Primary Graft Dysfunction (PGD) after Heart Transplantation

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PGD (Primary graft dysfunction) after HT

- **Primary!!!**

  Without discernable cause (hyperacute rejection, bleeding, etc)
- Diagnosis within 24 hrs

- Leading cause of **early mortality** after HT

- Firstly defined in **2014 ISHLT consensus statement**

Before **2014 ISHLT consensus**

- **Lack of standardization** of **diagnostic criteria** of PGD after HT
- Different set of criteria across literature

- **Incidence of PGD** in this era
- **2.3~28.2%** (too wide range d/t different definition)

At the **33rd Annual ISHLT meeting**

held in April 23, 2013

- **71 participants** from **42 HT centers** from North America, Australia, Europe, and Asia
- Online survey

Table 1 Primary Graft Dysfunction in Heart Transplantation, Results of Pre-conference Online Survey (47 centers participating) January 2013–March 2013

- Total number of transplant patients at all participating centers was 9,901 with 733 patients thought to have PGD—rate 7.4%
- 30-day mortality was 30% and 1-year mortality was 34.6%.
- Most common causes of death for 30-day mortality: Multiorgan failure (70%), graft failure (20%), and sepsis (10%)
- Definition parameters for PGD:
  - 79% of centers felt that LVEF $\leq$ 40% was a criteria of PGD
  - 68% of centers felt that a time frame of within 24 hours should be used to define PGD
  - 70% of participating centers felt that mechanical support is a mandatory criteria for the definition of PGD

Exclusion criteria for PGD: Hyperacute rejection, 85%;

- sepsis, 85%; right ventricular dysfunction with pulmonary artery systolic pressure >40%–59%; bleeding, 67%
- Precautions against PGD: descending order of importance
  - Cooling of the heart during implantation (by using devices such as cooling jackets, ice, cooling via vent into left atrium/ventricle)
  - Controlled reperfusion
  - Special cardioplegic solution protocol during surgery
  - Temperature control during transport
- Treatment
  - Retransplantation for PGD offered at 64% of participating transplant centers
  - Type of mechanical support routinely utilized (in order of most common to least common): Intra-aortic balloon pump, ECMO, VAD (paracorporeal), VAD (intracorporeal)

ECMO, extracorporeal membrane oxygenation; LVEF, left ventricular ejection fraction; PGD, primary graft dysfunction; VAD, ventricular assist device.

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

From the [a]Cedars-Sinai Heart Institute, Los Angeles, California; [b]Medical University of Vienna, Vienna, Austria; [c]St. Vincent's Hospital, Sydney, New South Wales, Australia; [d]Pierre et Marie Curie University La Pitie-Salpétrière Hospital, Paris, France; [e]Columbia University, New York, New York; [f]University Heart Centre, Hamburg, Germany; [g]Johns Hopkins Hospital, Baltimore, Maryland; [h]Hospital de Puerta De Hierro, Madrid, Spain; [i]Cleveland Clinic, Cleveland, Ohio; [j]University of Utah, Salt Lake City, Utah.

Jon et al. *J Heart Lung Transplant.* 2014

Consensus statements

1. Graft dysfunction classified into PGD or secondary graft dysfunction with a discernible cause such as hyperacute rejection, pulmonary hypertension, or known surgical complications (e.g.,uncontrolled bleeding).

2. The diagnosis of PGD is to be made within 24hours after completion of the cardiac transplant surgery.

3. PGD is to be categorized into PGD-LV or PGD-RV.

4. A severity scale for PGD–LV will include mild, moderate or severe grades based on specified criteria.

5. Risk factors categorized into donor, recipient, or surgical procedural factors.

Consensus statements

6. Medical management with inotropic support should initially be instituted for PGD such as levosimendan. For PGD-RV, NO and phosphodiesterase inhibitors

7. Mechanical circulatory support such as ECMO for patients refractory for medical management

8. Retransplantation for severe PGD may be indicated in select patients if risk factors are minimal.

9. All patients in whom mechanical circulatory support is placed directly into the heart should have a heart biopsy performed at that time.

10. It was recommended that an autopsy should be performed in all patients who are diagnosed with PGD and subsequently expire.

11. Potential future studies include creation of a PGD registry, impact of preservation solutions on PGD, mechanistic studies to understand pathophysiology of PGD, and study of donor management to minimize PGD, among others.

Table 5 Classification of Graft Dysfunction

1. Primary graft dysfunction (PGD):
   a. PGD-left ventricle (PGD-LV): Includes left and biventricular dysfunction.
   b. PGD-right ventricle (PGD-RV): Includes right ventricular dysfunction alone.
2. Secondary Graft Dysfunction: Occurs when there is a discernible cause for graft dysfunction (e.g., hyperacute rejection, pulmonary hypertension, known surgical complication).

Jon et al. *J Heart Lung Transplant.* 2014

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

1. **PGD-Left ventricle (PGD-LV):**	*Mild PGD–LV*: *One* of the following criteria must be met:	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
	Moderate PGD-LV: Must meet one criterion from I *and* another criterion from II:	I. *One* 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. *One* criteria from the following: i. High-dose inotropes—Inotrope score $>$ 10[a] *or* ii. Newly placed IABP (regardless of inotropes)
	Severe PGD–LV	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.

[a]Inotrope 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 µg/kg/min.

Jon et al. *J Heart Lung Transplant.* 2014

Epidemiology and Incidence of PGD

References	Year of publish	Years of data obtained	PGD/Total patient number of cohort (%)	Mild LV PGD	Moderate LV PGD	Severe LV PGD	RV PGD	30-day mortality PGD vs no-PGD
Daronavalli et al.* UK [10]	2015	2007–2011	94/290 (32%)					37.2% versus 4.1%
Sabatino M., et al. [8] Italy	2017	1999–2013	72/518 (14%)	4/72 (5%)	33/72 (46%)	35/72 (49%)		27% versus 3% mild (0%), moderate (12%), severe (65%)
					8/			
Foroutan F. et al. [11] Canada	2019	2004–2015	82/412 (20%)	15/82 (18%)	39/82 (48%)	19/82 (23%)	12/82 (15%)	
Singh S., et al. [5] UK	2019	2012–2015	163/450 (36%)	4/163 (3%)	72/163 (44%)	81/163 (50%)	6/163 (4%)	19% versus 4.5%
Rhee Y., et al. [4] South Korea	2021	1992–2017	35/570 (6%)	1/35 (3%)	14/35 (40%)	20/35 (57%)	3/35 (8.6%)	mild (0%), moderate (14.3%), severe (25%) versus 0.6%

Applied PGD criteria within 72 h after transplantation.

PGD incidence, 6~36%
In single center series

30-day mortality
in PGD: 19~37.2%
in no-PGD: 0.6~4.5%

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Incidence and impact of primary graft dysfunction in adult heart transplant recipients: A systematic review and meta-analysis

Tayler A. Buchan, MSc,[a,b] Yasbanoo Moayedi, MD,[a] Lauren K. Truby, MD,[c] Gordon Guyatt, MD, MSc,[b] Juan Duero Posada, MD,[a] Heather J. Ross, MD, MHSc,[a] Kiran K. Khush, MD, MAS,[d] Ana C. Alba, MD, PhD,[a] and Farid Foroutan, PhD[a,b]

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KEYWORDS:
prognosis;
heart transplant;
primary graft dysfunction;
mortality;
meta-analysis

PURPOSE: Primary graft dysfunction (PGD) is a leading cause of early mortality after heart transplant (HTx). To identify PGD incidence and impact on mortality, and to elucidate risk factors for PGD, we systematically reviewed studies using the ISHLT 2014 Consensus Report definition and reporting the incidence of PGD in adult HTx recipients.

METHODS: We conducted a systematic search in January 2020 including studies reporting the incidence of PGD in adult HTx recipients. We used a random effects model to pool the incidence of PGD among HTx recipients and, for each PGD severity, the mortality rate among those who developed PGD. For prognostic factors evaluated in ≥2 studies, we used random effects meta-analyses to pool the adjusted odds ratios for development of PGD. The GRADE framework informed our certainty in the evidence.

RESULTS: Of 148 publications identified, 36 observational studies proved eligible. With moderate certainty, we observed pooled incidences of 3.5%, 6.6%, 7.7%, and 1.6% and 1-year mortality rates of 15%, 21%, 41%, and 35% for mild, moderate, severe and isolated right ventricular-PGD, respectively. Donor factors (female sex, and undersized), recipient factors (creatinine, and pre-HTx use of amiodarone, and temporary or durable mechanical support), and prolonged ischemic time proved associated with PGD post-HTx.

CONCLUSION: Our review suggests that the incidence of PGD may be low but its risk of mortality high, increasing with PGD severity. Prognostic factors, including undersized donor, recipient use of amiodarone pre-HTx and recipient creatinine may guide future studies in exploring donor and/or recipient selection and risk mitigation strategies.

