

Influence of right ventricular function on the development of primary graft dysfunction after lung transplantation



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KEYWORDS:

primary graft
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BACKGROUND: Primary graft dysfunction (PGD) remains a significant cause of lung transplant postoperative morbidity and mortality. The underlying mechanisms of PGD development are not completely understood. This study analyzed the effect of right ventricular function (RVF) on PGD development.

METHODS: A retrospective analysis of a prospectively assessed cohort was performed at a single institution between July 2010 and June 2013. The primary outcome was development of PGD grade 3 (PGD3). Conventional echocardiographic parameters and speckle-tracking echocardiography, performed during the pre-transplant evaluation phase up to 1 year before surgery, were used to assess preoperative RVF.

RESULTS: Included were 120 lung transplant recipients (LTr). Systolic pulmonary arterial pressure (48 ± 20 vs 41 ± 18 mm Hg; $p = 0.048$) and ischemia time (349 ± 73 vs 306 ± 92 minutes; $p < 0.01$) were higher in LTr who developed PGD3. Patients who developed PGD3 had better RVF estimated by basal free wall longitudinal strain (BLS; $-24\% \pm 9\%$ vs $-20\% \pm 6\%$; $p = 0.039$) but had a longer intensive care unit length of stay and mechanical ventilation and higher 6-month mortality. $BLS \geq -21.5\%$ was the cutoff that best identified patients developing PGD3 (area under the receiver operating characteristic curve, 0.70; 95% confidence interval, 0.54–0.85; $p = 0.020$). In the multivariate analysis, a $BLS \geq -21.5\%$ was an independent risk factor for PGD3 development (odds ratio, 4.56; 95% confidence interval, 1.20–17.38; $p = 0.026$), even after adjusting for potential confounding.

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CONCLUSIONS: A better RVF, as measured by BLS, is a risk factor for severe PGD. Careful preoperative RVF assessment using speckle-tracking echocardiography may identify LTrs with the highest risk of developing PGD.

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Despite significant progress in recent decades, the morbidity associated with lung transplant (LT) remains unacceptably high.^{1–3} Primary graft dysfunction (PGD) is a form of acute respiratory distress syndrome that occurs in the first 72 hours after allograft reperfusion in LT recipients (LTrs).⁴ It remains the most common early complication of LT and contributes significantly to patients' morbidity and mortality.^{1,2,5–7} PGD is the end result of a series of hits occurring from the time of brain death to the time of lung reperfusion. Ischemia-reperfusion injury has been identified as its main cause.⁸

Preoperative pulmonary hypertension (PH) is common among patients with respiratory diseases who are undergoing LT⁹ and is associated with worse outcomes.^{10,11} One possible explanation for this link is PGD.^{12,13} In fact, a recent meta-analysis has identified primary PH and mean pulmonary arterial pressure (mPAP) as significant risk factors for severe PGD development.⁷ Several studies have analyzed factors involved in the pathogenesis of PH and PGD in LTr, including a greater endothelial injury from hemodynamic forces, inherent abnormalities in coagulation or inflammation, platelet activation, and cell adhesion.^{14,15} But its underlying mechanism is not completely understood. It has also been hypothesized that an exacerbation of ischemic-reperfusion lung injury, due to the hemodynamic forces caused by a “well-trained” hyperdynamic right ventricle (RV) contracting against a reduced pulmonary vascular resistance of the implanted lungs, may also play a role in PGD development.^{8,16} To our knowledge, however, the role of RV in the development of PGD has not been clarified.

