# Left Ventricular Dysfunction After Lung Transplantation for Pulmonary Arterial Hypertension

S. Gupta*, F. Torres, S. Bollineni, M. Mohanka, and V. Kaza

Division of Pulmonary and Critical Care Medicine, University of Texas–Southwestern, Dallas, Texas

ABSTRACT

Background. Lung transplantation (LT) is the final treatment option for patients with pulmonary arterial hypertension (PAH). Perioperative challenges after LT are unique and commonly include excessive bleeding, arrhythmias, and primary graft dysfunction. Transient left ventricular dysfunction (LVD) is a known postoperative complication, but not fully explored. We describe our experiences at a single institution.

Methods. We reviewed our database for patients with PAH who underwent LT from July 2008 to July 2012. The data were analyzed for preoperative inotrope use, intravenous prostacyclin, cardiac catheterization, and imaging. Also measured were perioperative ischemic time, bypass time, primary graft dysfunction, ventilator days, length of stay, and mortality. LVD is defined as acute cardiopulmonary compromise (acute worsening of hypoxia with new bilateral infiltrates on imaging) with a drop in LV systolic function of 15% from baseline. We compared data between patients with LVD and without LVD.

Results. Sixteen patients met the criteria, the majority of patients (10) with World Health Organization (WHO) group 1 PAH. Thirteen received intravenous prostacyclin therapy, and 6 required inotropes before surgery. Five patients (31%) developed LVD after transplantation. Average time to onset of LVD was 4.2 days. Preoperative vasopressors were required in 60% of those developing LVD. Patients with LVD had lower right and left ventricular ejection fraction with higher left ventricular end diastolic volume before surgery. All patients recovered from LVD within 4 months after LT.

Conclusions. LVD is a phenomenon observed mostly in patients with WHO group 1 PAH receiving LT. Prompt recognition and treatment of this condition reduced morbidity.

LUNG TRANSPLANTATION (LT) is recognized as the final line of management in patients with severe pulmonary arterial hypertension (PAH). Over time, changes in management of PAH have led to improved long-term survival and prolonged time to death or transplantation. Additionally, the Lung Allocation Scoring System implemented in 2005 plays a role in how patients are listed based on severity of disease. This resulted in an upsurge in the number of transplantations being performed for idiopathic pulmonary fibrosis compared with PAH [1]. Together, these changes have culminated in patients living longer than ever before with PAH and associated right ventricular (RV) dysfunction. Patients with PAH who receive lung transplants have the worst 3-month mortality compared with other transplants per diagnosis [2]. Once beyond this critical time, their survival rates are 2nd only to those with cystic fibrosis. The available data for early mortality center on graft failure, bleeding, infection, and left ventricular dysfunction (LVD) as the major causes of morbidity and mortality [3–8]. Furthermore, few reports present anecdotal evidence as to management.

It is clear that RV function improves after lung transplantation, but there is little evidence as to the changes to the left ventricle after transplantation [9]. This is relevant because of the changes in ventricular interaction related to both mechanical forces and electrical synchrony. A retrospective analysis of transthoracic echocardiography (TTE) performed perioperatively in single lung transplant for PAH patients found early persistent LV diastolic dysfunction, despite the

*Address correspondence to Sachin Gupta, MD, Kaiser Permanente 2500 Merced Street, San Leandro, CA 94577. E-mail: sachin.gupta@kp.org

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anatomic return of normal LV geometry [10]. Although acute LVD has been described, the clinical characteristics of these effected patients have not been evaluated [3–8,11–14]. Our aim was to describe the experiences at a single center with PAH patients undergoing bilateral lung transplantation: defining the variables affecting LV function in PAH patients, evaluating clinical associations, and suggesting a management algorithm.

## METHODS

Chart review was performed through an electronic medical record (EMR) system and transplant data collected was from July 2008 to July 2012. Institutional Review Board (IRB) approval at the University of Texas–Southwestern was obtained in October 2012. The requirement of informed consent was waived by the IRB. Patients with World Health Organization (WHO) group 2 PAH as well as congenital heart disease–associated PAH were excluded. Patients with WHO group 2 PAH have left-sided systolic or diastolic disease or have valvular disease that would have confounded results because our aim was to identify patients with PAH who developed acute new-onset LVD in the perioperative period and to describe risk factors and management. Similarly, patients with congenital heart disease have complex patterns of septal defects, right or left ventricular dysfunction, and/or hypertrophied chambers or shunts which would similarly have confounded the results of this study. Additional exclusion criteria included patients who were <18 years or >75 years of age and patients lost to follow-up. The date of last chart follow-up was in April 2012.