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Including 36 Studies

8120 HT patients

Pooled analysis

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All severities	20.5% (95% CI 17.2% – 24.1%)
Mild	3.5% (95% CI 0.9% – 7.5%)
Moderate	6.6% (95% CI 4.5% – 9.0%)
Severe	7.7% (95% CI 5.1% – 10.9%)
RV-PGD	1.6% (95% CI 0.6% – 2.8%)

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Pathophysiology of PGD

- Brainstem death
- Cold ischemia
- Warm ischemia
- Ischemia-reperfusion injury (IRI)

Pathophysiology of PGD

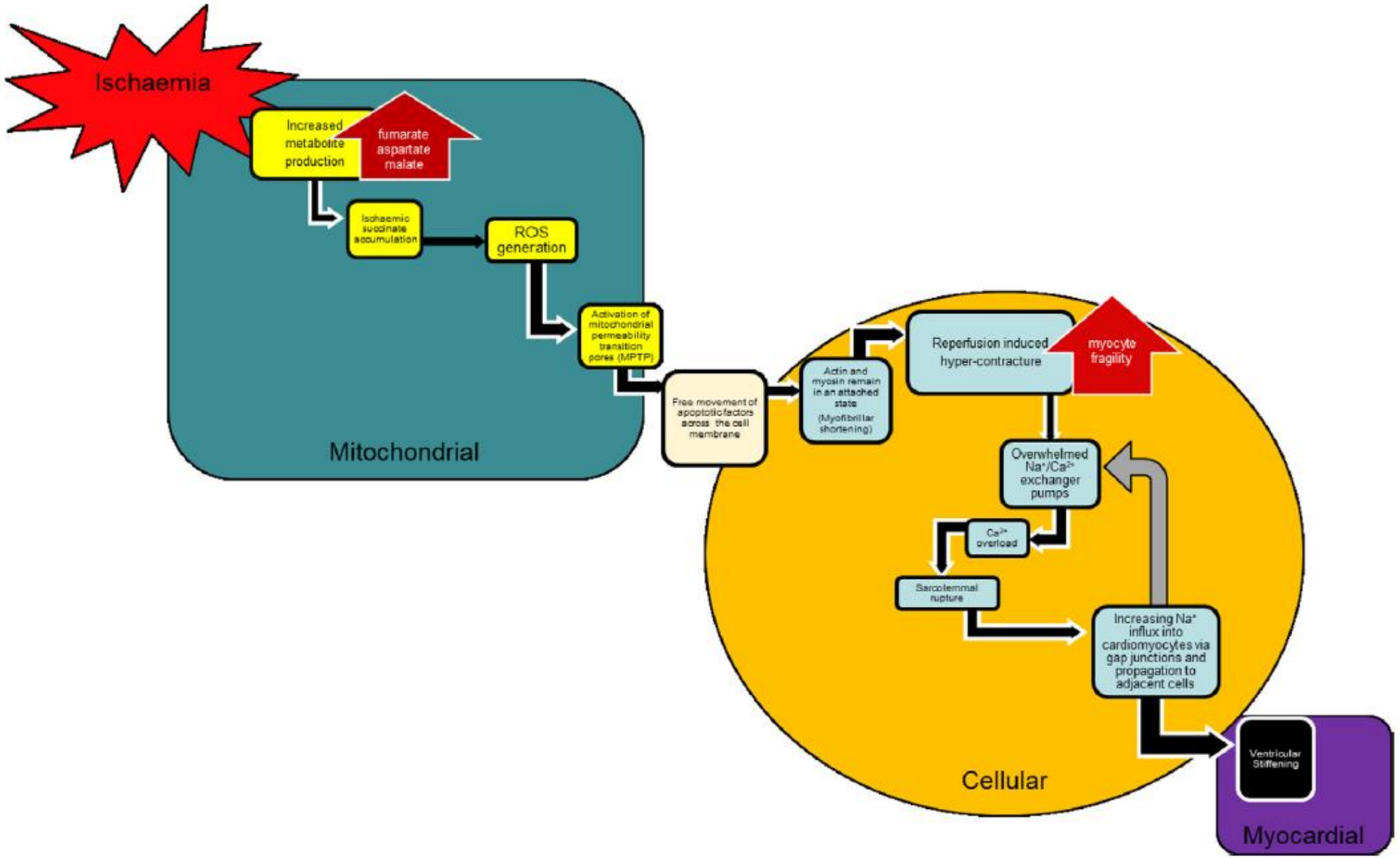
- **Brainstem death**
  - Catecholamine surge
    → myocardial ischemia & intracellular Ca^{2+} overload

- **Cold ischemia (0-4℃)**
  - 12-fold decrease in metabolic rate in hypothermic state & less accumulation of oxygen-free radical
  - Prolonged cold storage
    Cellular swelling & lactic acidosis → intracellular Ca^{2+} overload
    Oxygen-free radial formation↑

Pathophysiology of PGD

- **Warm ischemia (surgical implant time)**
  - Increased metabolic rate
  - Acceleration of deleterious effects during cold ischemic phase
    (Oxygen-free radial formation & intracellular Ca^{2+} overload↑)

- **Ischemia-reperfusion injury (IRI)**
  - Ca^{2+} overload (ACC release)
    Myocardial hypercontraction & End-diastolic pressure↑(myocardial stiffness)
  - MPTP (mitochondrial permeability transition pores) formation
    Non-specific channel allow free movement of apoptotic factors across cell membrane



Ahmed et al. *Curr Probl Cardiol.* 2022

Risk factors for PGD

Jon et al. *J Heart Lung Transplant.* 2014

Table 2 Risk Factors for Development of Primary Graft Dysfunction

Donor risk factors	Recipient risk factors	Surgical procedural risk factors
Age[5,11,39,66]	Age[11]	Ischemia time[5,9,42]
Cause of death[40,68]	Weight[42]	Donor-recipient sex mismatch[41]
Trauma[8,11]	Mechanical support[5,39–41]	Weight mismatch[5,40]
Cardiac dysfunction[40,69]	Congenital heart disease as etiology of heart failure[5]	Non-cardiac organ donation[a,10]
Inotropic support[8,40]	Multiple reoperations	Experience of procurement team and center volume[5]
Comorbidities: diabetes, hypertension[2]	LVAD explant	Cardioplegic solution[15]
Downtime of cardiac arrest	Comorbidities: renal dysfunction, liver dysfunction (high MELD), DM	Increased blood transfusion requirement
Drug abuse: alcohol, cocaine, amphetamines	Ventilator dependent	Elective vs emergency transplant[b,70]
Left ventricular hypertrophy	Multiorgan transplant	
Valvular disease	Elevated PVR	
Hormone treatment	Allosensitization	
CAD/wall motion abnormalities on TTE	Infection	
Sepsis	Retransplant	
Alternate list/marginal donor allocation—not increased risk[7]		
Troponin trend		
Hypernatremia		

CAD, coronary artery disease; DM, diabetes mellitus; LVAD, left ventricular assist device; MELD, Model for End-stage Liver Disease; PGD, primary graft dysfunction; PVR, peripheral vascular resistance; TTE, transthoracic echocardiogram; UNOS, United Network for Organ Sharing.

[a]Donation of all noncardiac organs, with the exception of lung donation, was associated with decreased incidence of PGD using data from UNOS.[5] Alternative study shows a high degree of correlation between heart and lung PGD in patients undergoing a paired transplant

[b]Single-center study showed an incidence of 36% of PGD in the group that received an emergency heart transplant whereas the incidence was 16% in those for which the transplant was done electively.

Factors	Non-modifiable	Modifiable
Donor	• Age [46, 47] • Death from trauma [48] • Cardiac dysfunction • Cardiac resuscitation time • Substance abuse • Left ventricular hypertrophy [49] • Valvular disease • Coronary artery disease	• Sepsis • Inotropic support [50]
Procurement		• Procurement team experience • Cardioplegic solution
Recipient	• Age [50] • Mechanical support [5] • Congenital heart disease • Multiple thoracic operation [2] • Comorbidities (DM, CKD, Liver dysfunction) [5, 50] • Ventilator dependence • Pulmonary hypertension [8] • LVAD bridging [6]	• Amiodarone usage [51] • Infection
Surgery	• Non-cardiac organ donation • Center volume	• Ischemic time [4, 6] • Female to male recipient [5] • Undersized donor (≥30%) [9] • Blood transfusion requirement