The assessment of RV function (RVF) has become increasingly important in the management of patients with PH.^{17,18} This may also be the case in LTrs. Quantification of RVF remains a challenge; because of its complex geometry, conventional 2-dimensional (2D) echocardiography does not provide a comprehensive evaluation.¹⁹ Speckle-tracking echocardiography is a relatively new, non-invasive method to estimate RVF by means of the analysis of wall deformation that has been widely applied to the left ventricle.^{20,21} More recently, it has been shown to highlight changes in RVF, particularly in PH.^{22,23} Furthermore, free wall 2D-strain quantifies the longitudinal RVF, which is one of the main mechanisms of blood ejection from the RV^{24,25} and makes it possible to differentiate active from passive motion regardless of the Doppler angle.^{25–27}

The main objective of this study was to analyze the possible role of RVF in severe PGD development. We hypothesized that pulmonary hyperflow generated by a “well-trained” RV, facing reduced pulmonary vascular

resistance after LT, may generate a higher degree of pulmonary edema and hence may be a risk factor for PGD development. To assess this possibility we evaluated RVF using conventional echocardiography techniques and speckle-tracking echocardiography.

Methods

The Vall d'Hebron University Hospital Clinical Research Ethics Committee approved this study (PR (AG) 144/2013). The need for informed consent was waived because of the non-interventional nature of the study.

Study design

A retrospective analysis of a prospectively assessed cohort was performed at a single institution (Vall d'Hebron University Hospital, Barcelona, Spain). All LTrs admitted between July 2010 and June 2013 were included. Healthy individuals matched by age and sex were used as controls.

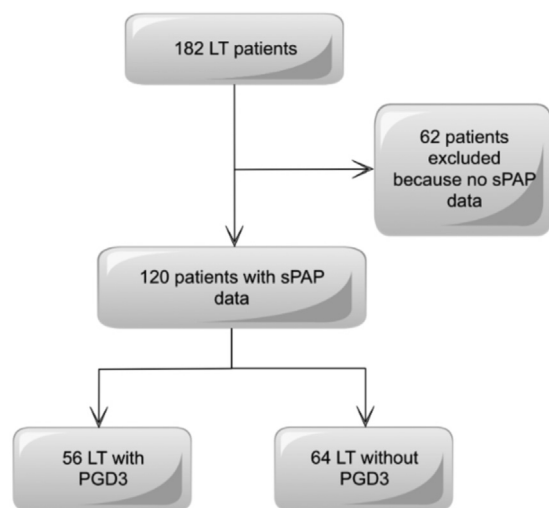
Study population

Considered for inclusion were 182 LTrs, of whom 62 were excluded for lack of systolic PAP (sPAP) data (Figure 1). In addition to echocardiographic or cardiac catheterization sPAP data, demographic data (sex, age, and lung pathology) were recorded. Also collected were data regarding intraoperative multiple transfusion, use of inhaled nitric oxide (iNO), cardiopulmonary bypass, and ischemic time.

Because current guidelines stress the lack of normative data regarding RV strain,¹⁹ 20 healthy volunteers recruited from the database of the Vall d'Hebron Hospital Echocardiography Department and matched for age and sex were included as a control group.

Definition of primary graft dysfunction

The primary outcome was PGD grade 3 (PGD3) recorded during the first 72 hours after surgery. In accordance with the report of the International Society for Heart and Lung Transplantation Working Group on Primary Lung Graft Dysfunction, PGD3 was defined as the presence of radiographic infiltrates consistent with pulmonary edema and a partial pressure of arterial oxygen (P_{aO_2})/fraction of inspired oxygen (F_{iO_2}) ratio of less than 200 mm Hg.⁴ PGD3 development was evaluated at 6, 24, 48, and 72 hours after the start of graft perfusion.⁴ The P_{aO_2}/F_{iO_2} ratio was carefully measured in mechanically ventilated patients. Patients who were not intubated at the time of the P_{aO_2}/F_{iO_2} measurement were graded as no PGD3.⁴ PGD3 development in the single-lung recipients was determined by a P_{aO_2}/F_{iO_2} ratio of less than 200 mm Hg and the presence of radiographic infiltrates in the implanted lung.⁴



LT: Lung Transplant, sPAP: Systolic Pulmonary Arterial Pressure, PGD3: Pulmonary Graft Dysfunction Grade 3.

Figure 1 Recruitment flowchart.

The researchers who graded PGD were blinded to the echocardiographic results and other clinical findings.

