or percutaneous LVAD. Excludes requirement for IABP.
2. PGD-right ventricle (PGD-RV):	Diagnosis requires either both i and ii, or iii alone:	i. Hemodynamics with RAP $>$ 15 mm Hg, PCWP $<$ 15 mm Hg, CI $<$ 2.0 L/min/m ² ii. TPG $<$ 15 mm Hg and/or pulmonary artery systolic pressure $<$ 50 mm Hg, or iii. Need for RVAD

BiVAD, biventricular assist device; CI, cardiac index; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; PCWP, pulmonary capillary wedge pressure; RAP, right atrial pressure; RVAD, right ventricular assist device; TPG, transpulmonary pressure gradient.

^aInotrope score = dopamine (\times 1) + dobutamine (\times 1) + amrinone (\times 1) + milrinone (\times 15) + epinephrine (\times 100) + norepinephrine (\times 100)⁶⁷ with each drug dosed in μ g/kg/min.

PGD: risk factors

Recipient

Donor

Surgery

Recipient and surgical factors trigger severe primary graft dysfunction after heart transplant

Lillian Benck, MD, MPH¹ • Evan P. Kransdorf, MD, PhD¹ • Dominic A. Emerson, MD • ...
Joseph E. Ebinger, MD, MS • Jon A. Kobashigawa, MD • Jignesh K. Patel, MD, PhD • Show all authors •
Show footnotes

Published: June 09, 2021 • DOI: <https://doi.org/10.1016/j.healun.2021.06.002> • Check for updates

Donor predicted heart mass as predictor of primary graft dysfunction

Timothy A. Gong, MD • Susan M. Joseph, MD • Brian Lima, MD • Gonzalo V. Gonzalez-Stawinski, MD •
Aayla K. Jamil, MPH • Joost Felius, PhD • Huanying Qin, MS • Giovanna Saracino, MS • Aldo E. Rafael, MD •
Parag Kale, MD • Shelley A. Hall, MD • Show less

Published: March 17, 2018 • DOI: <https://doi.org/10.1016/j.healun.2018.03.009> • Check for updates

> [J Heart Lung Transplant](#). 2018 Dec;37(12):1433-1442. doi: 10.1016/j.healun.2018.07.013.
Epub 2018 Jul 26.

Risk of severe primary graft dysfunction in patients bridged to heart transplantation with continuous-flow left ventricular assist devices

A COR Lauren K Truby¹, Koji Takeda², Veli K Topkara³, Hiroo Takayama², A Reshad Garan³,
Melana Yuzefpolskaya³, Paolo Colombo³, Yoshifumi Naka², Maryjane Farr³

> [Interact Cardiovasc Thorac Surg](#). 2018 Sep 1;27(3):343-349. doi: 10.1093/icvts/ivy084.

Reoperative sternotomy is associated with primary graft dysfunction following heart transplantation

Sasha Still¹, Asad F Shaikh², Huanying Qin³, Joost Felius³, Aayla K Jamil³,
Giovanna Saracino³, Themistokles Chamogeorgakis^{3 4}, Aldo E Rafael^{3 4},
Juan C MacHannaford^{3 4}, Susan M Joseph^{3 5}, Shelley A Hall^{3 5},
Gonzalo V Gonzalez-Stawinski^{3 4}, Brian Lima^{3 4}

Dose-dependent association between amiodarone and severe primary graft dysfunction in orthotopic heart transplantation

Matthew Wright, BM • Koji Takeda, MD, PhD • Christine Mauro, PhD • Douglas Jennings, PharmD •
Paul Kurlansky, MD • Jiho Han, BS • Lauren Truby, MD • Samantha Stein, BS • Veli Topkara, MD •
Arthur R. Garan, MD • Melana Yuzefpolskaya, MD • Paolo Colombo, MD • Yoshifumi Naka, MD, PhD •
Maryjane Farr, MD • Hiroo Takayama, MD, PhD • Show less

Published: May 20, 2017 • DOI: <https://doi.org/10.1016/j.healun.2017.05.025> • Check for updates

Original Article | [Published: 16 April 2020](#)

Intraoperative hemoglobin level and primary graft dysfunction in adult heart transplantation

Yuki Nakamura, Shunsuke Saito, Shigeru Miyagawa, Yasushi Yoshikawa, Hiroki Hata, Daisuke Yoshioka,
Ryoto Sakaniwa, Koichi Toda & Yoshiki Sawa

[General Thoracic and Cardiovascular Surgery](#) **68**, 1260–1269 (2020) | [Cite this article](#)

Prediction tools

RADIAL SCORE
(score total 6)

Recipient age >60 years
Recipient diabetes
Recipient on inotropes
Recipient RAP >10
Donor age >30
Ischemic time >240 min

PREDICTA
(score total 14)

Preoperative MCS (short term VAD / ECMO)
Recipient diabetes
Cardiopulmonary bypass time > 180 min
Implant time (<45, 45-60, 60-90, >90 min)
Donor age (<21, 21-40, 41-50, >50 years)

ABCE
(score max 66)

Treatment with ACEi/ARB/ARNI plus MRA
Treatment with BB + Amiodarone
History of Cardiac surgery
Ischemic TimE

Case Study

Mr A is a 44 year old man, blood group B, height 1.7 m, weight 70 kg with a history of dilated cardiomyopathy on GDMT. He does not have diabetes. He is supported with a durable LVAD and has required acute dialysis preoperatively. Hemodynamic are relevant for a CVP 5, PA 30/12 mmHg

The donor is a 33 yo woman, height 1.65 m weight 65 kg, blood group O who died as a result of head trauma with normal LV function and coronary arteries.

The anticipated total ischemic time is 3 hours and 30 mins

WHAT IS THIS PATIENT'S RISK OF PGD?

BY RADIAL = 1/6 8%

WHAT IS THIS PATIENT'S RISK OF PGD?

BY partial PREDICTA = Low

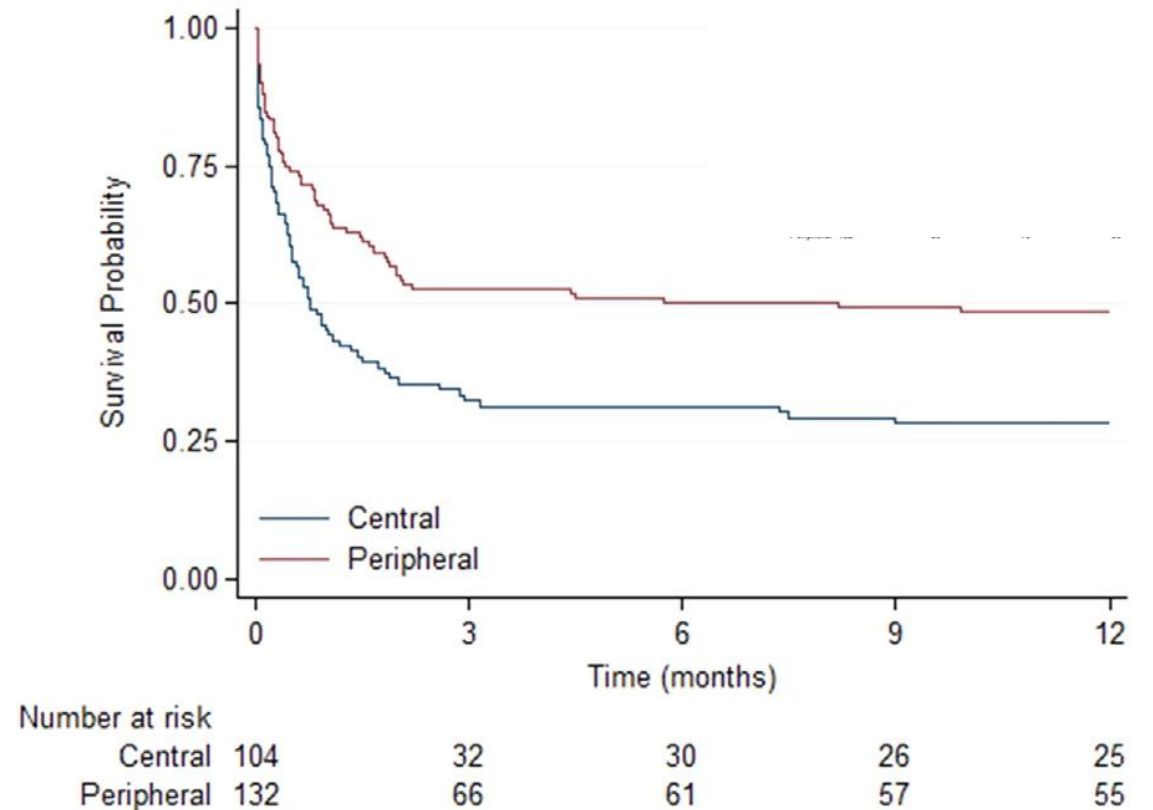
WHAT IS THIS PATIENT'S RISK OF SEVERE PGD?