Donor selection

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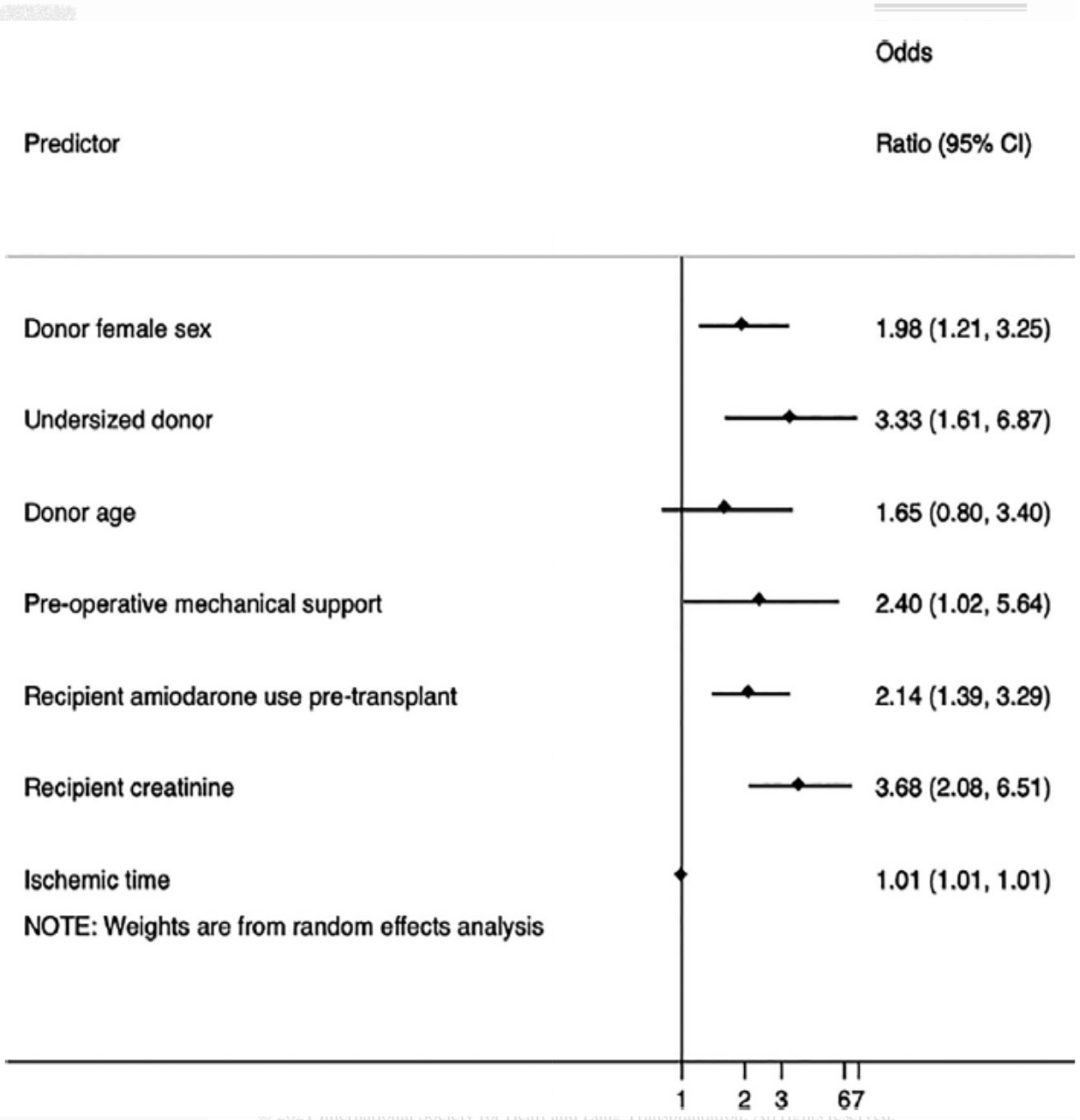

Tayler et al. *J Heart Lung Transplant.* 2021

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

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Dominic A. Emerson, MD,[a] Joshua Rushakoff, MD, MPP,[a]
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Single center analysis

734 HT patients

From Jan 2012 to Dec 2018

ischemia-reperfusion injury;
clinical risk prediction

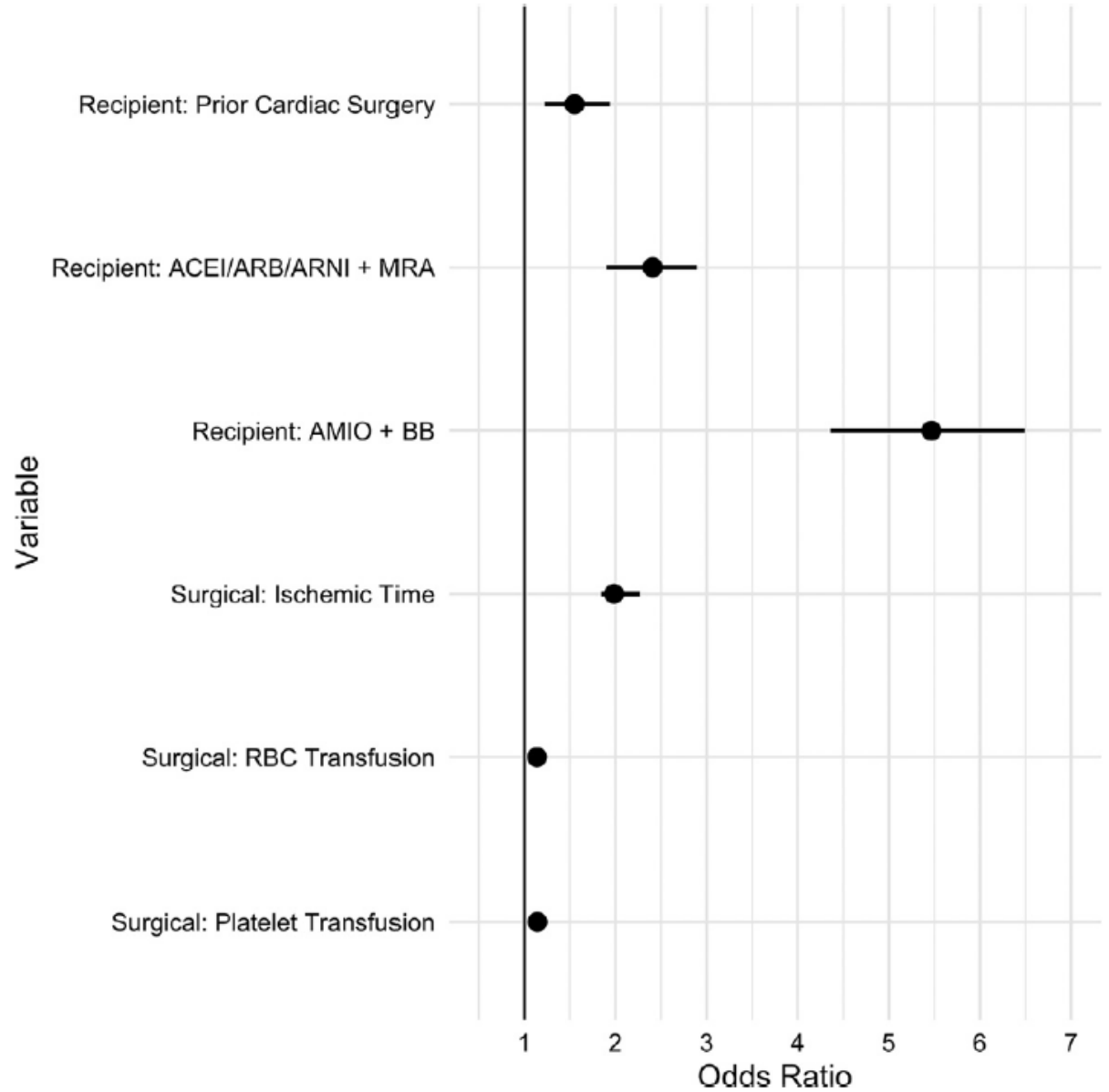
METHODS: We identified 734 heart transplant recipients at our institution transplanted between January 1, 2012 and December 31, 2018. PGD was defined according to modified ISHLT criteria. Recipient, donor and surgical variables were analyzed by multinomial logistic regression with mild/moderate or severe PGD as the response. Variables significant in single variable modeling were subject to multivariable analysis via penalized logistic regression.

RESULTS: PGD occurred in 24% of the cohort (n = 178) of whom 6% (n = 44) had severe PGD. One-year survival was reduced in recipients with severe PGD but not in those with mild or moderate PGD. Multivariable analysis identified 3 recipient factors: prior cardiac surgery, recipient treatment with ACEI/ARB/ARNI plus MRA, recipient treatment with amiodarone plus beta-blocker, and 3 surgical factors: longer ischemic time, more red blood cell transfusions, and more platelet transfusions, that were associated with severe PGD. We developed a clinical risk score, ABCE, which provided acceptable discrimination and calibration for severe PGD.