### Perioperative Management

A standard protocol of perioperative testing was performed as described elsewhere [15]. Hemodynamic evaluation via right heart catheterization was performed yearly on all patients as part of their management of PAH. Coronary angiography also was performed during the evaluation process if the patient was ≥45 years old or considered to be at high risk for coronary lesions. High coronary risk factors were considered to be hypertension, diabetes, hypercholesterolemia, smoking, and a personal or family history of coronary artery disease (CAD). Patients with significant CAD, defined as single or multiple coronaries with >50% stenosis, generally were precluded from receiving LT. TTE and cardiac magnetic resonance imaging (cMRI) were also a part of the evaluation.

The surgical approach to lung transplantation followed by our institution has been described previously [3,16]. Cardiopulmonary bypass (CPB) was used as indicated in the cases that were performed. Postoperative care was assumed in a multidisciplinary team approach by the cardiothoracic and pulmonary transplant teams. Perioperative care was provided per established guidelines [15]. Patients needing CPB received interleukin-2 receptor antagonist, basiliximab, per protocol on days 0 and 4. Standard immunosuppressive regimen included azathioprine, tacrolimus, and prednisone.

Primary graft dysfunction (PGD) was identified and defined according to standard criteria [17,18]. This included exclusion of infectious etiologies with the use of serial bronchoscopy and cultures, and possible acute decompensated heart failure was evaluated with the use of TTE or transesophageal echocardiography (TEE).

Hemodynamic instability also led to an extended work-up, including evaluation for sepsis and cardiogenic etiologies. Extubation after surgery was performed as the cardiopulmonary status allowed, with the target being 24–48 hours. Routine post-transplantation follow-up was performed per protocol at months 1, 3, 6, and 12 and then yearly. None of the patients were lost to follow-up.

**Table 1. Demographics ($n$ = 16)**

| Characteristic | $n$ | Mean | SD |
|---|---|---|---|
| Age (y) | | 46.2 | |
| Sex (female:male) | 10:6 | | |
| Race (African American:Hispanic:white) | 1:9:6 | | |
| PAH WHO subtype | | | |
| 1 | 11 | | |
| 3 | 3 | | |
| 4 | 1 | | |
| 5 | 1 | | |
| LHC: coronary disease* | 12 | | |
| RHC | | | |
| Mean PAP (mm Hg) | | 50.1 | |
| PAOP | | 9.6 | |
| CO/CI (mm Hg) | | 5.8/3.3 | 2.2/0.9 |
| cMRI ($n$ = 13) | | | |
| RVEF | | 39.1% | 10.3 |
| LVEF | | 63.2% | 18.7 |
| LVEDV (mL) | | 111.8 | 34.1 |
| RVEDV (mL) | | 252.4 | 126.6 |
| TTE: LVEF before transplantation | | 69.8% | 12.9 |
| ICU LOS (d) | | 16.1 | 9.5 |
| Hospital LOS (d) | | 30.6 | 18.6 |
| Mortality <30 d | 1 | | |
| Mortality <1 y | 3 | | |
| Mortality during study period† | 5 | | |

Abbreviations: PAH, pulmonary arterial hypertension; WHO, World Health Organization; LHC, left heart catheterization; RHC, right heart catheterization; PAP, pulmonary arterial pressure; PAOP, pulmonary arterial occlusion pressure; CO, cardiac output; CI, cardiac index; cMRI, cardiac magnetic resonance imaging; RVEF, right ventricular ejection fraction; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; RVEDV, right ventricular end-diastolic volume; TTE, transthoracic echocardiography; ICU, intensive care unit; LOS, length of stay.

*Coronary disease described as clinical significant.

†Study period: July 2008–April 2012.

TTE was evaluated by cardiology staff for several key measures, including LV ejection fraction (LVEF), gross LV and RV function, RV systolic pressure, valvular function and flows, and diastolic function.

Previous studies observed LVD in the setting of acute clinical compromise (worsening hypoxia, bilateral infiltrates on imaging, peripheral edema) and either an undefined increase in pulmonary arterial occlusion pressure or a drop in LVEF on imaging. We used similar criteria to define LVD, including acute cardiopulmonary compromise (acute worsening of hypoxia with new bilateral infiltrates on imaging) with a drop in LV systolic function of 15% from baseline [6,11,12].

### Statistical Methods

Descriptive statistics were used to evaluate demographic data. Fisher exact tests were used to compare categoric variables between LVD and non-LVD groups, and Wilcoxon rank sum tests were used to compare continuous variables between LVD and non-LVD groups.

## RESULTS

From July 2008 to July 2012, 133 lung transplantations were performed at our institution, with 16 patients receiving bilateral lung transplantation for PAH. Demographics of the group are described in Table 1, including age, sex,