BY partial ABCE = Mod-sev

Management strategies

Central vs peripheral cannulation

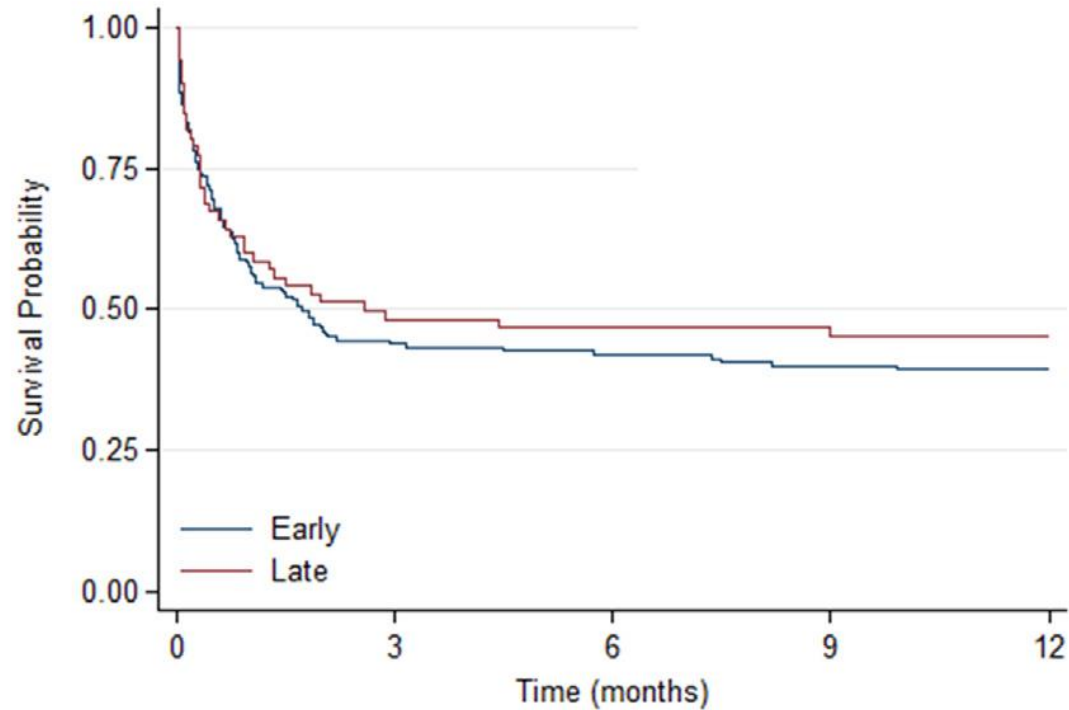
- No consensus on medical management
 - PLEX?
- ECMO vs other devices
- Cause of death: multiorgan



Olivella et al, JHLT 2023

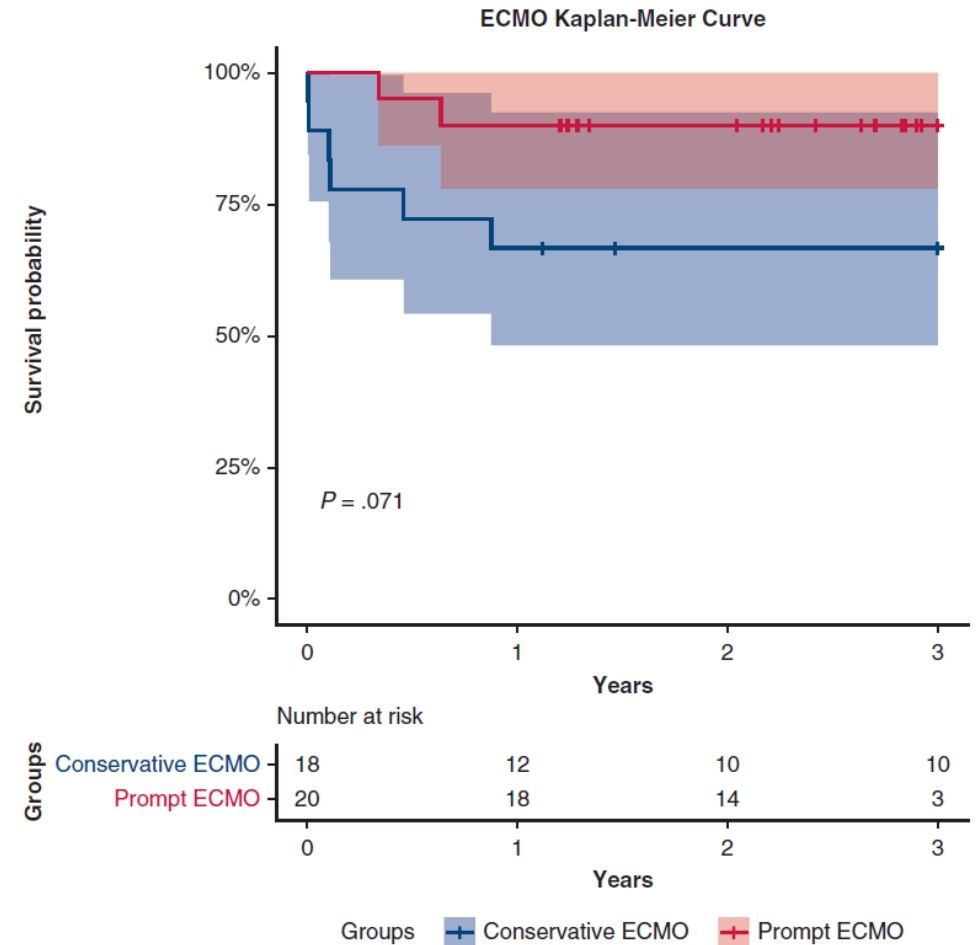
Management strategies

Early vs late MCS



Number at risk		0	3	6	9	12
Early	171	71	66	60	58	
Late	71	33	31	29	28	

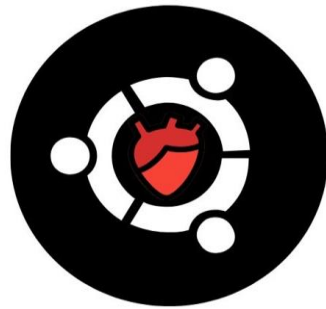
Olivella et al, JHLT 2023

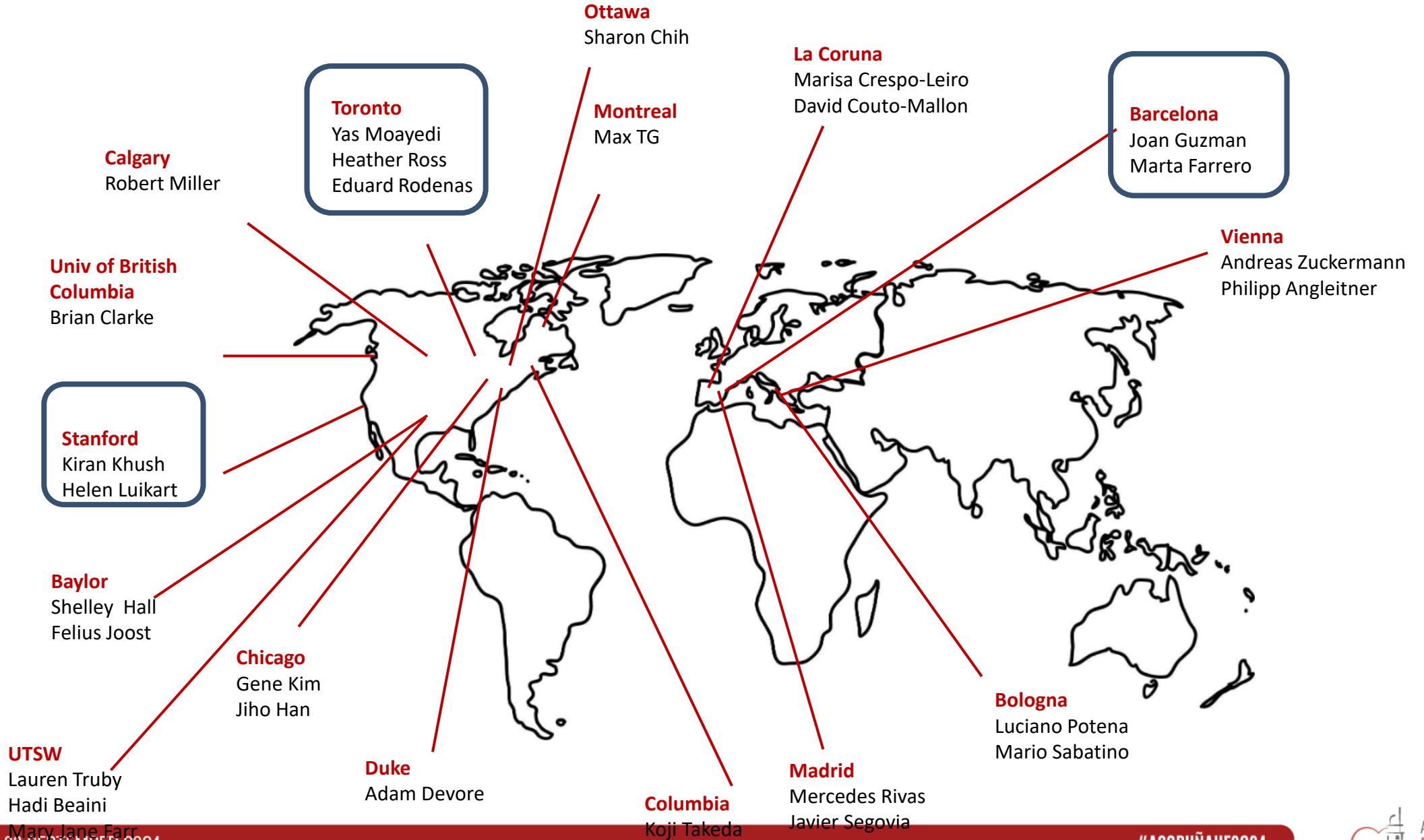
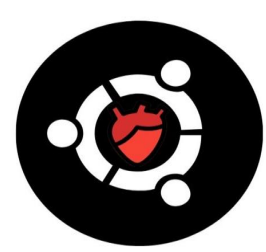