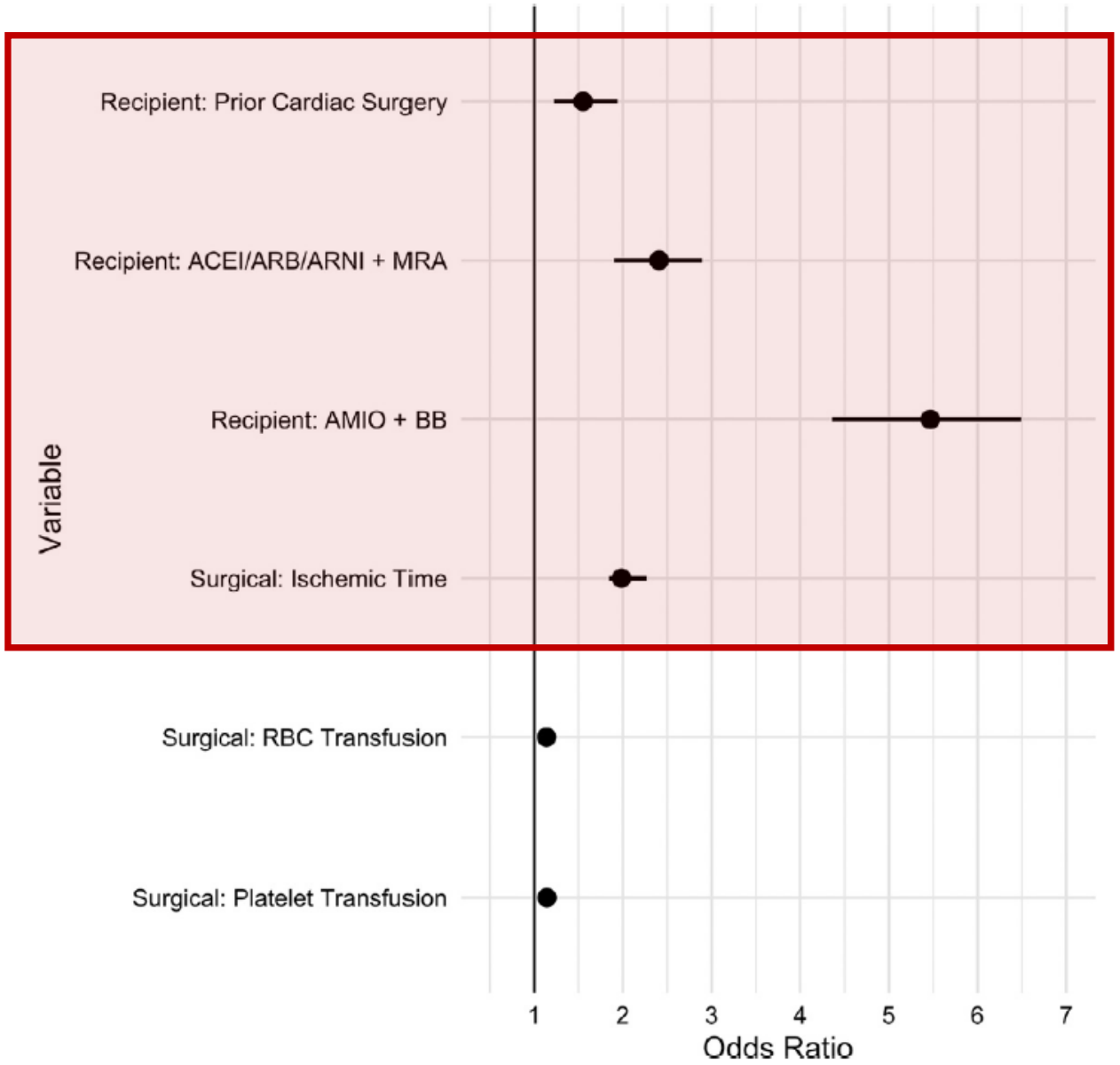
CONCLUSIONS: Risk factors for mild/moderate PGD were largely distinct from those for severe PGD, suggesting a differing pathophysiology involving several biological pathways. Further research into mechanisms underlying the development of PGD is urgently needed.

J Heart Lung Transplant 2021;40:970–980

Lillian et al. *J Heart Lung Transplant.* 2021



Lillian et al. *J Heart Lung Transplant.* 2021



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rigger severe

Table 3 Risk Score for Severe PGD

Variable	Points	Abbreviation
Treatment with **A**CEI/**A**RB/ **A**RNI + MRA	9	A
Treatment with AMIO + **B**eta-**B**locker	17	B
Previous **C**ardiac Surgery	4	C
Ischemic tim**E**	7 / hour	E

ACEI, angiotensin converting enzyme inhibitor; AMIO, amiodarone; ARB, angiotensin receptor antagonist; ARNI, angiotensin receptor-neprilysin inhibitors; MRA, mineralocorticoid receptor antagonist.

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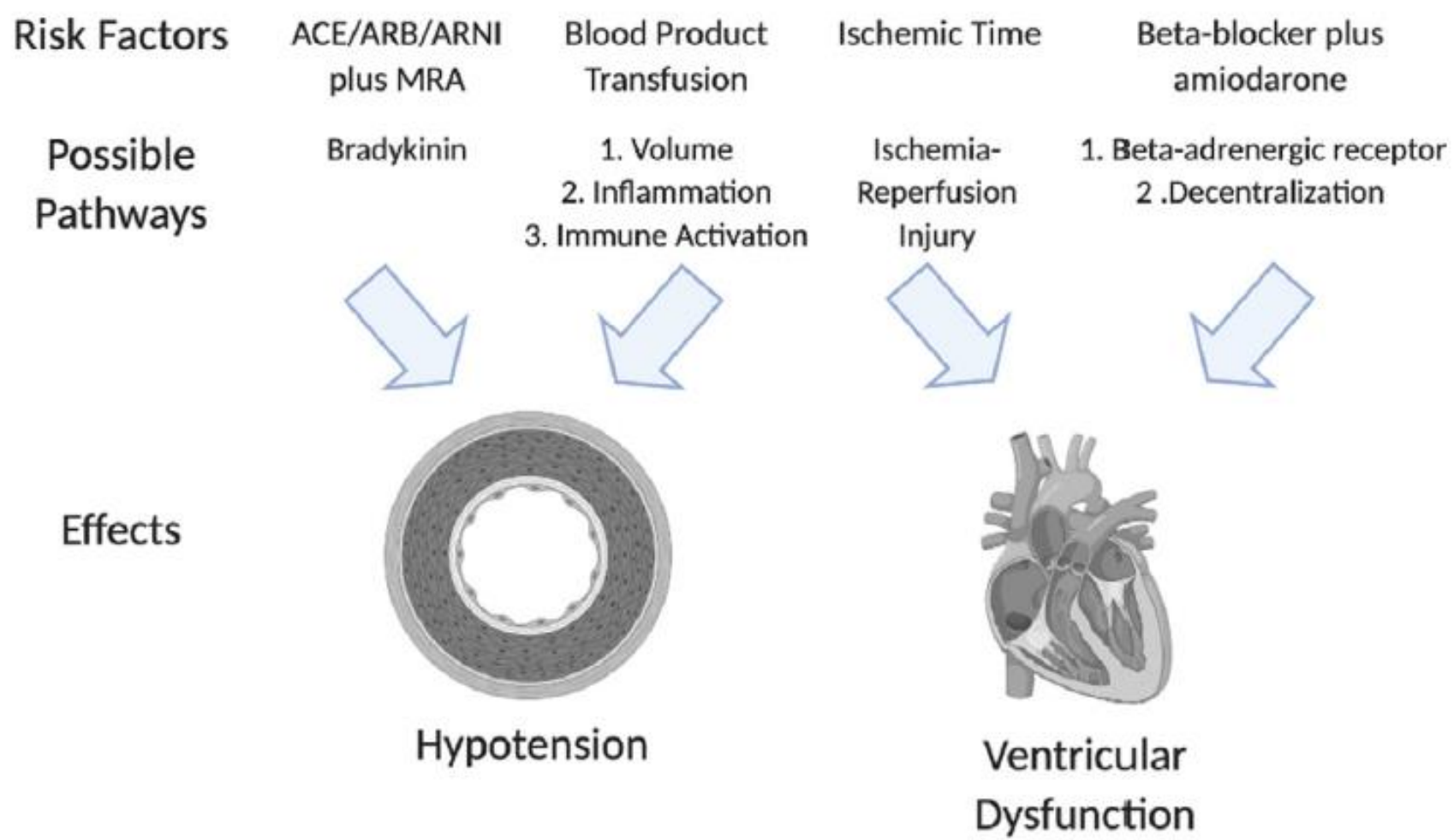
0–980

Lillian et al. *J Heart Lung Transplant.* 2021



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Prediction of PGD

- **RADIAL score: 0~6**
  - Proposed in 2011 (before 2014 ISHLT consensus)
  - PGD, Defined by 4 criteria (myocardial dysfunction, hemodynamic impairment, early onset <24hr, w/o secondary cause)
  - **R**A pressure/recipient **A**ge/**D**iabetes/**I**notropes/donor **A**ge/**L**ength of ischemic time

- **PREDICTA score: 0~14**
  - Proposed in 2019 (after 2014 ISHLT consensus)
  - Diabetes/preoperative mechanical support/implant time/donor age/bypass time>180min

RADIAL: A novel primary graft failure risk score in heart transplantation

Javier Segovia, MD, PhD, M. Dolores G. Cosío, MD, Juan M. Barceló, MD,
Manuel Gómez Bueno, MD, Pablo García Pavía, MD, Raúl Burgos, MD, PhD,
Santiago Serrano-Fiz, MD, PhD, Carlos García-Montero, MD, PhD,
Evaristo Castedo, MD, PhD, Juan Ugarte, MD, and Luis Alonso-Pulpón, MD, PhD

From the Unidad de

Single center analysis

621 HT patients

From Jan 1984 to Dec 2006

KEYWORDS:
primary early gra
failure;
heart transplantat
risk score

heart trans-
dictive risk

tion, severe
lysfunction.
onstructed a
e validation

ctively. We
nt Age ≥60
time ≥240

minutes—i.e., RADIAL). Analysis of isolated right ventricular failure showed similar predictors. The RADIAL score was obtained by adding 1 point for each of these factors present in a given HT. PGF incidence increased significantly as the RADIAL score increased ($p < 0.001$ for trend). Rates of actual and predicted PGF incidence for RADIAL subgroups showed a good correlation (C-statistic = 0.74). In a prospective validation cohort, RADIAL score kept its predictive ability.

CONCLUSIONS: PGF as defined by these criteria showed a high impact on early post-HT mortality in our series. The RADIAL score showed good ability to predict the development of PGF, and could be useful in the prevention and early treatment of this complication.