Definition of PH

In accordance with European and American Guidelines, sPAP was measured by right-sided heart cardiac catheterization (RHC) or alternatively by echocardiography.^{28,29} In both cases, sPAP was obtained at the time of LT evaluation. sPAP echocardiography measures were attempted in all patients based on the modified Bernoulli equation: $sPAP = 4v^2 + \text{right atrial pressure}$, where v is the peak velocity of the tricuspid regurgitation jet and the right atrial pressure was estimated by the collapsibility of the inferior vena cava on inspiration.¹⁹

Echocardiography

We collected data from echocardiograms performed by expert echocardiographers from the Cardiology Department during LT evaluation (acquired during the year before the LT). Routine digital gray scale 2D and tissue Doppler cine loops were obtained in accordance with current guidelines.³⁰ RVF was evaluated from apical 4-chamber images.¹⁹ After images were acquired, an expert echocardiographer performed the blinded off-line study.

Conventional echocardiographic assessment of the RV was performed using 3 different parameters. First, RV fractional area change was obtained by tracing the RV endocardium in systole and diastole and was calculated as follows: $\text{RV fractional area change} = \frac{[\text{RV end-diastolic area} - \text{RV end-systolic area}]}{\text{RV end-diastolic area}} \times 100\%$.

Second, the tricuspid annular plane systolic excursion was calculated as the total excursion of free wall tricuspid annulus from its highest position to the peak descent during ventricular systole by means of the M-mode.

Finally, the Doppler-derived tricuspid lateral annular systolic velocity was measured by the peak systolic velocity of the lateral corner of the tricuspid annulus.¹⁹

Speckle-tracking echocardiography of the RV free wall was performed using a routine gray-scale modified apical 4-chamber

view.¹⁹ The measurements were performed off-line with dedicated EchoPAC BT08 software (GE Vingmed Ultrasound). The RV free wall was divided into 3 standard segments (basal, middle, and apical) and time-strain curves were generated. We evaluated only the RV free wall because previous studies have demonstrated a good correlation between free wall RV 2D strain, RV ejection, and RV end-systolic volume measured using cardiac magnetic resonance imaging.^{19,22,25,26}

Longitudinal strain and strain rate data were collected. Longitudinal strain measures the percentage of myocardial deformation. As the RV contracts, the muscle shortens in the longitudinal and circumferential dimensions (negative strain). Strain rate measures the time course of deformation.

Outcome measures

The primary outcome was to study the relationship between PGD3 development and preoperative RVF. Secondary outcomes analyzed were other possible risk factors for PGD3 development, morbidity, and mortality, as well as the characterization of LTr RVF changes by conventional ultrasound methods and 2D strain.

Statistical analysis

The statistical analysis was performed with SPSS 18.0 software (IBM Corp, Armonk, NY). Baseline characteristics were expressed as mean \pm standard deviation for continuous variables and frequencies (percentage) for categorical variables. Comparisons between groups were made with the chi-square or Fisher's test for categorical variables and analysis of variance or Student's *t*-test for continuous variables. Differences in these variables were assessed according to PGD3 development. Comparisons were considered significant in the presence of a *p*-value of <0.05 .

Discrimination of significant variables was tested by calculating the area under the receiver operating characteristic curve. Multivariate logistic regression was used to identify the variables that were independently associated with PGD3 development. Variables with $p < 0.1$ in the univariate analysis were introduced into the multivariate model.

Finally, we assessed the effect of all potential confounding variables on the variables that were independently associated with the development of PGD3. Confounding was defined as a change in the odds ratio (OR) of 15% or greater on adjustment. To prevent model overfitting, we introduced all potential confounding variables one at a time.

