

# Lung transplantation and concomitant cardiac surgery: Is it justified?

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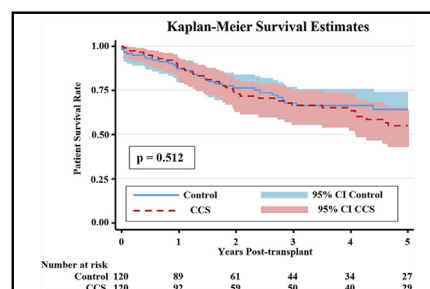
## ABSTRACT

**Objective:** Increasing numbers of lung transplant candidates have cardiac conditions that affect their survival after transplantation. Our objective was to determine if patients who undergo concomitant cardiac surgery (CCS) during the lung transplant procedure have similar outcomes, as a cohort of isolated lung transplant recipients.

**Methods:** This was a retrospective, observational, matched-cohort analysis. The records of lung transplant recipients who underwent CCS from August 2000 to August 2013 were reviewed. A cohort of isolated lung transplant recipients, matched on the basis of age, lung allocation score, diagnosis, type of procedure, and era, was identified. The primary endpoint of this trial was 5-year survival. The secondary endpoints were primary graft dysfunction, grade III, at 72 hours, intensive care unit and hospital length of stay, and 5-year major adverse cardiac event rates.

**Results:** A total of 120 patients underwent lung transplantation and CCS. Compared with the isolated lung transplant group, the donor, recipient, and operation characteristics were similar. No difference was found in the survival of the 2 groups for up to 5 years, or in the incidence of primary graft dysfunction Grade III at 72 hours, intensive care unit length of stay, invasive ventilation, hospital length of stay, or incidence of 5-year major adverse cardiac events.

**Conclusions:** Lung transplant recipients undergoing CCS have early and midterm clinical outcomes similar to those of isolated lung transplant recipients. Given that this report is the largest published experience, offering cardiac surgery at the time of lung transplantation, to selected patients, remains justified. (*J Thorac Cardiovasc Surg* 2016;151:560-7)



Survival of lung transplant recipients who had, versus did not have, concomitant cardiac surgery.

## Central Message

Lung transplantation and concomitant cardiac surgery can be performed with clinical outcomes similar to those for isolated lung transplantation.

## Perspective

Increasingly, lung transplant candidates have concomitant cardiac conditions that require cardiac surgical repair. Our study suggests that lung transplant recipients who require CCS have early and midterm outcomes similar to those of isolated lung transplant recipients. The implications of this study need to be weighed against the scarcity of donor organs.

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Lung transplantation is now an accepted form of therapy in many patients who have end-stage lung diseases. With improved peritransplant care and posttransplant outcomes, many patients previously deemed ineligible are now considered for lung transplantation. Many of these recipients have

comorbidities that may affect their posttransplant outcomes.<sup>1</sup> Given the limited number of donors, acceptance of potential recipients with comorbidities (with unknown or possibly inferior clinical outcomes) becomes an ethical dilemma.

An increasing number of patients being considered for lung transplantation have cardiac conditions that require repair prior to, or concomitant with, lung transplantation.<sup>1,2</sup> Most of these patients are not candidates for cardiac surgery prior to transplantation, owing to the severity of their lung disease. Concomitant cardiac surgery (CCS) and lung transplantation often necessitate cardiopulmonary bypass (in most cases), prolong operative time, and can affect short- and medium-term posttransplant outcomes.

Several reports have examined the clinical outcomes of lung transplantation and concomitant coronary revascularization procedures.<sup>3-5</sup> Information is limited on the clinical outcomes of lung transplantation in patients who need

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### Abbreviations and Acronyms

CABG = coronary artery bypass grafting  
CCS = concomitant cardiac surgery

CCS. A contemporary report with a large number of patients will broaden the knowledge base and rationalize the current policy of offering lung transplantation to patients who have concomitant cardiac diseases.

Our program has offered lung transplantation and CCS for >10 years. We hypothesized that in highly selected patients who need corrective cardiac procedures, simultaneous lung transplantation and CCS can be performed with clinical outcomes comparable to those for patients undergoing isolated lung transplantation. The purpose of this report is to compare 5-year survival; postoperative clinical outcomes; and 5-year major adverse cardiac events of patients who underwent lung transplantation and CCS (CCS group), compared with a matched group who underwent lung transplantation alone (control group).

## METHODS

Institutional review board approval was given for this study. The records of 620 patients were reviewed who had undergone lung transplantation in the period from August 2000 to August 2013. Of these, 120 had undergone CCS; this cohort was the subject of this report.

### Cardiac Evaluation in Lung Transplantation Candidates

All potential lung transplantation candidates were screened with a transthoracic echocardiogram. Male patients aged >40 years, female patients aged >45 years, and younger patients who had symptoms suggestive of coronary artery disease underwent coronary angiography to rule out coronary artery disease.