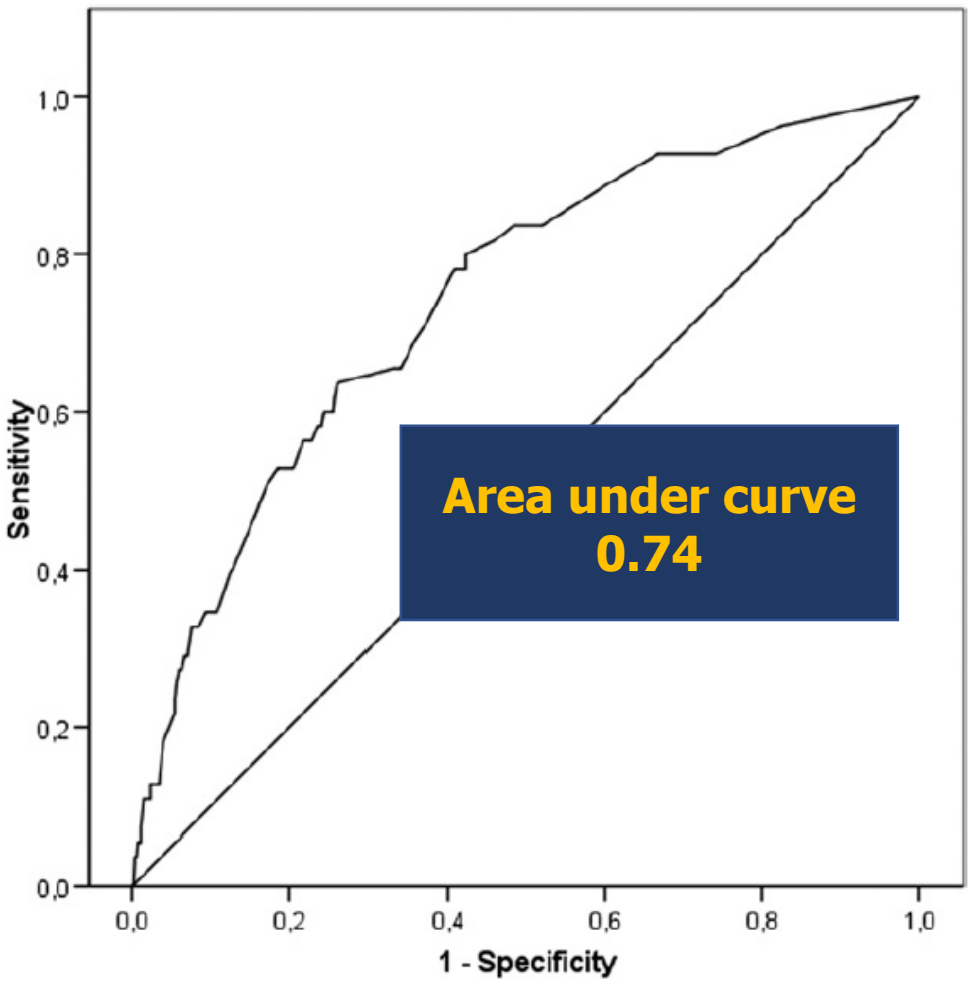
J Heart Lung Transplant 2011;30:644–51

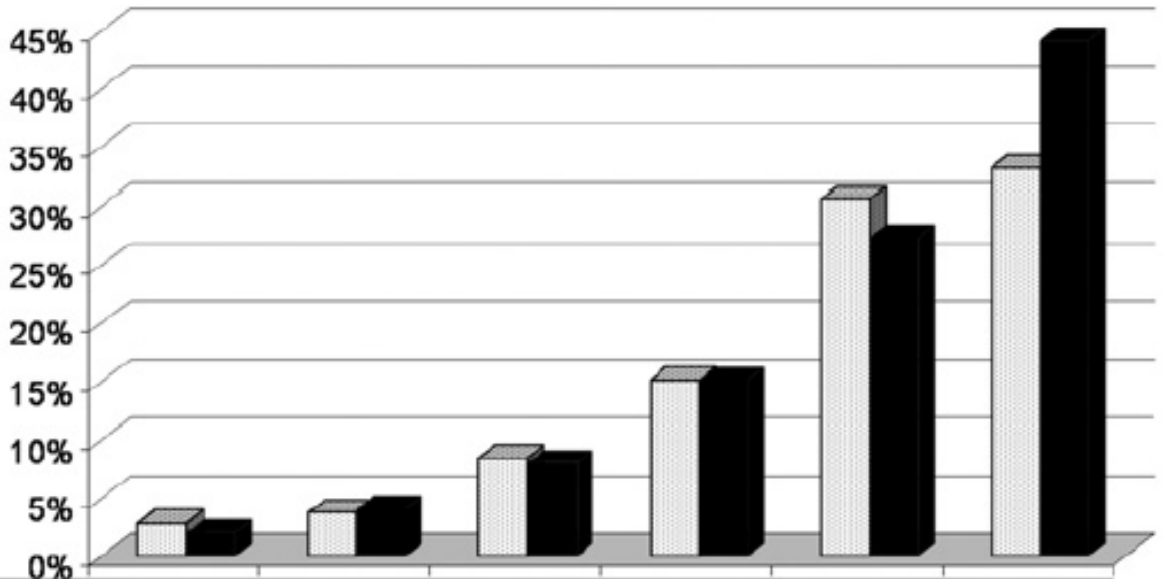
Javier et al. *J Heart Lung Transplant.* 2011

Table 2 Multivariate Model for Primary Graft Failure

	PGF			
Risk factors	Prev	RR	CI 95%	*p*-value
Recipient age ≥60 years	20.2%	1.9	1.1–3.7	0.047
Recipient diabetes mellitus	12.1%	2.5	1.2–5.1	0.008
Recipient inotrope therapy	38.3%	2.1	1.1–3.7	0.016
Recipient RAP ≥10 mm Hg	40.9%	2.2	1.2–4.0	0.009
Donor age ≥30 years	39.3%	1.7	1.1–3.1	0.04
Ischemic time ≥240 min	20.6%	1.9	1.1–3.5	0.04

Javier et al. *J Heart Lung Transplant.* 2011





RADIAL Score	0	1	2	3	4	≥5
N. patients	103	189	165	119	36	9
Actual PGF	2,9%	3,7%	8,5%	15,1%	30,6%	33,3%
Predicted PGF (CI 95%)	2.1% (0-5,3)	4,1% (3-4.7)	8,1% (4-12)	15,2% (13-17)	27,4% (15-39)	44,2% (17-68)

Javier et al. *J Heart Lung Transplant.* 2011

Journal of Cardiac Failure Vol. 25 No. 12 2019

PREDICTA: A Model to Predict Primary Graft Dysfunction After Adult Heart Transplantation in the United Kingdom