Results

Included were 120 LTrs, of whom 46% developed PGD3 in the first 72 hours of the post-operative period (Figure 1). Table 1 reports the pre-operative, intraoperative, and post-operative characteristics and outcomes of the LTrs included in our study. Patients with PGD3 presented higher preoperative sPAP (48 ± 20 vs 41 ± 18 mm Hg; $p = 0.048$), a longer ischemic time (349 ± 73 vs 306 ± 92 minutes; $p = 0.005$), and a higher use of intraoperative iNO (63% vs 19%; $p < 0.001$). Patients who developed PGD3 in the early post-operative period had a longer intensive care unit (ICU) length of stay (40 ± 35 vs 25 ± 35 days; $p = 0.032$), length of mechanical ventilation (34 ± 35 vs 20 ± 34 days; $p = 0.037$), and also higher ICU (16% vs

3%; $p = 0.023$), 90-day (14% vs 3%; $p = 0.044$), and 6-month mortality (25% vs 8%; $p = 0.027$).

Compared with healthy volunteers, LTRs presented a worse RVF (Table 2). However, basal longitudinal strain (BLS) was higher (better RVF) in LTRs who developed PGD3 ($-24\% \pm 9\%$ vs $-20\% \pm 6\%$; $p = 0.039$; Table 3). BLS $\geq -21.5\%$ was the cutoff that best identified patients developing PGD3 (area under the receiver operating characteristic curve, 0.70; 95% confidence interval [CI], 0.54–0.85), with a sensitivity of 68%, specificity of 64%, positive predictive value of 62%, and negative predictive value of 70% ($p = 0.020$). However, the positive likelihood ratio was 2.45. This means that, for a pre-test PGD3 incidence of 46%, the incidence would be 31% if BLS were $< -21.5\%$ and might increase to 161% if BLS were $\geq -21.5\%$. Therefore, a BLS $\geq -21.5\%$ increases the probability of PGD3 by 30%.

All variables with $p < 0.1$ in the univariate analysis were included in a multivariate model to identify risk factors independently associated with PGD3 development. iNO was not included because in all probability it was used mainly to treat intraoperative hypoxemia secondary to the appearance of PGD and might therefore be considered as a consequence rather than a risk factor. A BLS $\geq -21.5\%$ was the only variable independently associated with PGD3 development

(odds ratio, 4.56; 95% CI, 1.20–17.38; $p = 0.026$; Table 4). Finally, to assess the effect of potential confounding, several models were also constructed including BLS (as the independent risk factor of PGD3) and other potential confounding variables (Table 5). No effect of confounding variables on BLS was observed, and the effect of BLS on PGD3 development was significant at all times.

Discussion

This study tries to evaluate the role of RVF in the pathogenesis of PGD, and 2 important results should be highlighted. First, PGD had an important effect on short-term and long-term morbidity and mortality. Second, we demonstrate that a better RVF, measured by BLS, is an independent risk factor for PGD3 development even after adjusting for potential confounding. This result provides new evidence to further our understanding of PGD pathophysiology.

The incidence of PGD3 varies between 12% and 32% depending on the time chosen for grading.^{1,2,7,13,31} A PGD3 incidence of 46% results from selecting the most severe grade recorded during the 72-hour period. However, 72-hour PGD3 incidence is approximately 17%. The point is that PGD remains a significant cause of post-transplantation

Table 1 Lung Transplant Recipient Characteristics Versus Primary Graft Dysfunction Grade 3