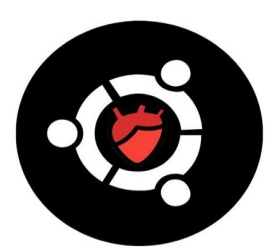
De Roo et al, J Thorac CV Surg, 2019

Too many unanswered questions...

International PGD Consortium







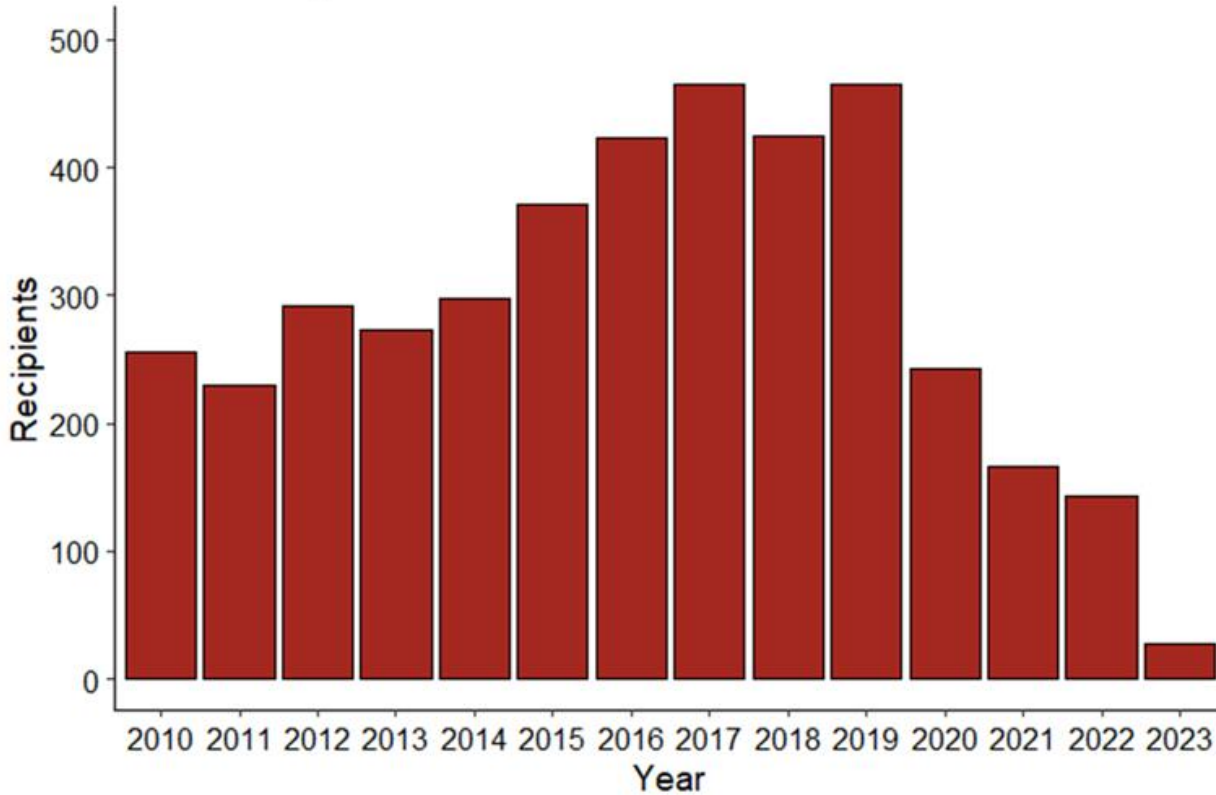
International PGD consortium: results

1. Current incidence of PGD
2. Risk factors – prediction model (role of ML)
3. Regional differences analysis

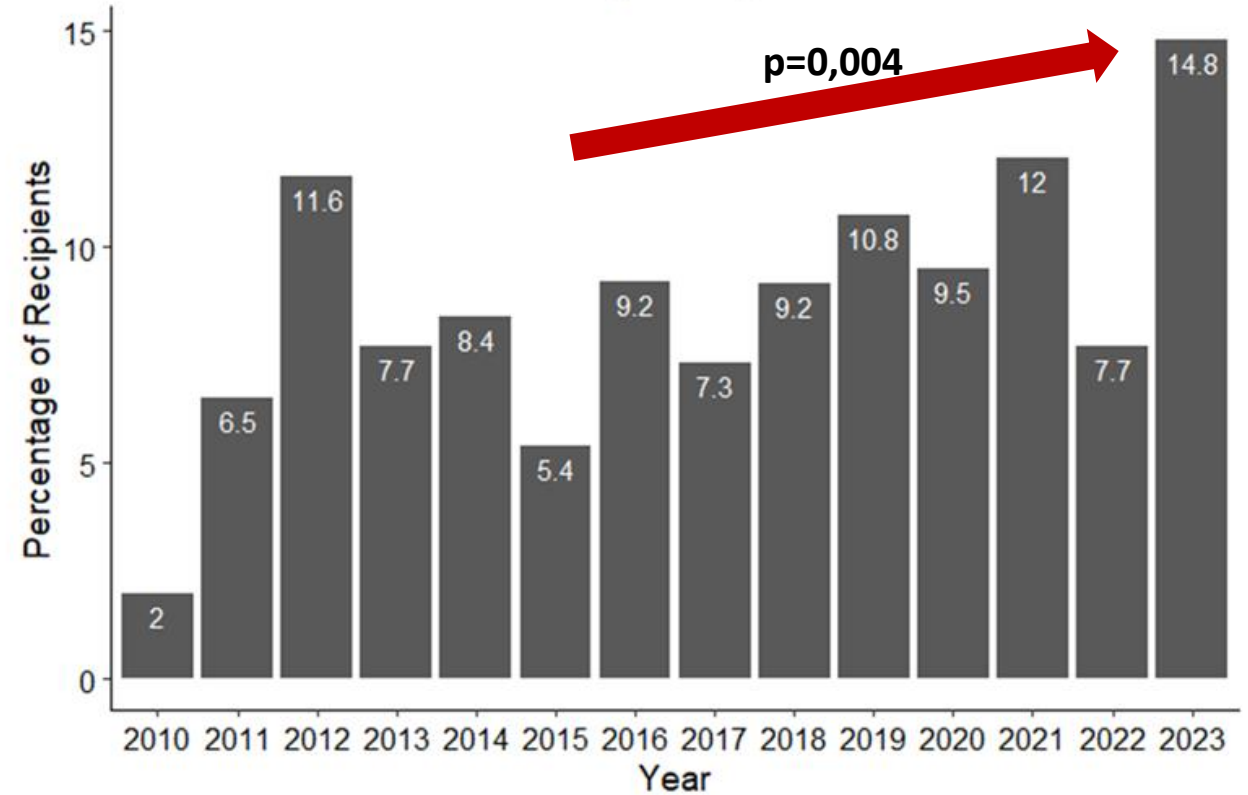


PGD Remains A Common Complication of HT

Heart Transplants Per Year



Prevalence of Severe PGD by Transplant Year

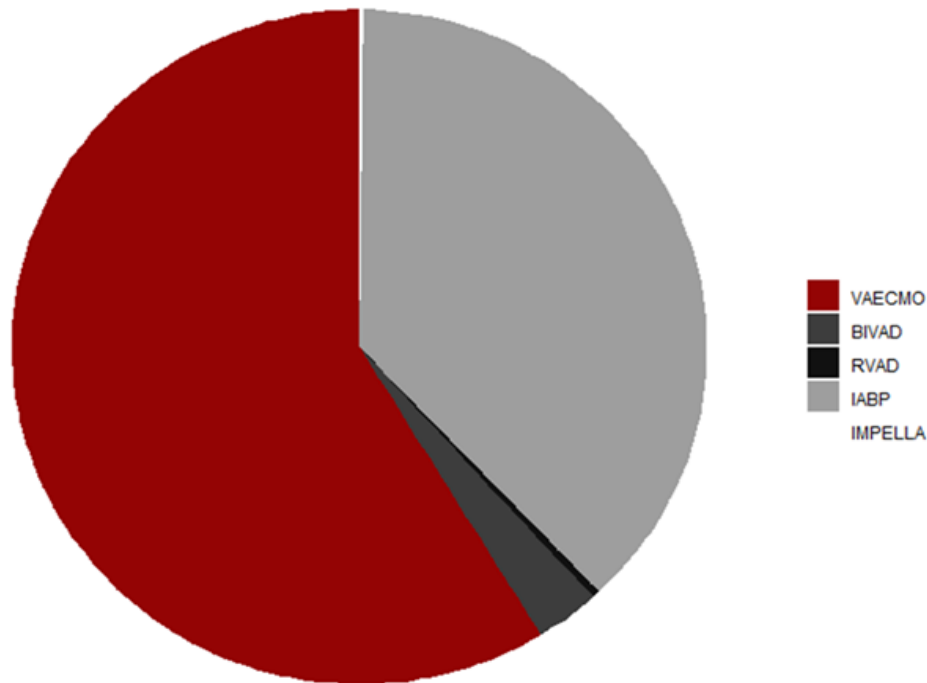


Incidence of Severe PGD: 8.2%

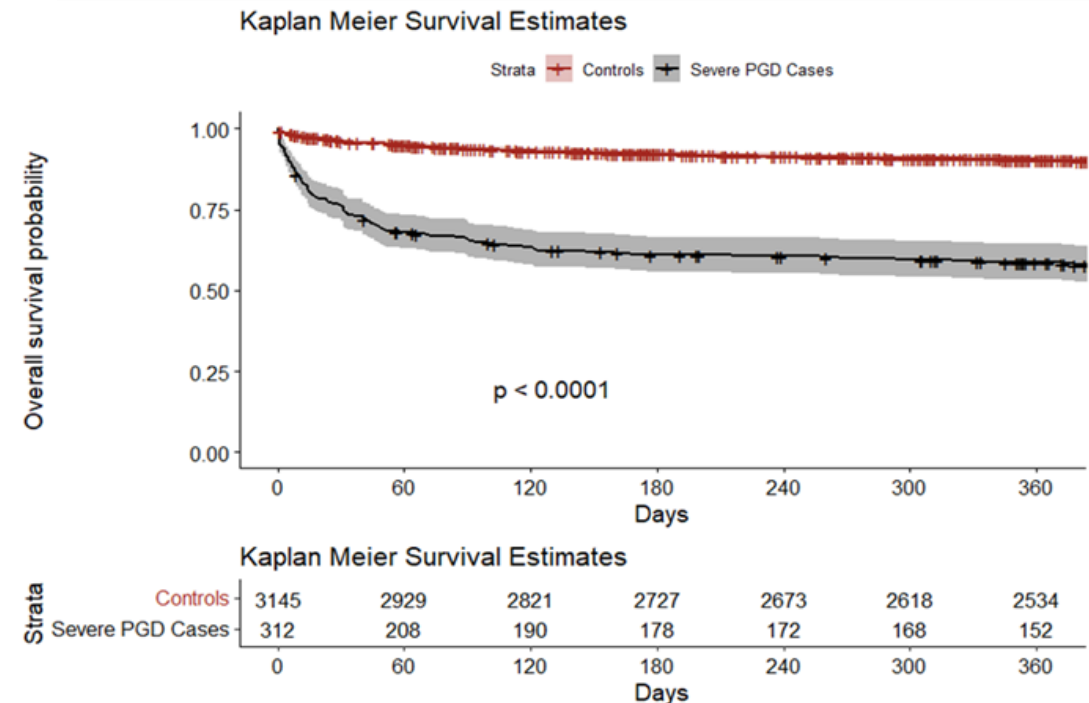


Despite MCS, PGD Mortality Remains High

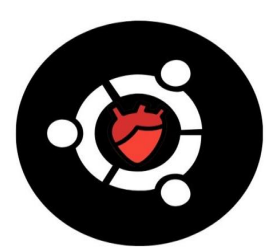
PGD Supportive Care by Type of Mechanical Circulatory Support Deployed



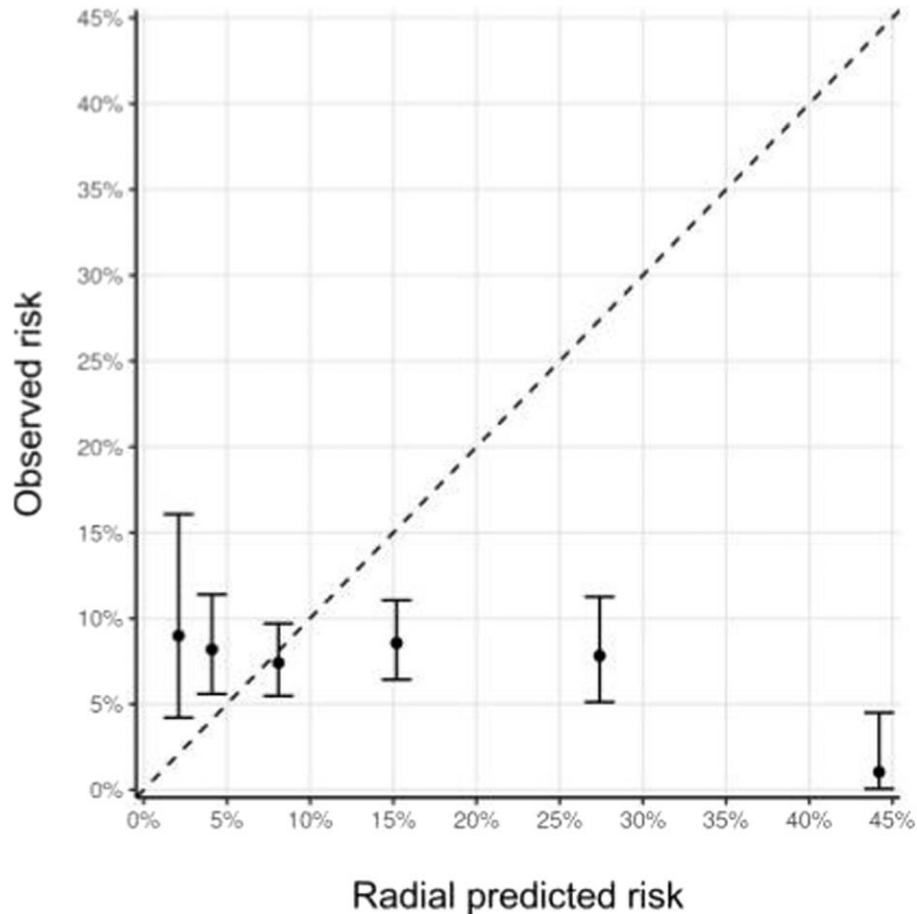
1-Year Kaplan Meier Survival Curves By Severe PGD Status