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6 UK HT centers

613 HT patients

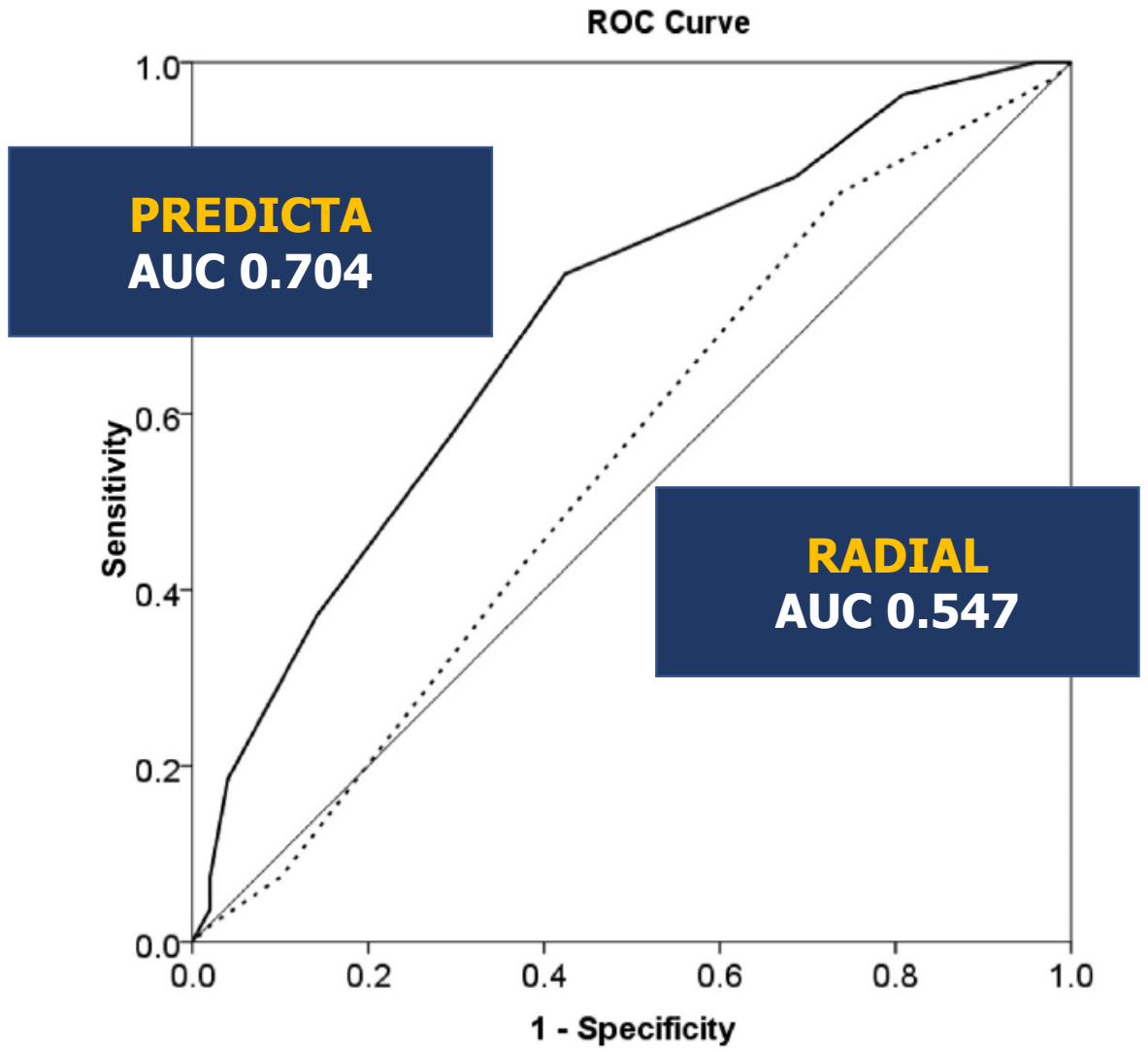
From 2012 to Dec 2016

Backgrou
transplant
increasing
system ba
to a previ
Methods:
2012 and
recipient
the PGD
Multivari
characteristics curve was used to test the novel scoring system (PREDICTA) versus the RADIAL score.
Results: Six hundred and thirteen heart transplants were included in the study. There were 233 patients who had PGD. The variables included in the model were recipient diabetes mellitus, preoperative mechanical circulatory support (short-term ventricular assist devices/extracorporeal membrane oxygenation), implant time, donor age, and bypass time >180 minutes. The C statistic of the PREDICTA score was 0.704 versus 0.547 for the RADIAL score indicating an acceptable discriminatory value.
Conclusion: The PREDICTA score is a novel scoring tool with improved ability to predict the development of PGD compared with the RADIAL score. Its application in the prevention and early management of PGD needs further evaluation. (*J Cardiac Fail 2019;25:971–977*)
Key Words: Primary graft dysfunction, scoring systems, heart transplantation, mechanical circulatory support.

Sanjeet et al. *J Cardiac Fail.* 2019

Table 5. PREDICTA Score Points Allocation

Variable	Points
Preoperative MCS (ST-VADs and ECMO)	3
Recipient diabetes mellitus	3
Cardiopulmonary bypass time >180 min	2
Implant time	
≤45 min	0
46-60 min	1
61-90 min	2
>90 min	3
Donor age	
<21 years	0
21-40 years	1
41-50 years	2
>50 years	3
Total	__/14



Sanjeet et al. *J Cardiac Fail.* 2019

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The Journal of Heart and Lung Transplantation

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Donor hyperoxia is a novel risk factor for severe cardiac primary graft dysfunction

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KEYWORDS:
heart transplant;
donor risk factors;
primary graft dysfunction;
hyperoxia;
donor management

BACKGROUND: Primary graft dysfunction (PGD) is a major cause of early mortality following heart transplant (HT). Donor risk factors for the development of PGD are incompletely characterized. Donor management goals (DMG) are predefined critical care endpoints used to optimize donors. We evaluated the relationship between DMGs as well as non-DMG parameters, and the development of PGD after HT.

METHODS: A cohort of HT recipients from 2 transplant centers between 1/1/12 and 12/31/19 was linked to their respective donors in the United Network for Organ Sharing (UNOS) DMG Registry (n = 1,079). PGD was defined according to modified ISHLT criteria. Variables were subject to univariate and multivariable multinomial modeling with development of mild/moderate or severe PGD as the outcome variable. A second multicenter cohort of 4,010 donors from the DMG Registry was used for validation.

RESULTS: Mild/moderate and severe PGD occurred in 15% and 6% of the cohort. Multivariable modeling revealed 6 variables independently associated with mild/moderate and 6 associated with severe PGD, respectively. Recipient use of amiodarone plus beta-blocker, recipient mechanical circulatory support, donor age, donor fraction of inspired oxygen (FiO_2), and donor creatinine increased risk whereas predicted heart mass ratio decreased risk of severe PGD. We found that donor age and $FiO_2 \geq 40\%$ were associated with an increased risk of death within 90 days post-transplant in a multicenter cohort.

CONCLUSIONS: Donor hyperoxia at heart recovery is a novel risk factor for severe primary graft dysfunction and early recipient death. These results suggest that excessive oxygen supplementation should be minimized during donor management.

J Heart Lung Transplant 2023;42:617–626

Evan et al. *J Cardiac Fail.* 2023

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Donor hyperoxia is a novel risk factor for severe

CrossMark

Risks factor analysis using
Donor Management Goals (DMG) registry

1079 HT patients

btw Jan 2012 and Dec 2019

in 2 HT centers

40% were associated with an increased risk of death within 90 days post-transplant in a multicenter cohort.

CONCLUSIONS: Donor hyperoxia at heart recovery is a novel risk factor for severe primary graft dysfunction and early recipient death. These results suggest that excessive oxygen supplementation should be minimized during donor management.

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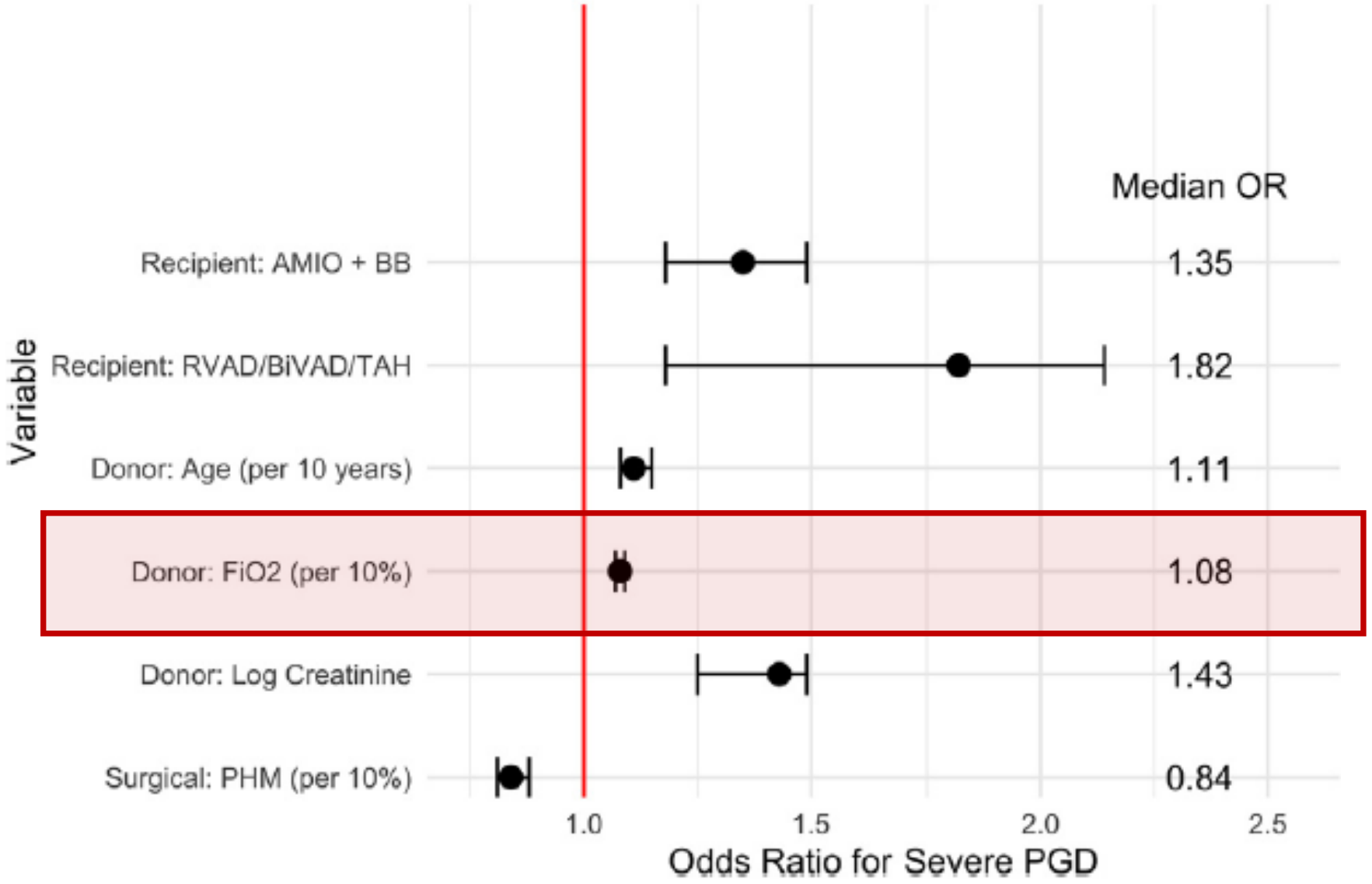