Characteristics ^a	No PGD3 (n = 64)	PGD3 (n = 56)	OR	95% CI	p-value
Pre-operative					
Age, years	55 \pm 11	51 \pm 11	0.97	0.94–1.00	0.065
Male gender	36 (56)	36 (64)	0.71	0.34–1.49	0.456
Body mass index, kg/m ²	26 \pm 8	27 \pm 5	0.27	–4.17 to 2.65	0.658
Etiology					0.697
Pulmonary fibrosis	18 (28)	10 (36)	1.420.58	0.66–3.07	
COPD	34 (53)	23 (41)	1.16	0.28–1.19	
Pulmonary hypertension	5 (8)	10 (9)	0.56	0.32–4.22	
Cystic fibrosis	3 (5)	2 (4)	1.76	0.50–6.39	
Others	4 (6)	6 (11)		0.28–10.90	
Systolic PAP, mm Hg	41 \pm 18	48 \pm 20	1.06	1.01–1.13	0.048
Intraoperative					
Procedure type					0.098
Single-lung transplant	33 (52)	20 (36)	0.52	0.25–1.09	
Bilateral-lung transplant	41 (48)	26 (64)	1.91	0.02–3.99	
CPB use	14 (22)	20 (30)	0.96	0.37–2.52	0.305
Inhaled nitric oxide use	12 (19)	35 (63)	7.22	3.15–16.54	<0.001
Multiple transfusions	19 (30)	17 (40)	1.54	0.72–3.31	0.333
Ischemic time, min	306 \pm 92	349 \pm 73	1.01	1.00–1.01	0.005
Post-operative					
Mortality					
ICU	2 (3)	9 (16)	5.95	1.23–28.77	0.023
28 days	1 (2)	5 (9)	6.18	0.67–54.56	0.096
90 days	2 (3)	8 (14)	5.17	1.05–25.45	0.044
6 months	4 (8)	12 (25)	4.08	1.22–13.70	0.027
ICU length of stay, days	25 \pm 35	40 \pm 35	1.01	1.00–1.02	0.032
MV length, days	20 \pm 34	34 \pm 35	1.01	1.00–1.02	0.037

CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; ICU, intensive care unit; MV, mechanical ventilation; OR, odds ratio; PAP, pulmonary arterial pressure; PGD3, primary graft dysfunction grade 3.

^aContinuous data are presented as mean \pm standard deviation and categoric data as number (%).

Table 2 Right Ventricular Function in Controls Versus Lung Transplant Recipients

Variables	Control group (n = 20) Mean ± SD	LTrs (n = 120) Mean ± SD	p-value
FAC, %	50 ± 9	38 ± 10	<0.001
TAPSE, mm	22 ± 3	20 ± 4	0.032
S', cm/sec	13.0 ± 1.1	12.0 ± 3.0	0.189
Longitudinal strain, %			
Free wall	-25 ± 5	-18 ± 6	<0.001
Basal	-31 ± 9	-22 ± 8	<0.001
Medium	-27 ± 6	-19 ± 6	<0.001
Apical	-18 ± 6	-13 ± 6	0.002
Strain rate, s ⁻¹			
Basal	2.53 ± 0.82	2.15 ± 0.94	0.120
Medium	1.66 ± 0.41	1.54 ± 0.72	0.497
Apical	1.22 ± 0.35	1.29 ± 0.52	0.590

FAC, fractional area change; LTr, lung transplant recipients; S', Doppler-derived tricuspid lateral annular systolic velocity; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

morbidity and mortality. Reported 30-day mortality rates of patients who develop PGD are nearly 8 times higher. PGD also leads to increased length of mechanical ventilation and ICU stay, increased peri-operative complications, and poor functional outcomes.^{1,7}

Despite the significant morbidity and mortality in patients who develop PGD, the associated risk factors remain controversial. A recent meta-analysis showed that female gender, pre-operative diagnosis of pulmonary fibrosis or primary PH, use of cardiopulmonary bypass, multiple transfusions, and mPAP were significantly and consistently associated with development of PGD.⁷ Our study observed no differences in gender, pre-operative diagnosis, use of CPB or multiple transfusions; however, we found that a longer ischemic time is related to the development of PGD3.^{8,13} Intraoperative use of iNO was more frequent in patients with PGD but should not be considered a risk factor for PGD but a consequence of the

appearance of intraoperative hypoxemia.^{7,8} However, we cannot rule out the possible role of iNO in decreasing RV afterload and enhancing RVF.

