Lobar Lung Transplantation From Deceased Donors: A Valid Option for Small-Sized Patients With Cystic Fibrosis

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ABSTRACT

Background. Small-sized patients with cystic fibrosis usually face long waiting times for a suitable lung donor. Reduced-size lung transplantation (LTx) was promoted to shorten waiting times. We compared donor and recipient characteristics and outcome in lobar ([L]) versus full-size ([FS]) lung recipients.

Methods. Between July 1, 1991, and February 28, 2011, 535 isolated LTx were performed, including 74 in cystic fibrosis patients (8 L, 66 FS). Patients were followed up until September 2012.

Results. [L] recipients were younger, smaller, and lighter. Sex, waiting times, and donor data (age, sex, height, weight, PaO_2/FiO_2, and ventilation time) were comparable. Cardiopulmonary bypass was used more often in [L]; cold ischemia was comparable for first lung but longer in [L] for second lung; implantation times were comparable. In-hospital mortality rate was 0% in [L] versus 3% in [FS]. Both intensive care unit and hospital stay were longer in [L]. Grade 3 primary graft dysfunction was more pronounced in [L] at T0 and at T48. FEV_1 increased significantly in both groups from preoperative value. Bronchiolitis obliterans syndrome was absent in [L] and diagnosed in 18 patients in [FS], accounting for 6 of 15 late deaths. All [L] are still alive. No differences in survival were found between the groups.

Conclusions. Although hindered by a higher incidence of primary graft dysfunction, L-LTx is a viable option with excellent survival and pulmonary function comparable to FS-LTx.

SHORTENING time on the waiting list is a key point in lung transplantation (LTx) for patients at risk of premature death. Despite the efforts made in this direction, including a wider acceptance of marginal donors and donors after circulatory death, median waiting time on list is longer now than 10 years ago. The increasing number of patients listed for lung transplantation as the result of an improved confidence in this technique also contributes to this phenomenon.

Broadening the standard criteria leads to acceptance of organs from older donors, which reflects in an increase in mean donor age [1]. It is thus not surprising that small-sized patients, most of which in the Belgian population belong to the pediatric age, face longer waiting times compared with their taller counterparts.

As a matter of fact, few years ago, when looking back at the results of the transplant activity (from the beginning to transplant No. 500) at University Hospitals in Leuven, the mean waiting time for patients smaller than 166 cm turned out to be 257 days versus 189 days in other recipients [2].

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Reduced-size lung transplantation has been proposed to overcome the lack of short donors, allowing the use of larger lungs for a smaller recipient. Besides the original technique of pulmonary bipartitioning proposed by Couetil et al [3] in 1994, several other strategies have been attempted, including lobar-lung transplantation from both deceased and living donors. Given the ethical problems related to living donation, living-donor lobar transplantation never received widespread attention outside the United States [4] and Japan [5–7]. On the other hand, concerns about the safety and long-term results of lobar transplantation per se initially limited the use of deceased-donor lobar LTx to sicker patients who cannot afford a long waiting time [8]. As a consequence, in the literature we can either find studies including a miscellanea of reduced-size LTx techniques altogether [9–11] or reports of large series of lobar lung transplantation from living donors [4–7]. Papers focusing on deceased donor lobar lung transplantation alone usually deal with very small numbers [12,13], and no comparative analysis with full-size transplantation is available in the literature.

We chose to focus on the latter, and, for that purpose, we retrospectively compared donor and recipient characteristics and outcomes after lobar (L) versus full-size (FS) transplantation in our cystic fibrosis population since the beginning of the lung transplant program in Leuven to the present days.