Evan et al. *J Cardiac Fail.* 2023

Long-term survival in PGD

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

Lillian Be
Dominic A
Michelle M
Dominick
Alfredo Tr
David H. (
Jon A. Ko

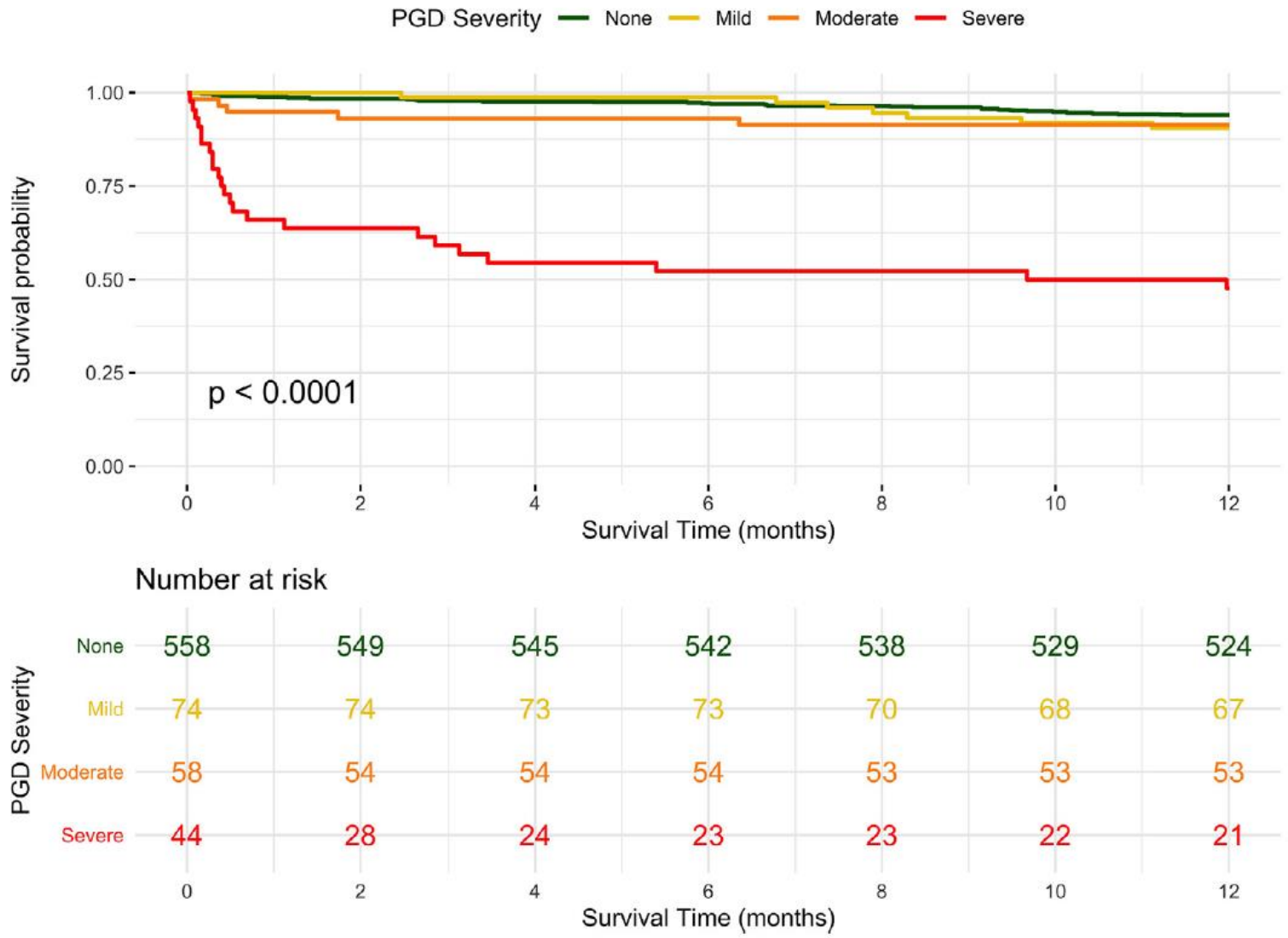
From the [a]Smi *e,*
Department of

Single center series

734 HT patients

From Jan 2012 to Dec 2018

Lillian et al. *J Heart Lung Transplant.* 2021



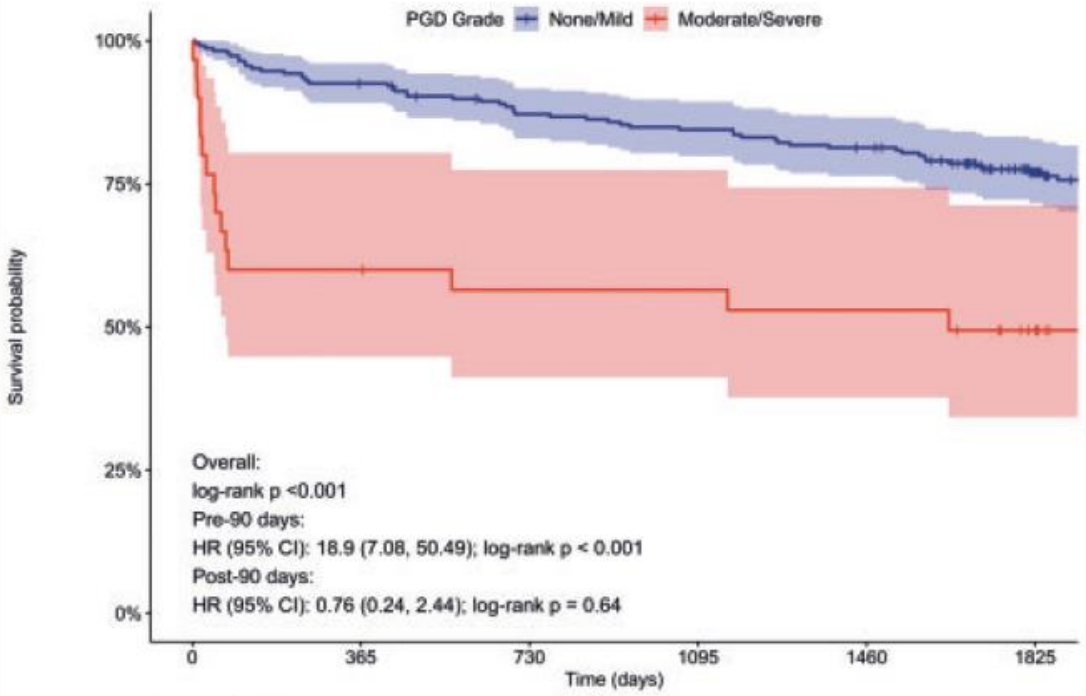
Non-severe PGD

Severe PGD

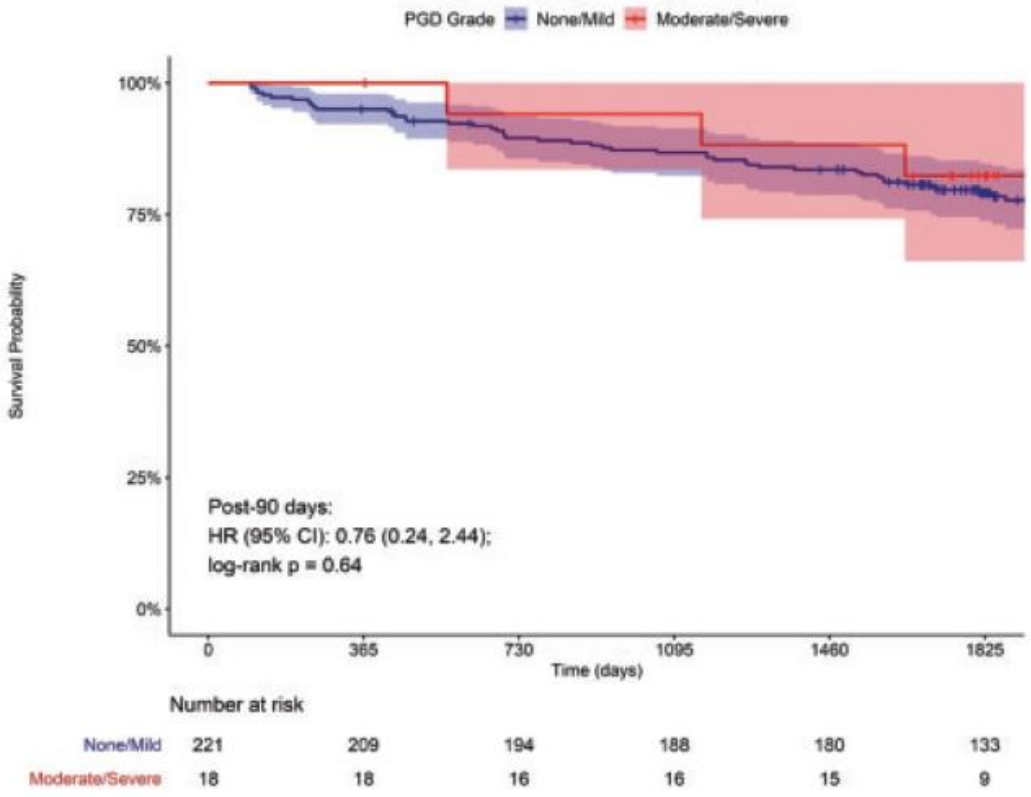
10-year survival: 50%

Lillian et al. *J Heart Lung Transplant.* 2021

Kaplan-Meier survival curves of consecutive patients undergoing isolated orthotopic cardiac transplantation, stratified by severity of primary graft dysfunction (PGD): none/mild (blue) versus moderate/severe (red). Hazard ratios for mortality at the specified time intervals are also listed

