Cardiac Procedures in Lung Transplant Recipients Do Not Increase Mortality in Selected Patients

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Background. Associated comorbidities in potential lung transplant recipients may significantly impact operative morbidity and mortality. We undertook this review to specifically study whether patients who underwent associated cardiac procedures either before (as a prerequisite) or during their lung transplantation had different outcomes when compared with the overall cohort of lung transplant recipients.

Methods. A retrospective chart review was performed of all patients who underwent lung transplantation at the University of Texas Health Science Center at San Antonio from January 1994 to June 2004. The records of these patients were analyzed for patient-days on the ventilator, hospital length of stay, operative morbidity and mortality, and long-term survival. The patients were then divided into two groups and compared: patients who had a cardiac intervention either prerequisite to or concurrent with their transplant (group C, n = 13) and patients who did not (group NC [no cardiac intervention], n = 120).

Results. Although the median length of stay was longer in group C when compared with group NC, the number of patient-days on the ventilator and the operative morbidity and mortality were similar for both groups. Likewise, overall long-term survival was not significantly different (Kaplan-Meier method, p = 0.70).

Conclusions. Patients who are otherwise deemed to be good candidates for lung transplantation but are found to have an associated cardiac condition that could adversely affect their candidacy may still be considered for transplantation in selected cases if the cardiac abnormality can be addressed either before or during transplantation.

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The criteria used to select recipient patients for lung transplantation continues to evolve and be institutional dependent [1, 2]. Criteria guidelines based on degree of lung dysfunction, underlying pulmonary disease, and age have been well defined [3–5]. However, patients who are potential lung transplant recipients often have associated comorbidities such as cardiac disease, renal disease, or systemic illnesses that may be important to consider when evaluating a patient as a potential lung transplant recipient. These comorbidities may be directly related to the patient’s primary pulmonary illness, and may be just as important as the patient’s underlying diagnosis in determining the patient’s overall risk for postoperative mortality and morbidity, as well as overall long-term survival [6]. Given the relative scarcity of donor organs, especially for lungs, recipient selection criteria must be continuously reevaluated so that organ allocation remains appropriate [7]. There have been a limited number of studies published regarding associated comorbidities in lung transplant recipients, and as a result, little is known based on scientific study whether specific comorbidities should be regarded as either relative or absolute exclusion criteria when evaluating someone as a potential recipient [8–10].

We undertook this study to specifically look at our experience regarding whether patients who underwent lung transplantation who also had an associated cardiac condition that was treated either before (as a prerequisite for transplantation) or during their transplantation had different outcomes when compared with the overall cohort of lung transplant recipients.

Material and Methods

A retrospective chart review was performed of all patients who underwent lung transplantation at the University of Texas Health Science Center at San Antonio from January 1994 to June 2004. Permission was granted from both the University of Texas Health Science Center Institutional Review Board and the University Hospital Institutional Review Board to conduct the study, with initial approval granted June 2004. Individual patient consent was waived. The records of these patients were analyzed for the following: age at transplantation, sex, indication for transplant, type of transplant performed (single versus bilateral), days on the ventilator, hospital length of stay, operative morbidity (to include, but not be limited to, atrial fibrillation requiring treatment; pneumonia as evidenced by pulmonary infiltrates, leukocytosis or fever or both, and positive blood cultures or...
sputum samples; rejection as evidenced clinically or by biopsy or both; reperfusion injury defined clinically as pulmonary dysfunction and radiographic consolidation occurring within the first 24 hours after transplant; acute renal failure requiring dialysis; and need for reoperation for any reason, operative mortality, and long-term survival. The patients were then divided into two groups and compared: those who had a cardiac intervention either prerequisite to or concurrent with their transplant (group C), and those who did not (group NC [no cardiac intervention]).

Bivariate analyses were performed with t tests, non-parametric Wilcoxon rank-sum tests, χ² tests, and Fisher’s exact tests. Median survival times were calculated using the Kaplan-Meier method. Overall survival time (in years) was calculated using the difference between the date of transplantation and date of last follow-up or date of death, depending on the patient’s status. All statistical analyses were conducted using the SAS System for Windows, version 9.1.3 (SAS Institute, Cary, North Carolina).