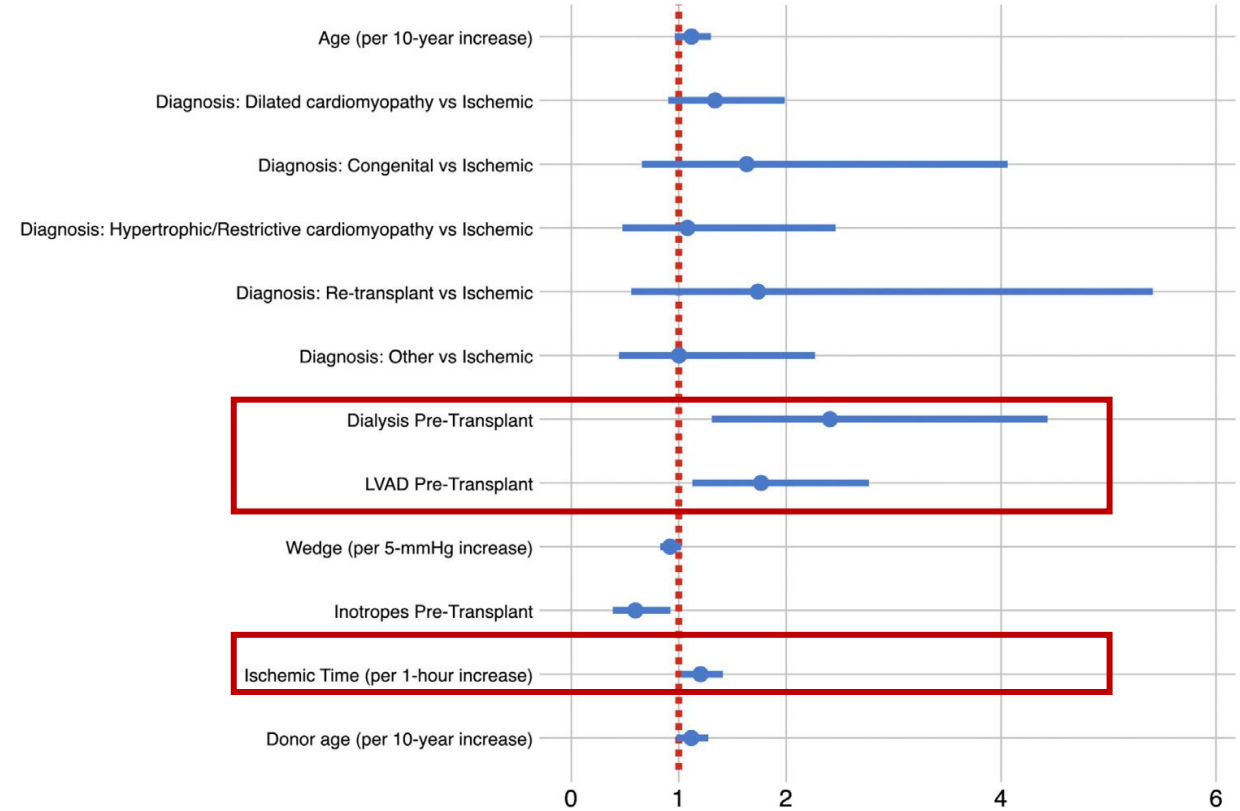
Impact: 1-Year Mortality 41.4% (35.7-46.8%)



