ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

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

Purificación Pérez-Terán, MD,[a,b] Oriol Roca, MD, PhD,[a,c] José Rodríguez-Palomares, MD, PhD,[d] Judit Sacanell, MD,[a] Sandra Leal, MD,[a] Joan Solé, MD, PhD,[e] María I. Rochera, MD,[f] Antonio Román, MD, PhD,[g] Juan C. Ruiz-Rodríguez, MD,[a] Joaquim Gea, MD, PhD,[c,h,i] Arturo Evangelista, MD, PhD,[d] and Joan R. Masclans, MD, PhD[c,i,j]

From the [a]Critical Care Department, Vall d'Hebron University Hospital, Institut de Recerca Vall d'Hebron (VHIR), Barcelona, Spain; [b]Departament de Medicina, Universitat Autònoma de Barcelona, Barcelona, Spain; [c]CibeRes (Ciber de Enfermedades Respiratorias), Instituto de Salud Carlos III, Madrid, Spain; [d]Cardiology; [e]Thoracic Surgery; [f]Anesthesiology and [g]Respiratory Departments, Vall d'Hebron University Hospital; [h]Universitat Pompeu Fabra, Barcelona, Spain; [i]Respiratory; and the [j]Critical Care Departments, Hospital del Mar - Parc de Salut Mar de Barcelona, Institut Hospital del Mar d'Investigacions Mèdiques (IMIM).

KEYWORDS:
primary graft dysfunction;
lung transplant;
right ventricle,
speckle-tracking echocardiography

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% ± 9% vs –20% ± 6%; $p = 0.039$) but had a longer intensive care unit length of stay and mechanical ventilation and higher 6-month mortality. BLS ≥ –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 ≥ –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.

Reprint requests: Purificación Pérez-Terán, MD, Critical Care Department, Vall d'Hebron University Hospital, Pg. Vall d'Hebron 119-129, 08035, Barcelona, Spain. Telephone: +34-932-74-62-09. Fax: +34-932-74-60-62.
E-mail address: puperez@vhebron.net

1053-2498/$ - see front matter
http://dx.doi.org/10.1016/j.healun.2015.05.026

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.
J Heart Lung Transplant 2015;34:1423–1429

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 LT[9] 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 (Pao_2)/fraction of inspired oxygen (Fio_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 Pao_2/Fio_2 ratio was carefully measured in mechanically ventilated patients. Patients who were not intubated at the time of the Pao_2/Fio_2 measurement were graded as no PGD3.[4] PGD3 development in the single-lung recipients was determined by a Pao_2/Fio_2 ratio of less than 200 mm Hg and the presence of radiographic infiltrates in the implanted lung.[4]