Results

There were a total of 132 lung transplants performed in 130 patients during the period analyzed. Of these, 13 patients had associated cardiac procedures: 6 of these had prerequisite cardiac procedures performed in anticipation of their lung transplantation (3 angioplasties/stent placements, 2 coronary bypass surgeries, and 1 mitral valve replacement); and the remaining 7 had concomitant cardiac procedures performed at the time of their transplant (5 closures of patent foramen ovale, 1 single-vessel coronary bypass surgery, and 1 closure of a ventricular septal defect). Of those 6 patients who underwent a cardiac procedure as a prerequisite to their lung transplant, the mean length of time between cardiac procedure and transplant was 79 days, with a range of 21 to 120 days. The mean age of the patients at the time of transplantation, the reason for transplant, and the type of transplant performed for each group are given in Table 1. Median length of stay was longer in group C when compared with group NC (16 days [range, 11 to 21] versus 11 days [range, 8 to 18], respectively; p = 0.09). If the 1 patient requiring ventilator support longer than 100 days in group NC is excluded, the mean number of patient-days on the ventilator was similar for each group: 4.0 ± 0.6 patient-days for group NC versus 3.8 ± 1.1 patient-days for group C (p = 0.66). Of note, 56 patients (47%) in group NC and 6 patients (46%) in group C were intubated less than a day.

Operative mortality was 9 of 120 (7.6%) in group NC versus 1 of 13 (7.7%) in group C (p = 1.0). The causes of death in the 9 patients in group NC were a combination of graft failure and sepsis in 4 patients, primary graft failure in 2 patients, arrhythmia in 2 patients, and primary cardiac failure in 1 patient. The 1 patient who died in group C reached postoperative day 11 after a bilateral lung transplant with concomitant patent foramen ovale closure and died from a presumed combination of septic shock and reperfusion injury, although no autopsy was performed. This patient had also required reoperation in the early postoperative period for bleeding from his bronchial arteries.

Of patients who survived their operation, 51 of 111 (46%) in group NC had a total of 101 complications, including 24 patients who had pneumonias, 20 who had reperfusion injuries, 18 who required take-backs to the operating room (for any reason), 6 who had atrial fibrillation, 5 who had acute renal failure, 4 who required treatment for graft rejection, 4 who required reintubation, 4 who had pneumothorax requiring chest tube placement, 3 who had heparin-induced thrombocytopenia, and 2 who sustained postoperative cardiopulmonary arrest. Additional complications in this group included 1 patient each in whom developed a compartment syndrome, a gallstone cholecystitis, a non–q-wave myocardial infarction, a pulmonary embolus, a Clostridium difficile infection, a vocal cord paralysis, a tracheobronchitis, an upper extremity neuropaxxia, a syndrome of inappropriate antiidiurectric hormone secretion, a stroke, and a phrenic nerve injury. Similarly, 7 of the 12 patients (58%) surviving their operation in group C had a total of 12 complications, to include 4 patients who required take-backs to the operating room (for any reason), and 3 who had reperfusion injury. Additional complications in this group included 1 patient each in whom developed pneumonias, a strangulated inguinal hernia requiring colostomy, a pulmonary embolus, and an ischemic colitis; 1 patient required reintubation. Overall difference in morbidity between the survivors of both groups was not significant (p = 0.42). Likewise, long-term survival was similar in both groups (Fig 1).