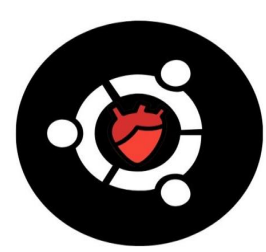
Performance of RADIAL



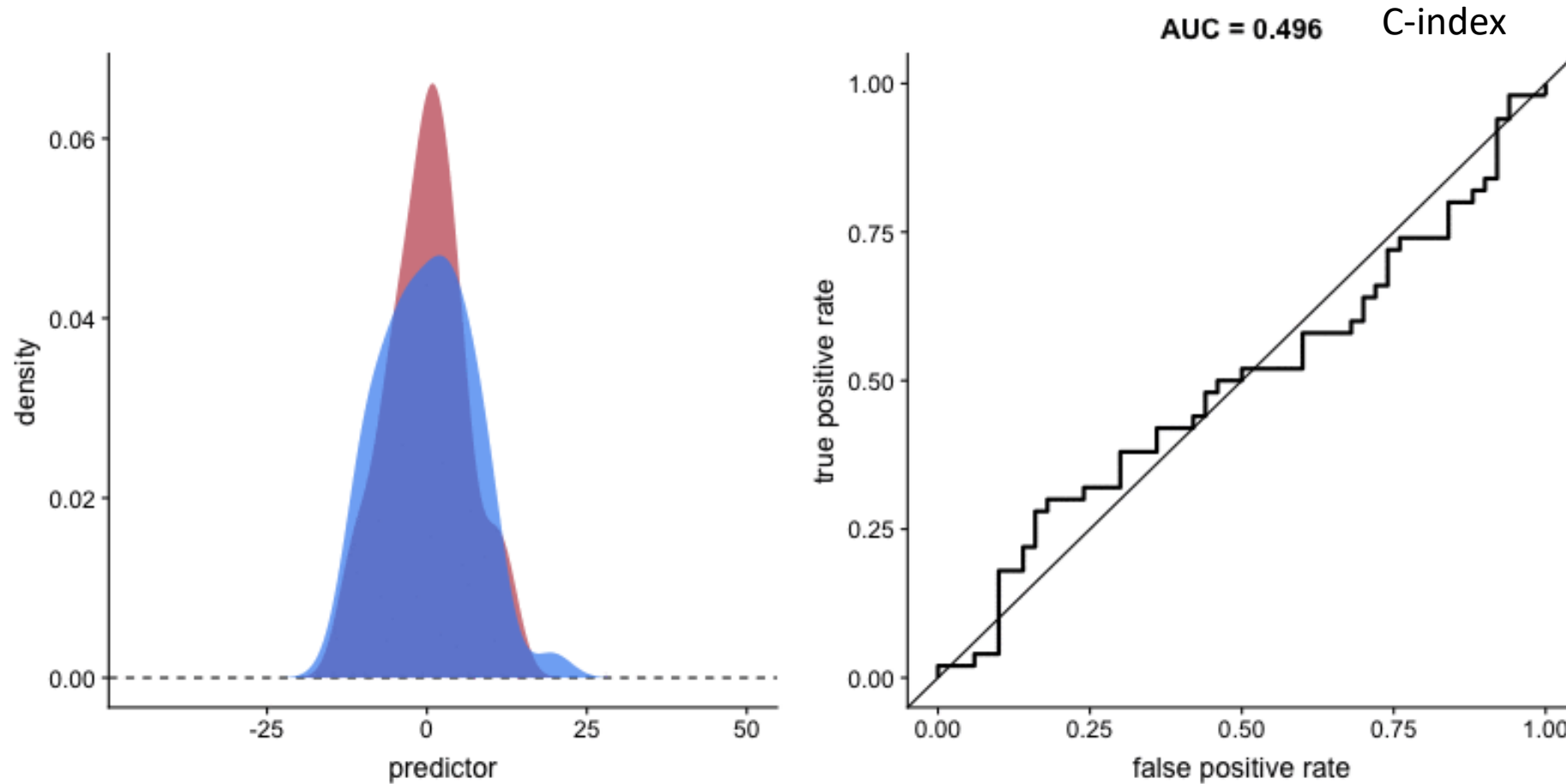
PGD Risk Factors



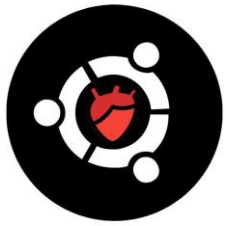
Moayed et al, J Cardiac Fail 2023



Ideal Model Performance

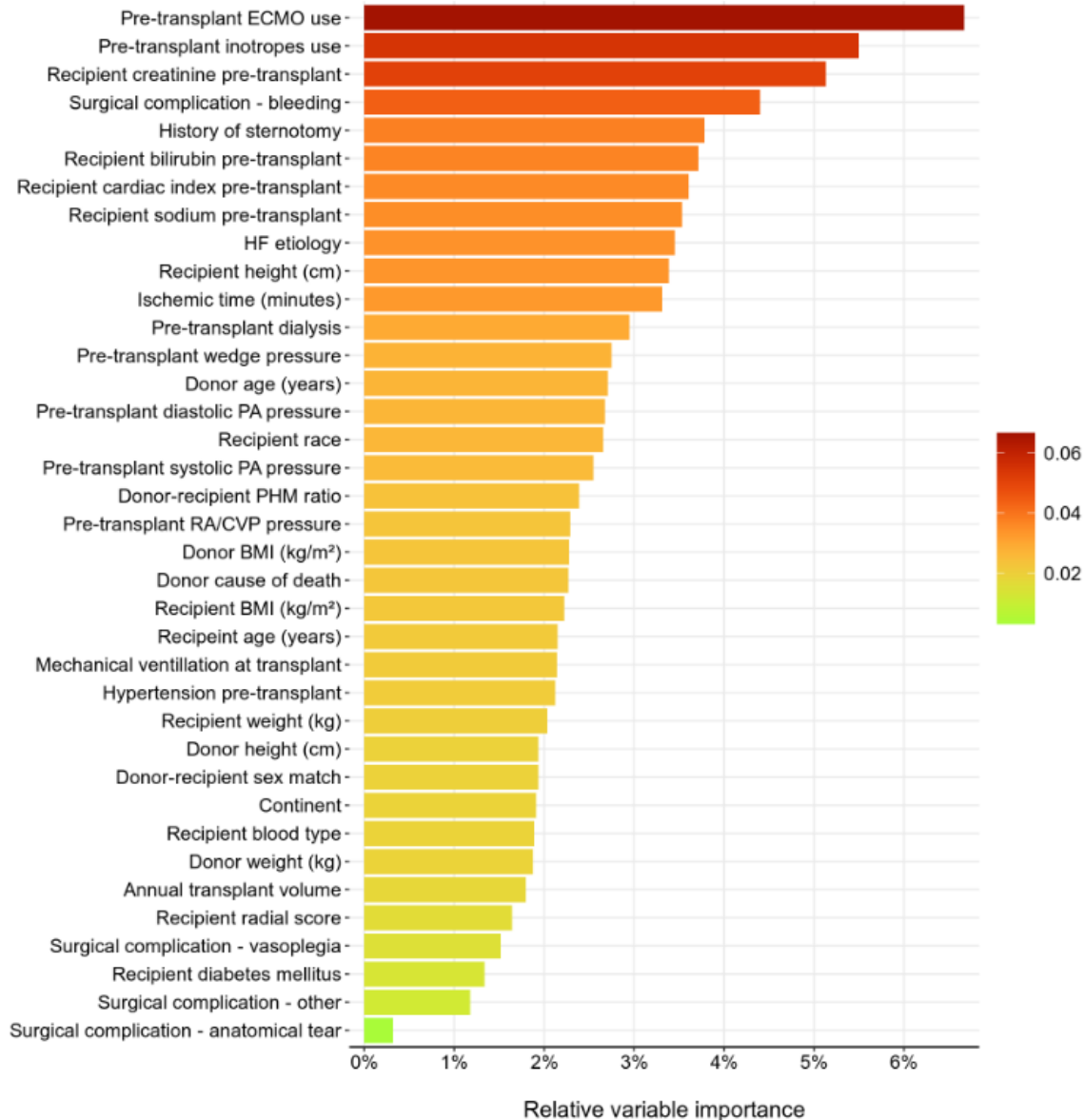


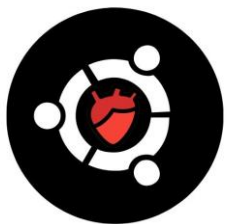
<https://paulvanderlaken.com/2019/08/16/roc-auc-precision-and-recall-visually-explained/>



Relative Variable Contribution

37 relevant variables ranked by ML Boosting approach





Severe PGD scoring tool

2

Recipient Age (years)
10 40 60

Recipient Sex
 Male
 Female

Recipient Weight (kg)
20 60 100 150

Recipient Height (cm)
100 160 180 215

HF Etiology
 Ischemic cardiomyopathy
 Dilated cardiomyopathy
 Congenital
 Hypertrophic or restrictive cardiomyopathy
 Re-transplant
 Other

Recipient Blood Type
 O
 A
 B
 AB