Primary PH is the most significant risk factor for PGD.^{11,14,32} As we pointed out above, the results of a recent meta-analysis showed strong associations between primary PH and mPAP with PGD.⁸ We also observed an association between sPAP and PGD3; however, the reason for this is not fully understood. Christie et al¹² showed that the diagnosis of primary PH was even more strongly associated with an increased risk of PGD after adjustment for recipient PAP. This suggests that factors other than the absolute value of PAP may be important in the pathogenesis of PGD. RV afterload is acutely reduced immediately after LT, leading to an increase in pulmonary blood flow and therefore a greater shear stress, which causes capillary leak and impairs graft function.^{8,14,15} Thus, PAP, or perhaps right cardiac output, during the initial 10 minutes after lung reperfusion is of prime importance, because a rapid perfusion after a period of ischemia may exacerbate the existing ischemia-reperfusion injury and increase pulmonary edema generation.^{32,33} That patients with pulmonary diseases and PH can also present a secondary RV dysfunction is also well known. This myocardial involvement may be variable, and some patients may present a hyperdynamic or compensatory response preceding the development of RV dysfunction.²³ Thus, a LTr with a normal or hyperdynamic RV will have a higher pulmonary blood flow after pulmonary implantation. For this reason, RVF can be also considered as a possible risk factor of PGD. We hypothesized that, regardless of PAP, patients with better RVF may present a greater pulmonary flow after LT and a higher risk of PGD as a consequence.

Quantification of RVF remains a challenge, however, because of its complex geometry.¹⁹ Conventional 2D echocardiography does not allow a comprehensive evaluation because of the RV's complex crescent-shaped structure, wrapped around the left ventricle.³⁰ Speckle-tracking echocardiography has been recently introduced for the

Table 3 Right Ventricular Function in Lung Transplant Recipients Versus Primary Graft Dysfunction Grade 3

Variable	LTV	No PGD3 (n = 64) Mean ± SD	PGD3 (n = 56) Mean ± SD	OR	95% CI	p-value
FAC, %	35	37 ± 9	40 ± 11	1.03	0.97–1.09	0.353
TAPSE, mm	16	21 ± 4	20 ± 4	0.95	0.87–1.05	0.316
S', cm/sec	10	12.0 ± 3.0	12.0 ± 3.5	1.01	0.84–1.22	0.913
LS, %						
Free wall	-19	-18 ± 5	-19 ± 7	1.03	0.94–1.13	0.558
Basal	-18	-20 ± 6	-24 ± 9	1.09	1.00–1.19	0.039
Medium	-20	-19 ± 6	-19 ± 9	1.01	0.94–1.09	0.807
Apical	-19	-14 ± 6	-12 ± 8	0.96	0.89–1.05	0.368
Strain rate, s ⁻¹						
Basal	0.70	1.93 ± 1.00	2.34 ± 0.86	0.61	0.32–1.20	0.145
Medium	0.85	1.44 ± 0.51	1.63 ± 0.69	0.67	0.28–1.61	0.368
Apical	0.86	1.27 ± 0.10	1.30 ± 0.56	0.87	0.30–2.52	0.802

CI, confidence interval; FAC, fractional area change; LTV, low reference values; LS, longitudinal strain; OR, odds ratio; S', Doppler-derived tricuspid lateral annular systolic velocity; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

Table 4 Multivariate Analysis for Primary Graft Dysfunction Grade 3 Development

Variable	β	SE	OR	95% CI	<i>p</i> -value
Age, years	-0.003	0.028	0.10	0.94–1.95	0.906
Procedure type	-0.321	0.599	0.73	0.22–2.35	0.592
Ischemia time, min	0.005	0.005	1.01	0.10–1.02	0.310
Systolic PAP, mm Hg	0.010	0.014	1.01	0.98–1.04	0.508
BLS \geq -21.5, %	-1.517	0.683	4.56	1.20–17.38	0.026

β , regression coefficient; BLS, basal free wall longitudinal strain; PAP, pulmonary arterial pressure; SE, standard error.

evaluation of global and regional RVF. Speckle-tracking assesses myocardial deformation without being limited by the Doppler beam angle,²⁶ allows active motion to be differentiated from passive motion,²⁷ and is more effective for evaluating subtle changes than other conventional echocardiographic techniques. Further, speckle-tracking has a good intraobserver and interobserver agreement, with low bias.^{22,23}