Table 1. Univariate Analysis of Characteristics Between Groups

<table>
<thead>
<tr>
<th></th>
<th>Group NC (n = 120)</th>
<th>Group C (n = 13)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51.0 ± 11.7</td>
<td>51.2 ± 10.2</td>
<td>0.91</td>
</tr>
<tr>
<td>Sex (males)</td>
<td>68 (57%)</td>
<td>6 (38%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Diagnosis*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>61</td>
<td>4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>2</td>
<td>0.2568</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>48</td>
<td>7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>E</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bilateral transplants</td>
<td>23 (19%)</td>
<td>6 (46%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

* Group A includes obstructive lung disease, including chronic obstructive pulmonary disease, alpha-1 antitrypsin deficiency, lymphangioleiomyomatosis, and sarcoidosis with mean pulmonary artery pressure ≥ 30 mm Hg; group B includes patients with pulmonary vascular disease, including primary pulmonary hypertension and Eisenmenger’s syndrome; group C includes cystic fibrosis and immunodeficiency disorders; group D includes restrictive lung diseases, including idiopathic pulmonary fibrosis, pulmonary fibrosis (other causes), sarcoidosis with mean pulmonary artery pressure > 30 mm Hg, and obliterator bronchiolitis (nonretransplant); group E includes retransplantation due to graft failure/chronic rejection [18].

NC = no cardiac intervention.
The purpose of this study was to determine whether the addition of a cardiac surgical procedure either pretransplant or concomitant to transplant would increase the morbidity and mortality of what is already considered relatively high. This is only one of a few studies that have specifically addressed cardiac comorbidities and their influence on surgical morbidity and mortality, long-term survival, and whether their existence should preclude lung transplantation.

The purpose of this study was to determine whether the addition of a cardiac surgical procedure either pretransplant or concomitant to transplant would increase the morbidity and mortality of what is already considered to be a relatively complex procedure. This is only one of a few studies that have specifically addressed cardiac comorbidity as it relates to lung transplantation outcomes [9, 10]. In our study, patient-days on the ventilator and operative morbidity and mortality between group NC and group C were not significantly different, and although group C patients tended to have a longer length of hospital stay, this, too, was not significant. In addition, long-term survival was also not appreciably different between the two groups.

A factor that may have contributed to group C’s overall similar short-term and long-term outcomes may be that all of our lung transplant recipient candidates are required to undergo an extensive preoperative evaluation that includes performing a preoperative left and right heart catheterization and an echocardiogram, and that they are all individually discussed at a monthly multidisciplinary transplant conference attended by pulmonologists, transplant coordinators, and thoracic surgeons to determine their candidacy. During this conference, each patient who is being considered for transplantation is discussed. Patients with concomitant cardiac abnormalities are given careful consideration, and the need to address the abnormality either pretransplant or concurrent to transplant is carefully weighed and discussed with respect to the type of transplant planned. In general, patients who are amenable to coronary stenting but are otherwise good candidates for transplantation who were stented pretransplant. If the patient is not a good stent candidate but bypass grafting can be performed at the time of transplant, then this is generally the preferred approach. Likewise, if the cardiac abnormality can be approached relatively easily at the time of transplant (e.g., closure of patent foramen ovale), then this is the preferred approach. If the cardiac abnormality cannot be adequately addressed or easily approached at the time of transplant owing to the incision or type of transplant planned, then careful consideration is given to correct the cardiac abnormality at a separate surgery pretransplant.

It must be stressed that the patient population presented in this study represents a highly select group of patients. Therefore, although this study would suggest that patients requiring cardiac intervention either before or during lung transplantation as a condition of their candidacy does not greatly influence either their short- or long-term outcome, it must be emphasized that each patient was carefully selected. Furthermore, it is not known exactly how many patients with associated cardiac conditions during this same period were actually declined transplantation based on other factors, or how many patients underwent unsuccessful cardiac intervention preoperatively (i.e., never made it to transplantation).

Despite the small sample size, this study suggests that patients who are otherwise deemed to be good candidates for lung transplantation but are found to have an associated cardiac abnormality that could adversely affect their candidacy may still be considered for transplantation if the cardiac condition can be addressed either before or during transplantation. Repair of cardiac defects (e.g., ventricular septal defects, patent foramen ovale), and performance of coronary bypass concomitant to transplantation does not necessarily increase operative morbidity or mortality in selected patients [10]. Further study is needed to determine whether (and to what degree) other comorbidities such as diabetes mellitus, osteoporosis, renal insufficiency, and obesity should be considered relative versus absolute contraindications to lung transplantation.