Recipient Diabetes (on oral hypoglycemic or insulin)
 Yes
 No

Durable LVAD Bridge
 Yes
 No

Pre-transplant dialysis
 Yes
 No

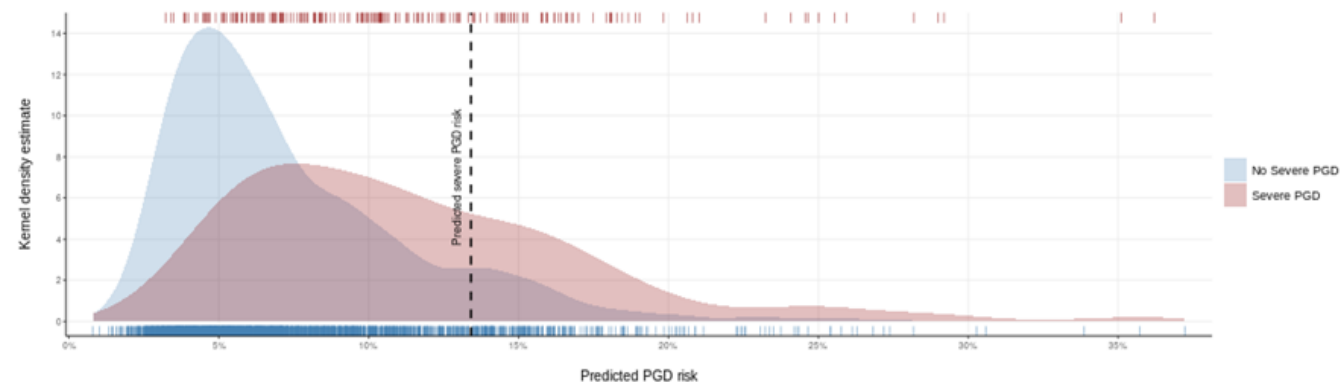
Pre-transplant ecmo
 Yes
 No

Disclaimer

The Severe PGD Risk Scoring Tool is intended for use only by healthcare professionals for informational purposes only. This tool has not been validated, does not give professional advice nor should it be used in the course of clinical care. Physicians and other healthcare professionals who use this calculator should exercise their own clinical judgment and not that based on results from this calculator. The tool is used at your own risk and we assume no liability for usage of the tool.

PHM Ratio (Donor:Recipient): 1.18
Donor-Recipient Mismatch: 17.8%

Severe PGD Risk 13.4%

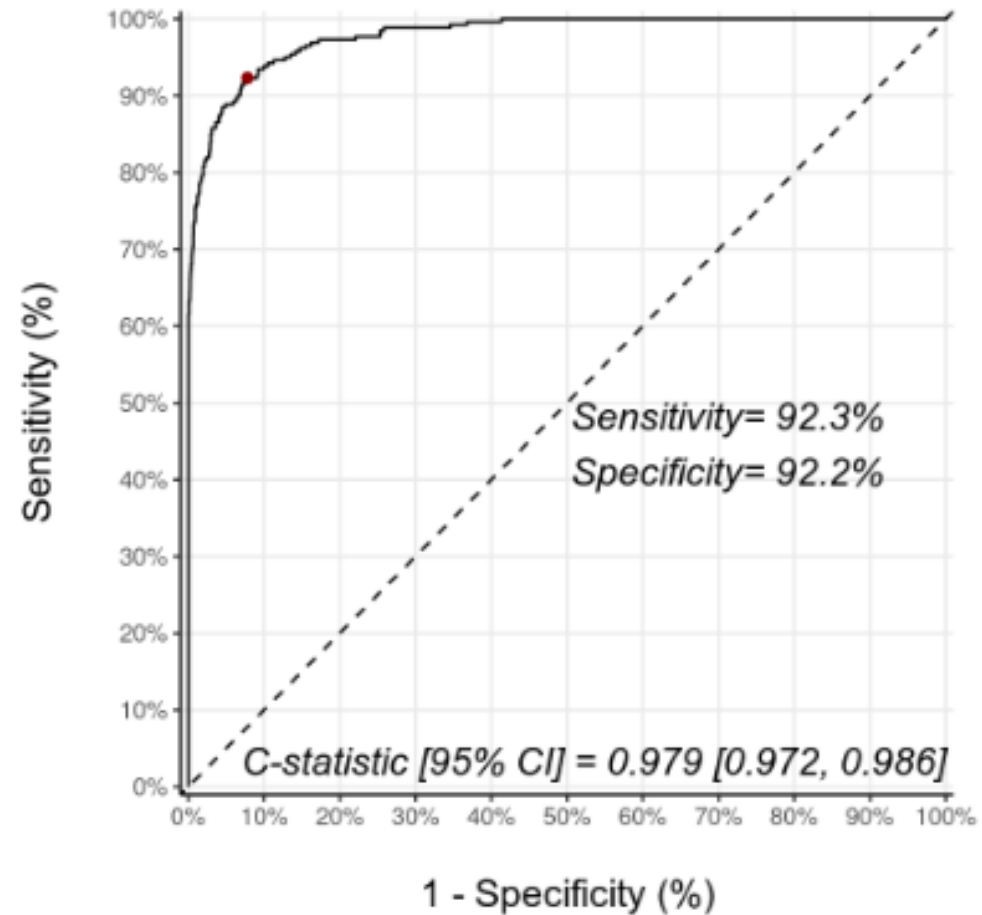
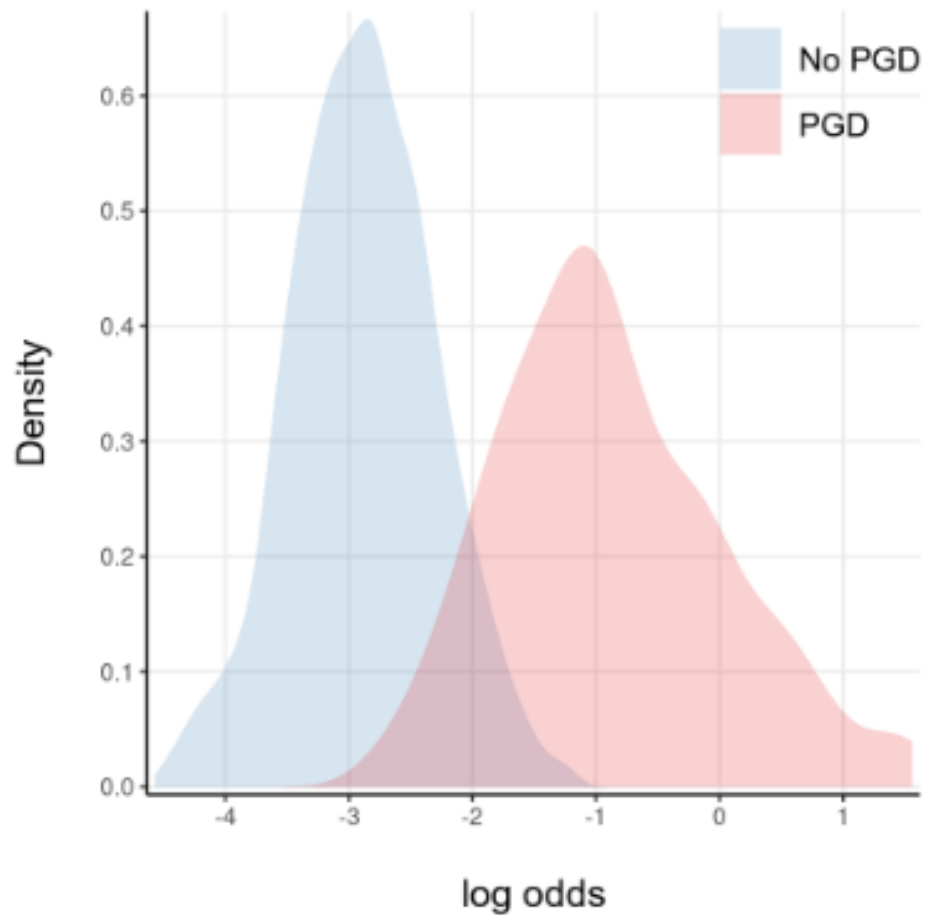