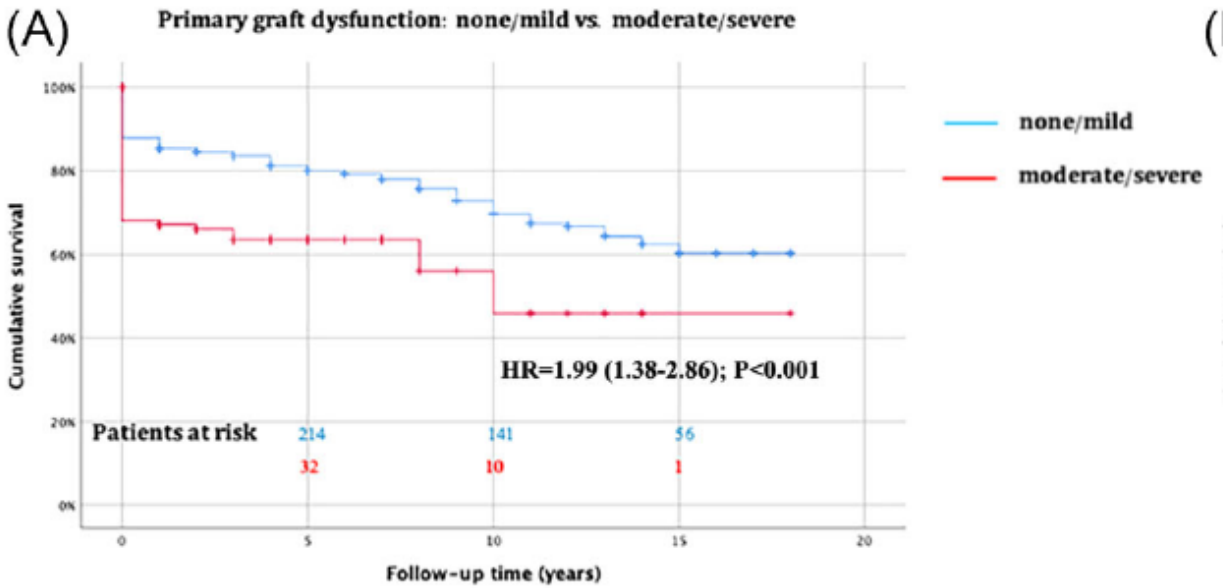


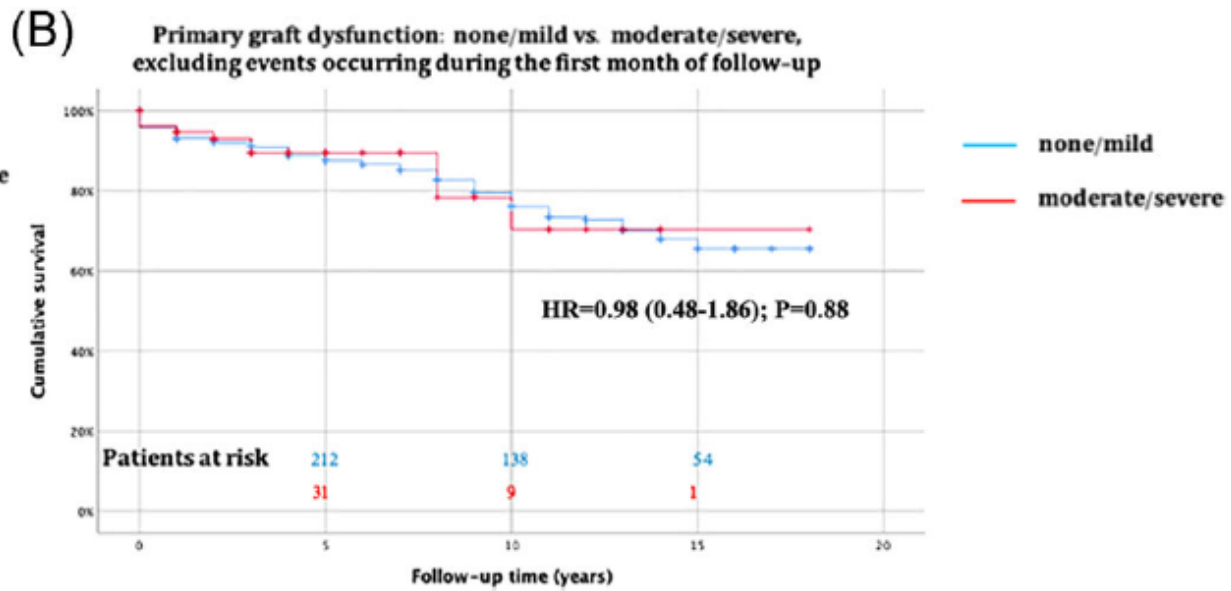
After 90 days



John et al. *Eur J Cardiothorac Surg.* 2021

After 30 days





Fabrizio et al. *J Card Surg.* 2021

After 90 days

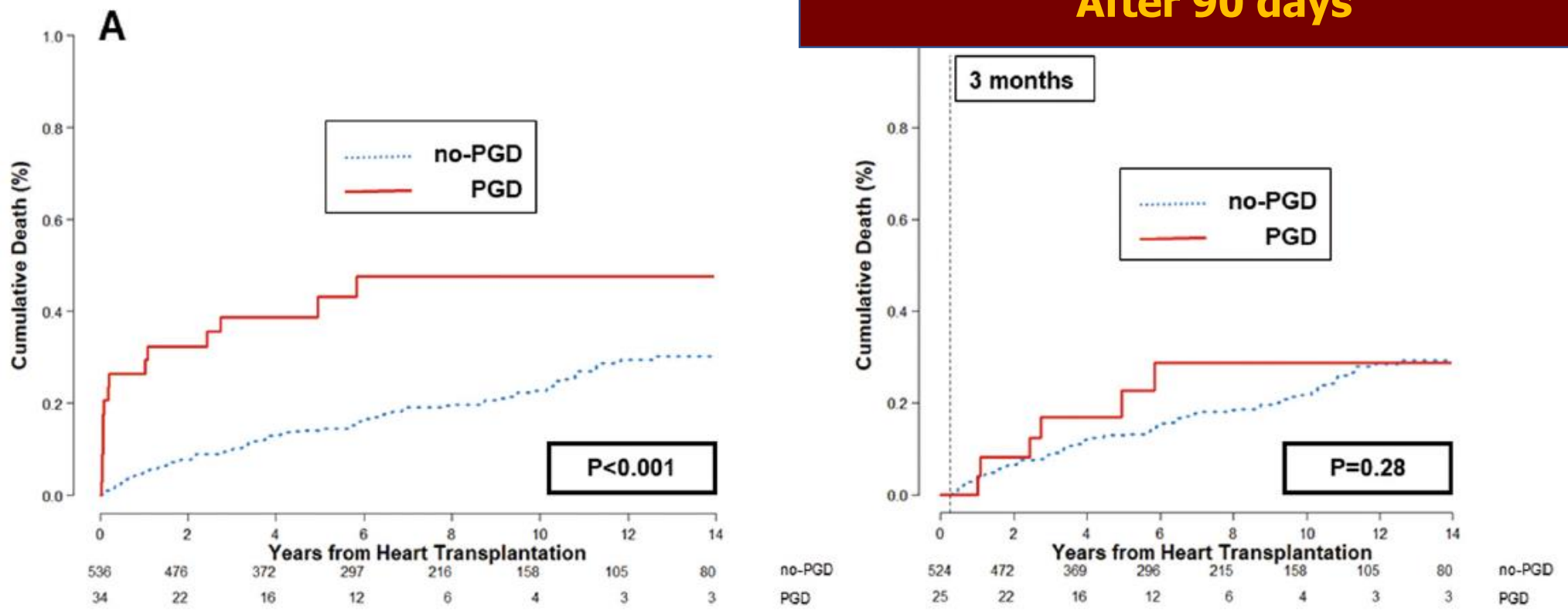


Figure 1. Overall mortality according to the development of (**A**) primary graft dysfunction (PGD) and (**B**) landmark analysis excluding in-hospital deaths occurring within 3 months after heart transplantation.

Rhee et al. *Circ J.* 2021

Summary

- Overall incidence of PGD after HT : about 20%

  Severe PGD: 5~10%

- **Higher 30-day mortality** in patients with **severe PGD**

- Definite pathophysiology, unknown,

  but, intracellular **Ca^{2+} overload** (d/t prolonged ischemia) may play important role

- Risk factor assessments are focused on Recipient & Surgical factor in previous studies

  Knowledge gap in Donor-specific risk factors

- **Long-term survival** is not affected by PGD for **survivors** in early postoperative period

Thank you for attention

Pathophysiology of PGD

- Hypothermic ischemia
- Hypothermic arrest of metabolism → 12-fold decrease in metabolic rate in hypothermic state (0-4℃)
- Pathologic LV hypertrophy → uniform & global cooling is impossible → susceptible to ischemic injury

- Prolonged cold storage → cellular swelling & lactic acidosis
- → intracellular H+ → Na+ → Ca2+

Pathophysiology of PGD

- Brainstem death
- Surge in the adrenergic response → Systemic & Pulmonary HTN → afterload ↑ & myocardial ischemia
- Loss of spinal cord sympathetic activity
- → Unopposed vasodilation
- → Reactive intense release of myocardial noradrenaline
- → Myocardial O2 demand & Impaired myocardial oxygenation