In this regard, RV free wall longitudinal strain quantifies the longitudinal RV systolic function, which is one of the main mechanisms of blood ejection from RV²⁵ and correlates significantly with the RV ejection fraction measured using cardiac magnetic resonance.^{19,22,25} However, previous studies of patients with PH have demonstrated that RV pressure overload reduces global and regional RV strain and increases regional heterogeneity.^{17,25,26,34} Owing to the progressive nature of the disease, the apical segments are the most affected and are then compensated for by the middle and basal RV region, which becomes the main determinant of the RV cardiac output.³⁵ Therefore, in these patients, the basal level segment is an accurate and reproducible estimator of RVF.³⁶

In our study, comparing the RVF of the control group and LTrs we observed decreases in conventional echocardiography parameters (except Doppler-derived tricuspid lateral annular systolic velocity) and longitudinal strain but not in strain rate. It is important to consider that (with the exception of apical longitudinal strain) all echocardiography parameters are within normal range.¹⁹ However, analyzing the RVF of LTrs who developed PGD3, we observed that they have a higher BLS, meaning that LTrs with better RVF have a higher prevalence of PGD3. Furthermore, patients with a BLS \geq -21.5% have an increased risk of developing severe PGD. These results argue in favor of performing a speckle-tracking echocardiography study in the echocardiography evaluation of LTrs to identify patients with a higher risk of developing PGD3.

These findings are especially important for 2 reasons. First, they provide further evidence of the pathophysiology of PGD. Second, they might allow an assessment of the effectiveness of new potential treatment strategies, such as the progressive intraoperative reintroduction of pulmonary flow, in patients with a high risk of PGD development in whom these strategies could provide more benefits in reducing pulmonary edema.^{8,32,33}

This study has some limitations. First, donor characteristics were not available because of its retrospective nature, and the time between echocardiographic evaluation and LT

was variable. Moreover, even though more than 100 patients were included, the possibility of a β -type error cannot be entirely ruled out. Therefore, the results obtained need to be confirmed in a prospective study in which echocardiography is evaluated immediately before LT.

Second, the speckle-tracking technique involves manual tracing of the endocardial border, which requires special care and may be particularly difficult in the apical regions of the free wall.

Finally, not all sPAP data were recorded from RHC; some data were obtained by echocardiography. However, in the 32 patients who had RHC and echocardiography sPAP data, mean catheterization sPAP was 46 ± 25 mm Hg and the mean echocardiography sPAP was 50 ± 26 mm Hg ($p = 0.148$), with a correlation coefficient of 0.77 ($p < 0.01$). Therefore, the 2 methods produced broadly similar clinical results.

Nevertheless, despite these potential limitations, this study demonstrates the importance of RVF in the appearance of PGD. We believe that the results provide new evidence regarding the pathophysiology of PGD, which is the most common early complication of LT and contributes significantly to patient morbidity and mortality. Understanding the mechanisms that lead to PGD is vital for designing therapeutic strategies focused on PGD prevention that can improve outcomes in LTr patients.

In summary, the present study demonstrates that RVF, measured by BLS, is an independent risk factor for severe PGD development. Therefore, accurate preoperative RVF assessment by means of 2D-strain is essential to identify LTrs at a higher risk of PGD development who would benefit the most from an extremely careful peri-operative management strategy able to limit pulmonary overflow.

Table 5 Bivariate Analysis of Association of Basal Free Wall Longitudinal Strain \geq 21.5% With Primary Graft Dysfunction Grade 3

Variable	OR	95% CI	<i>p</i> -value
Unadjusted base model	3.72	1.11–12.45	0.033
Base model adjusted for			
Age, years	3.71	1.09–12.55	0.035
Procedure type	3.73	1.11–12.54	0.034
Ischemia time, min	4.14	1.18–14.48	0.026
Systolic PAP, mm Hg	4.14	1.17–14.65	0.027

CI, confidence interval; OR, odds ratio; PAP, pulmonary artery pressure.

Disclosure statement

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