https://lx1r1o-yas-m.shinyapps.io/PGD-risk/?_ga=2.245274758.2032975790.1681416055-947814456.1681416055

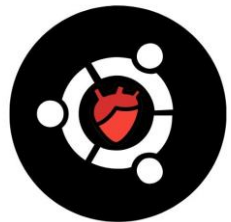
Late breaking, ISHL 2024



AI-PGD Derivation (n=3000)

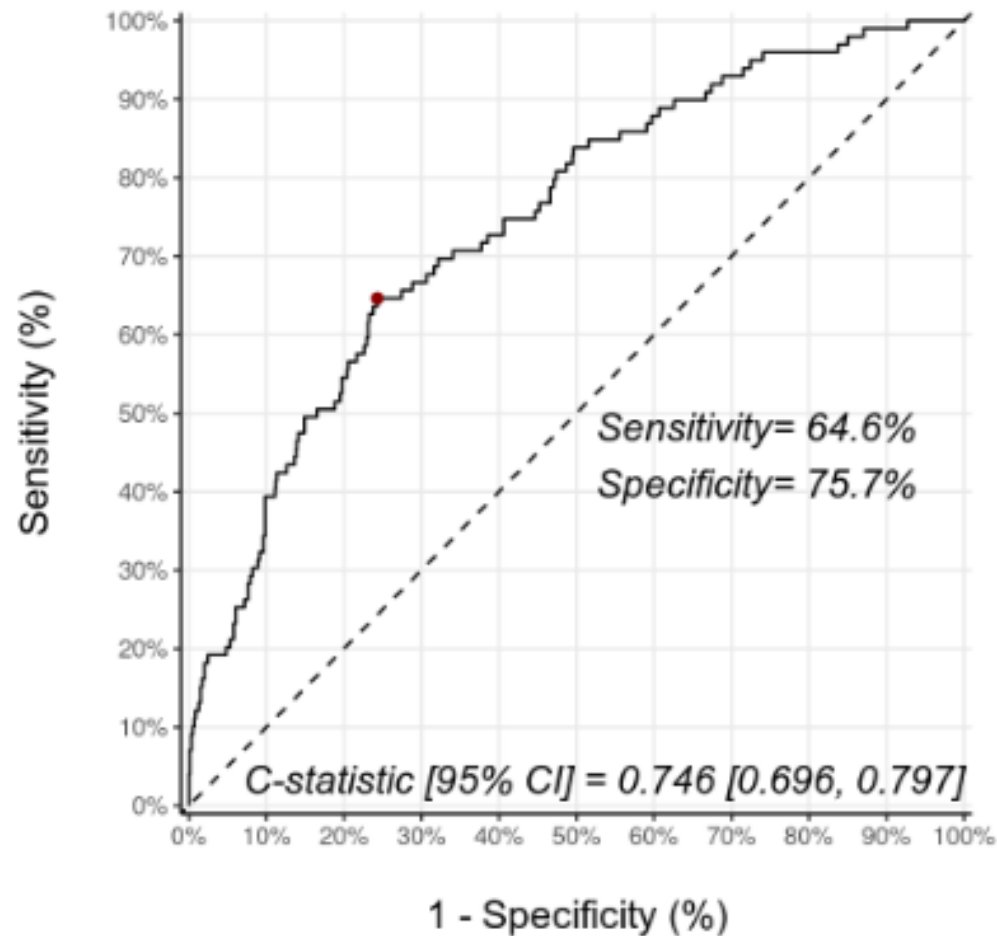
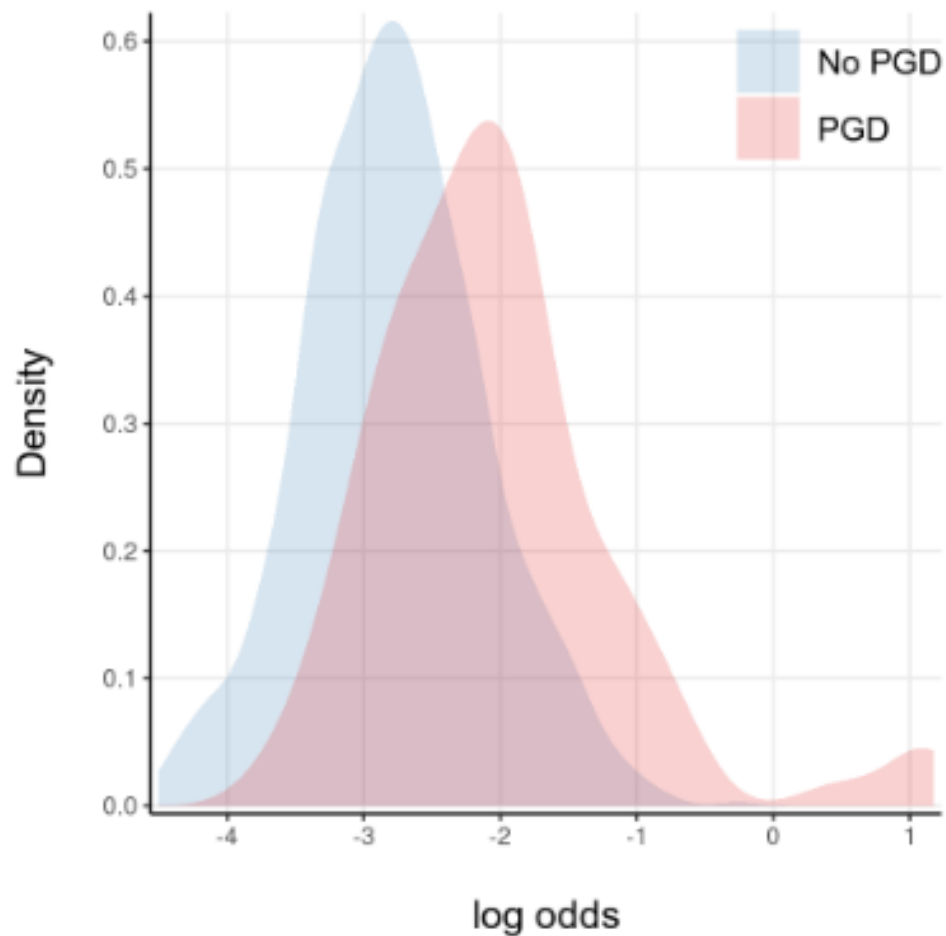