METHODS

Between July 1991 and February 2011, 535 isolated lung transplantations were performed at Leuven University Hospital. Prospectively collected data were retrospectively analyzed in September 2012. Seventy-four (13.8%) of these patients were affected by cystic fibrosis (CF) when referred to our lung transplantation center. Starting from 2005, lobar lung transplantation was performed in the case of considerable size mismatch between recipient lungs and donor chest cavity. Fourteen lobes from deceased donors were transplanted in 8 patients (10.8%), with the remaining 66 patients (89.2%) receiving a standard procedure. The final choice for lobar lung transplantation was made on the back table, immediately before starting implantation, according to the recipient's chest cavity. After downsizing, lungs were implanted in a standard fashion.

Surgical Technique

The surgical technique of lobar transplantation was consistent with what was previously described [14]: meanwhile, pneumonectomy was carried out in a standard fashion, and the corresponding donor lung was split on the back table. Fissures were divided with the use of linear staplers if necessary, and the vein from the removed lobe was closed and cut, preserving the whole atrial cuff for the venous anastomosis.

Shortening of the arterial stump was performed whenever necessary to avoid kinking. Anastomoses were carried out as usual: bronchus first, followed by artery and atrial cuff. If any discrepancy in the bronchial diameter occurred, it was adjusted with the use of interrupted sutures on the cartilaginous part of the bronchus, to obtain an end-to-end anastomosis, usually considered to be at lower risk for airway complications compared with the telescoping technique [15].

Extracorporeal Support

Since 2005, extracorporeal support consisted of veno-arterial extracorporeal membrane oxygenation (ECMO) whenever needed. Before that year, full cardiopulmonary bypass was used in the case of hemodynamic instability. It is our routine practice now to implant the second lobe on ECMO to avoid overperfusion of the first implanted lobe.

Postoperative Management and Follow-Up

Primary graft dysfunction (PGD) was evaluated according to ISHLT criteria [16]; PGD 0 and 1 were not further distinguished. Patient follow-up after discharge from the hospital consisted of a standardized outpatient care regimen. A thorough re-evaluation, including physical examination, blood tests, urine, sputum and pharyngeal swab cultures, pulmonary function tests, and chest radiography, was performed twice per week for the first 2 postoperative months, weekly or biweekly until the 6th month after transplantation, then every 2 to 4 weeks until the first postoperative year and, afterward, life-long at intervals of 2 to 3 months. Bronchoscopy with bronchoalveolar lavage was also performed routinely at established time points (at discharge, 3, 6, 12, 18, and 24 months after transplantation and yearly from then on); transbronchial biopsies were routinely performed at discharge and 3 months after transplantation. Both bronchoalveolar lavage and biopsies were additionally performed whenever necessary if rejection, infection, or bronchiolitis obliterans syndrome (BOS) were suspected. BOS was defined as a sustained decline in forced expiratory volume in 1 second (FEV_1) $\geq$20% from the patient's best postoperative value, in the absence of any other detectable causes [17].

Statistical Analysis

Continuous variables are expressed as median value and range; differences were analyzed with the use of the Mann-Whitney U test or the Wilcoxon signed-rank test for paired samples. Categorical data were analyzed by use of a 2-tailed Fisher exact test (95% confidence interval). Values of $P \leq .05$ were considered to indicate statistical significance. Survival data were analyzed by use of the Kaplan-Meier method.

RESULTS

Recipient Characteristics

Patients in the lobar group ([L]) were younger, with a median age of 21 years (13–25) versus 28 years (14–57) in the full-size group ([FS]); $P < .01$. They were also smaller and lighter: median height 152 cm (145–166) and weight 42 kg (34–52), versus height 168 cm (144–192) and weight 51 kg (30–82) in [L] and [FS], respectively ($P < .01$). No significant differences could be demonstrated in both male/female ratio and median waiting time, although >100 days longer on average in [L] (Table 1).

Donor Characteristics

Analysis of donor data showed the two populations to be homogenous when age, height, and weight were compared (Table 2). The final PaO_2/FiO_2 ratio was also not significantly different (460 mm Hg vs 493 mm Hg), as well as ventilation time, defined as time (in hours) from intubation to cross-clamp: 50 versus 44 hours, respectively.