Comment

The first successful lung transplant was performed by James D. Hardy and his associates at the University of Mississippi Medical Center on June 11, 1963 [11]. Since that time, lung transplantation as well as other forms of transplantation have become viable options for end-organ failure, and numerous societies and forums have been specifically created to study and report experiences regarding transplantation worldwide [12]. Lung transplantation in particular has been shown not only to improve quality of life, but also to improve long-term survival when performed for certain end-stage diseases [13–17]. Although guidelines have been well established regarding primary pulmonary disease processes and severity with respect to timing for referral for transplantation, relatively little has been written regarding concomitant comorbidities and their influence on surgical morbidity and mortality, long-term survival, and whether their existence should preclude lung transplantation.

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References

DISCUSSION

DR THOMAS M. EGAN (Chapel Hill, NC): I just wanted to congratulate you on nice results with challenging patients. How do you deal with the patient who has a coronary stent and the cardiologists who want to give them Plavix forever and you who want to operate on them and don’t want them to bleed to death?

DR JOHNSON: That is a very good question. It is often a tug of war. As you know, many cardiologists like to keep their patients on Plavix for a minimum of 6 months after a coronary stent. We have talked them into allowing us to stop the Plavix after 4 to 6 weeks and then convert them over to Coumadin, which is still a reasonable anticoagulant. We, again, individually approach each patient, and there are some patients who have had PFOs that we did not close them. If we can find good reason to avoid doing it, we probably would leave it alone, but again, I think we would tend to be more aggressive in those patients and close them if they are present.

DR SUDISH MURTHY (Cleveland, OH): I congratulate you on the study. Just a question about PFOs. These are some patients, which I suspect are symptomatic from a PFO because of pulmonary hypertension. When you unload the pulmonary vascular bed with the transplant, often the PFO becomes insignificant. Do you do intraoperative assessment on these patients (eg, TEE), and what is your criteria for repairing a PFO? This becomes important because the PFO repair mandates cardiopulmonary bypass in some patients who may otherwise be transplanted off pump.

DR JOHNSON: We, again, individually approach each patient, and there are some patients who have had PFOs that we did not close. Obviously, in every program there are anecdotal experiences, and one that we had was not closing a PFO in a patient who went on to die, partly from complications related to leaving the PFO alone. So in general, if they are found preoperatively, we tend to close them. If we can find good reason to avoid doing it, we probably would leave it alone, but again, I think we would tend to be more aggressive in those patients and close them if they are present.

DR DANIEL L. MILLER (Atlanta, GA): Can I just ask a question for the audience? Is there a difference in the restenosis rate between a drug-eluting stent and a nondrug-eluting stent, because I know at our institution, when our patients have been found to have a positive DSC and they are going to have to have...
a stent before lung cancer operation that they are going to a nondrug-eluting stent on those patients because we are going to take them off of Plavix because they saw a high incidence of restenosis when we take them off short term on the drug eluting, and we got into more trouble with myocardial problems? Are there any data out there on that short term? Do our cardiac colleagues know that?

DR ROBERT S. POSTON (Baltimore, MD): I don’t think there is a difference in restenosis but acute thrombosis is higher. I think that is probably why they would go with a noncoated stent, and the reason why is that endothelialization occurs better over a noncoated stent; the rapamycin or whatever coating inhibits their reendothelialization.

DR MILLER: Because we have always seen patients who have positive DSC before lung cancer, and we have gotten burned a couple of times when we did the intervention, but when we took them off Plavix, they developed thrombosis or stent occlusion.

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**Notice From the American Board of Thoracic Surgery**

The 2006 Part I (written) examination will be held on Monday, December 4, 2006. It is planned that the examination will be given at multiple sites throughout the United States using an electronic format. The closing date for registration is August 1, 2006. Those wishing to be considered for examination must apply online at www.abts.org.

To be admissible to the Part II (oral) examination, a candidate must have successfully completed the Part I (written) examination.

A candidate applying for admission to the certifying examination must fulfill all the requirements of the Board in force at the time the application is received.

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