Late breaking, ISHL 2024

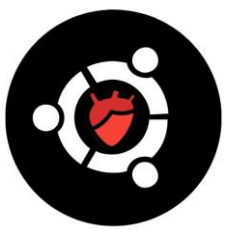


AI-PGD Validation (n=1000)

2



Late breaking, ISHL 2024

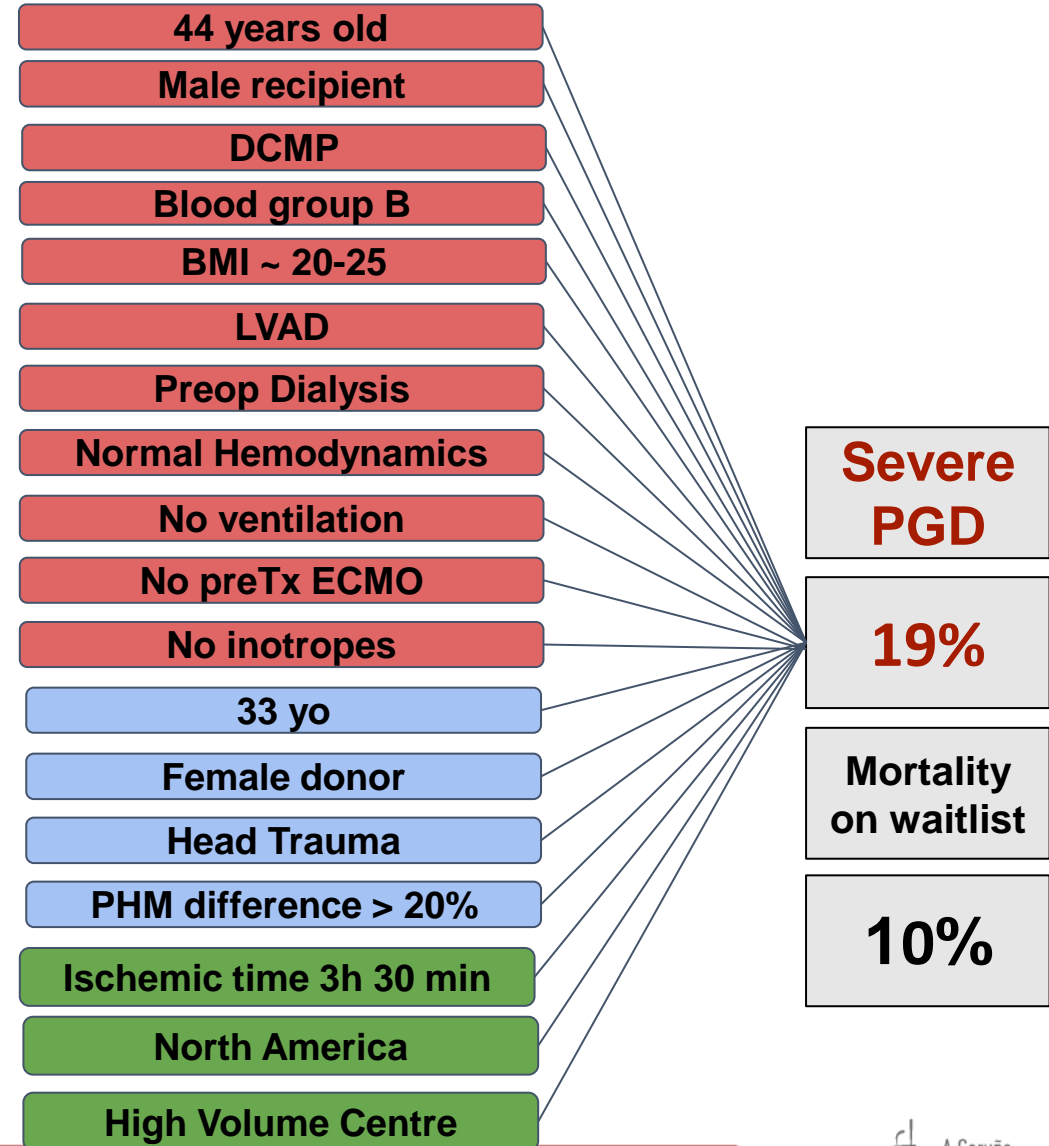


Case Study: Novel Prediction Model





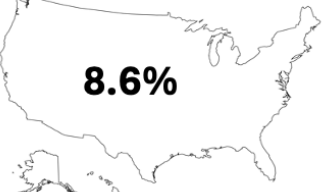


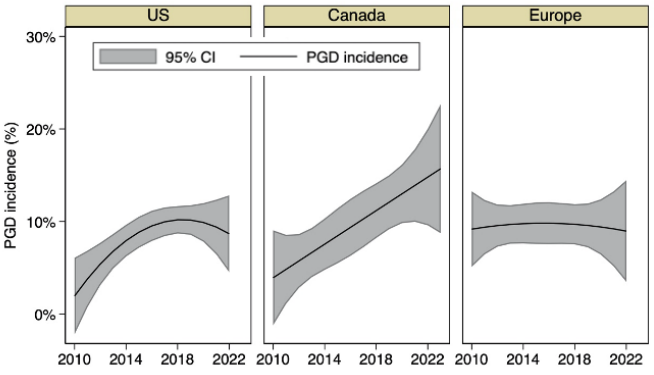
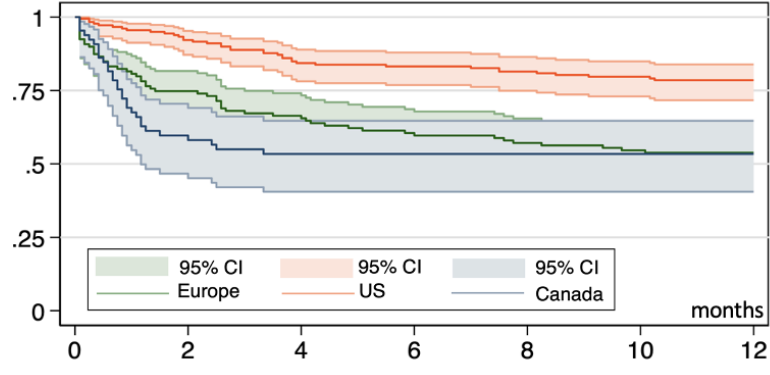
Mr A is a 44 year old man, blood group B, height 1.7 m, weight 70 kg with a history of dilated cardiomyopathy. He does not have diabetes. He is supported with a durable LVAD and has required acute dialysis preoperatively.

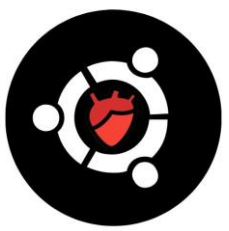
The donor is a 33 yo woman, 1.65 m weight 65 kg, blood group O who died as a result of head trauma with normal LV function.

The total ischemic time is 3 hours and 30 mins



Regional differences

	 <p>2,077</p>	 <p>730</p>	 <p>1,294</p>		
<p>Recipients</p>	<p>↑ BMI, T2DM, HTN ↓ dialysis 1/3 LVAD</p>	<p>↑ re sternotomy ↓ age 1/3 LVAD</p>	<p>↑ RAP, pulmonary pressures ↓ LVAD (15.5 %) ↑ MCS, mechanical ventilation</p>		
<p>Donors</p>	<p>↓ age ↑ BMI = CV risk factors</p>	<p>↓ age ↑ BMI = CV risk factors</p>	<p>↑ age ↓ BMI = CV risk factors</p>		
<p>Surgical factors</p>	<p>↓ ischemic time ↓ PHM mismatch</p>				
<p>Severe PGD incidence</p>	 <p>8.6%</p>	 <p>9.0%</p>	 <p>9.6%</p>		
<p>Severe PGD temporal trend</p>				<p>Severe PGD survival</p>	



In the pipeline

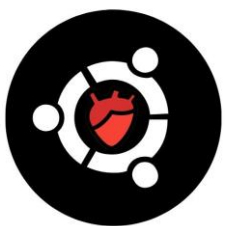


- Subgroup focus:
 - LVAD / short-term MCS
 - Sex
 - DCD / preservation
- Consortium 2.0 – prospective data collection
- Biobank: prediction, diagnosis, prognosis

Take home messages and future directions

- PGD is common and deadly
- Current definition (2014) difficult / based on treatment
 - Need for a new definition? – 2024 ISHLT consensus conference
- Need for risk stratifying tools:
 - Updated to current definition / situation
 - Validated
 - Evolving
 - Make simple the complex
 - Can they decrease PGD / improve post-tx mortality?
- Need for collaborative research
 - Understanding mechanisms
 - Defining phenotypes / severity
 - Management strategies





Acknowledgements