### Selection of Patients for Lung Transplantation and Concomitant Cardiac Surgery

Patients with patent foramen ovale or atrial septal defects;  $\geq$  moderate tricuspid regurgitation; tricuspid annulus  $>4$  cm or  $>2.1$  cm/m<sup>2</sup> (irrespective of pulmonary artery pressure);  $\geq$  moderate mitral regurgitation;  $\geq$  moderate aortic stenosis; and normal ejection fraction, all on transthoracic echocardiogram (valve area  $<1.5$  m<sup>2</sup>), were considered for lung transplantation and CCS. Patients with discrete coronary artery disease and preserved left ventricle ejection fraction were additionally considered for lung transplantation and concomitant coronary artery bypass grafting (CABG; part of this group's clinical outcome has been previously reported).<sup>3</sup> The presence of a cardiac condition necessitating concomitant repair was considered within the context of each patient's candidacy. Patients with several relative contraindications (ie, age >70 years) and in need of CCS were declined. Major CCS was defined as cardiac surgical procedures excluding isolated patent foramen ovale repair.

### Inclusion and Exclusion Criteria

All patients who underwent lung transplantation and CCS during the study period were included in the study. This group included redo lung transplantation recipients. Pediatric (age  $<18$  years), and multivisceral transplantation, patients were excluded.

### Control Group

Each lung transplant recipient who underwent CCS was matched to an isolated lung transplant recipient (1:1 ratio). Propensity-score matching was performed based on recipient age, era (within 1 year of the procedure), pulmonary diagnosis, lung allocation score, and the type of lung transplantation procedure.

### Peri- and Post-Operative Care

The timing of surgery for patients in need of lung transplantation and CCS was coordinated such that the cardiac procedure was usually done first (prior to arrival of the organ). Our strategy for coronary revascularization has been previously reported.<sup>3</sup> Patients who require tricuspid valve intervention underwent annuloplasty with either a pericardial strip or an Edwards MC3 tricuspid ring (Model 4900; Edwards Lifesciences, Irvine, Calif) annuloplasty. Patients with an annuloplasty ring were maintained on warfarin for 3 months.

The immunosuppressive regimen for all patients included induction therapy, with either: Thymoglobulin (Genzyme, Cambridge, Mass), for patients aged  $<60$  years in absence of infectious lung diseases; or basiliximab, for the remaining recipients. All lung transplant recipients received tacrolimus, mycophenolate mofetil, and steroids. All patients were treated with pravastatin, and aspirin (unless being treated with warfarin for the first 3 months) indefinitely.

### Data Endpoints

The following donor characteristics were collected: age, gender, body mass index, diabetes, cytomegalovirus status, smoking history, last ratio of arterial oxygen partial pressure to fractional inspired oxygen (prior to harvest), and cause of death. The collected recipient characteristics were as follows: age, gender, height, weight, body mass index, diabetes, systemic hypertension, cytomegalovirus status, 6-minute walk test, etiology of lung failure (obstructive, cystic fibrosis/bronchiectasis, pulmonary fibrosis, or pulmonary vascular disease), systolic, diastolic, and mean pulmonary artery pressures, right atrial pressure, pulmonary vascular resistance, cardiac output/index, lung allocation score, and days on the waitlist. In addition, the following data points were collected in reference to the transplantation procedure: type of procedure (single vs double lung transplant); donor/recipient gender mismatch; donor/recipient cytomegalovirus mismatch; allograft ischemia time; number performed on bypass; cardiopulmonary bypass time; and aortic crossclamp time.

The primary endpoint for this study was 5-year patient survival. Survival information was confirmed at the end of the study period. This study had 2 secondary endpoints: (1) postoperative clinical outcomes; and (2) 5-year major adverse cardiac events. The postoperative clinical outcomes that were collected and analyzed were as follows: duration of invasive mechanical ventilation, incidence of re-exploration for bleeding, incidence of operative wound revision, requirement for postoperative extracorporeal membrane oxygenation support, primary graft dysfunction grade III at 72 hours, intensive care unit length of stay, hospital length of stay, and 30-day or in-hospital mortality.<sup>6</sup>

In-hospital cardiac complications, including the incidence of atrial fibrillation (lasting for  $>30$  minutes and requiring treatment during the same hospital admission or within 30 days of surgery), myocardial infarction, and cerebrovascular accident were collected and analyzed. The category of 5-year major adverse cardiac events was defined as: episodes of atrial fibrillation (documented episode requiring treatment); episodes of acute coronary syndrome; redo revascularization or valvular procedure; episodes of congestive heart failure (requiring hospital admission); and cardiac-related deaths, including pulmonary embolism.

### Statistical Analysis

Our matching procedure was performed using propensity-score analysis. Variables selected for the matching procedure were chosen based

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