Atrial arrhythmias after lung transplantation: Incidence and risk factors in 652 lung transplant recipients

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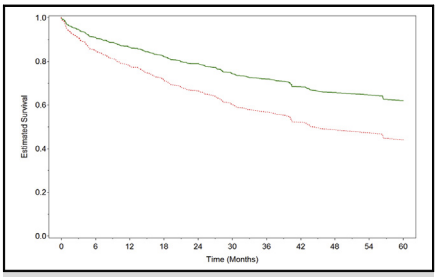
ABSTRACT

Objectives: Atrial arrhythmia (AA) after lung transplantation (LTx) is a potentially morbid event often associated with increased length of hospital stay. Predictors of postsurgical AA, however, are incompletely understood. We characterized the incidence and predisposing risk factors for AA in patients undergoing LTx.

Methods: A retrospective analysis of prospectively collected data was conducted to identify LTx recipients between January 2008 and October 2013. Patients were divided into 2 groups on the basis of postoperative AA development. Univariable and multivariable analyses were performed to define differences between groups and identify factors associated with AA. Survival differences were assessed by the use of competing risks methodology.

Results: A total of 198 of 652 (30.4%) patients developed AA at a median onset of 5 days after transplant. Increasing age (hazard ratio [HR] 1.03 per additional year, $P < .001$) and previous coronary artery bypass grafting (HR 2.77, $P = .002$) were found to be independent risk factors. Counterintuitively, patients with a medical history of AA before LTx had a lower incidence of postoperative AA. Preoperative beta-blocker usage was not a significant predictor of postoperative AA. Postoperative AA was a significant predictor of long-term mortality (HR 1.63, $P = .007$) when we adjusted for other risk factors.

Conclusions: AA is a common occurrence after LTx, occurring with greatest frequency in the first postoperative week, and results in a significant reduction in long-term survival. Increasing age and before coronary artery bypass grafting were identified as independent risk factors for AA development. Better understanding of these risk factors may improve identification of patients at heightened risk after transplantation. (J Thorac Cardiovasc Surg 2016;152:901-9)



Atrial arrhythmia after lung transplantation negatively impacts survival.

Central Message

Atrial arrhythmia after lung transplant is a common and morbid event that is associated with a significant negative impact on long-term survival.

Perspective

We found atrial arrhythmia after lung transplant to be a common event that is associated with significantly reduced long-term survival. We anticipate these findings will help guide physicians in identifying patients more susceptible to atrial arrhythmia after lung transplant, with the ultimate goal of implementing interventions that have a lasting therapeutic impact.

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Lung transplantation (LTx) is a potentially life-saving intervention for end-stage parenchymal lung and pulmonary vascular disease. Although there has been a reduction in the number of donor organs available, the annual procedure volume continues to increase.[1] The development of atrial arrhythmia (AA) after LTx has been demonstrated to increase perioperative morbidity.[2,3] The reported incidence of AA varies widely, ranging from 20% to 45%.[2,4] Furthermore, previous authors have demonstrated the development of AA may increase perioperative mortality.[4-6] A variety of mechanisms have been implicated in the postoperative development of AA, including inflammation, increased sympathetic tone, oxidative stress, structural predisposition, and operative technique (such as pulmonary venous line anastomosis).[7-11]

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Received for publication June 12, 2015; revisions received March 25, 2016; accepted for publication April 23, 2016; available ahead of print May 24, 2016.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2016.04.070

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Abbreviations and Acronyms

AA = atrial arrhythmia
BMI = body mass index
CABG = coronary artery bypass grafting
CAD = coronary artery disease
DC = direct current cardioversion
ICU = intensive care unit
LOS = length of stay
LTx = lung transplantation
PAP = pulmonary arterial pressure
POD = postoperative day
UPMC = University of Pittsburgh Medical Center

In the current study, we retrospectively reviewed our institutional experience with patients who developed AA after LTx. In this analysis of LTx recipients, we aimed to clarify the incidence, risk factors, and postoperative survival of LTx recipients who develop AA.

METHODS

Patients

The study population includes patients who underwent single or double LTx at the University of Pittsburgh Medical Center (UPMC) between January 2008 and October 2013. This was an institutional review board–approved study (PRO13040360). Patients undergoing combined heart–lung transplants during this time period were excluded; patients undergoing retransplant also were excluded. Data on all 652 patients were obtained from the prospectively collected Cardiothoracic Transplant Database at UPMC. Our standard surgical approach has been described previously.[12]

End Points

The primary end point of the study was the in-hospital development of AA. Given the fact that other similar studies to ours have not discriminated between the types of AA,[3,5] atrial fibrillation and atrial flutter were not distinguished in our study. Although this decision may be interpreted as a limitation, we chose this approach to be able to compare our study with those performed previously. AA was defined by the Society of Thoracic Surgeons Adult Cardiac Surgery Database definition as those that were clinically documented or treated. Transient AA noted only on telemetry was not captured in the database and thus is not included in our analysis. Patients who experienced their initial episode of AA subsequent to their postoperative discharge from the hospital were categorized as non-AA patients in the analysis, because the event did not occur as an in-hospital event. The first day of AA development was used to calculate time from transplantation to arrhythmia onset. Recipients were all treated according to an institutional lung transplant patient care pathway, which did not include the routine use of prophylactic beta blockade or alternative AA prophylaxis. Data were not available regarding the duration of AA before conversion or hemodynamic status during AA events.

Data Collection

This retrospective analysis included a review of data entered into the UPMC Cardiothoracic Transplant Database, with database information obtained directly from in-patient records. All patients were monitored with continuous telemetry throughout the stay in the intensive care unit (ICU) and surgical transplant unit. A 12-lead electrocardiogram was obtained to confirm the rhythm in cases of documented AA.

Statistical Analysis

Descriptive characteristics are presented as n (%) for categorical variables and median (interquartile range) for continuous variables. Univariable relationships between each of the baseline variables and development of postoperative AA were tested with either χ^2 tests (categorical variables) or *t* tests (continuous variables). Variables that were significantly associated with postoperative AA in univariable analyses were considered as potential predictors of postoperative AA in multivariable analysis: age at transplant, sex, body mass index (BMI), hypertension, hyperlipidemia, coronary artery disease (CAD), previous coronary artery bypass grafting (CABG), previous AA, and transplant indication.

Risk factors for postoperative AA were assessed with the Fine-Gray model for analysis of competing risks. We felt this was a more appropriate model than the standard Cox proportional hazards model for this particular question, and support for this model has been provided recently.[13] This model is appropriate for analysis of time-to-event data when the event of interest (in this case, AA within the hospitalization) can be impeded by a previous event of a different type; in this study, a patient's subsequent development of AA might be unobservable because the patient dies before development of AA is observed. Therefore, the patient is followed until the first of these 3 outcomes occurs: in-hospital development of AA, death in-hospital before diagnosis of AA, or discharge from hospital free of AA. The patient is censored from further analysis when the first of these occurs.

To evaluate the effects of postoperative AA on survival in the long term, we used a Cox proportional-hazards model with postoperative AA included as a time-varying covariate. This model was used to compute estimated survival curves for patients with AA versus patients without AA to visually display the independent effects of AA on long-term survival. To capture the vast majority of AA cases and the relationship to outcome, survival analysis was started at posttransplant day 25 (examining only patients who survived to this time point), which also approximates our median length of hospital stay at the time the study was designed. We chose this endpoint to be congruent with other similar studies[3] and enabled us to include more than 96% of AA cases that developed.

RESULTS

Patient Characteristics

A total of 652 patients underwent LTx during the study period. Median age at transplant was 61 years (interquartile range 50-67 years), and men represented 58% of the study population (379/652). Significant comorbid medical conditions in our population included hypertension (37.4%; 244/652), hyperlipidemia (30.7%; 200/652), diabetes (20.6%; 134/652), and CAD (24.6%; 161/652). Indications for LTx include fibrotic lung diseases (including scleroderma and idiopathic pulmonary fibrosis) (47.1%; 307/652), obstructive disease (including chronic obstructive pulmonary disease) (35.4%; 231/652), suppurative disease (12.3%; 80/652), pulmonary hypertension (1.5%; 10/652), and other (including retransplant from outside institutions) (3.7%; 24/652).

Incidence and Timing

AA developed in 198 of 652 patients (30.4%). The largest single-day incidence of AA occurred on postoperative day 3 with a total of 28 new cases (Figure 1). A total of 67.7% (134/198) of arrhythmias occurred within the first postoperative week, whereas 97.5% (193/198) of cases developed within the first 30 days (range postoperative day [POD] 0-POD104). Among all patients who developed