Is There an Age Limit to Lung Transplantation?

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Background. Lung transplantation in patients older than 65 years is increasingly common, but questions remain regarding risk vs benefit and procedure choice. We identified short-term and long-term outcomes in older single-lung transplant (SLT) and bilateral-lung transplant (BLT) recipients.

Methods. We performed a retrospective review of United Network for Organ Sharing data for patients who underwent lung transplantation between May 2005 and December 2012. Patients were grouped by age, and we calculated short-term and long-term survival rates and compared survival distributions.

Results. Of the 11,776 patients who received lung transplants, 9,317 (79%) were aged 12 to 64 years, 1,902 (16%) were 65 to 69, 486 (4%) were 70 to 74, and 71 (1%) were 75 to 79. Short-term survival was similar across all age groups and procedure types except those aged 75 to 79, who had lower short-term survival for BLT. Those

aged 12 to 64 had higher 5-year survival for SLT and BLT than all other groups ($p < 0.001$), and BLT offered a long-term survival advantage over SLT in this group ($p < 0.0001$). Older age groups trended toward better long-term survival for BLT compared with SLT (65 to 69, $p = 0.059$; 70 to 74, $p = 0.079$). Although data were lacking for 5-year survival for those aged 75 to 79, the 3-year survival for BLT in this group was inferior.

Conclusions. Lung transplant can be offered to select older patients up to age 74 with acceptable outcomes. SLT may be preferred for elderly patients, but BLT offers acceptable long-term outcomes without significant short-term risk. Patients older than 75 have acceptable short-term outcomes for SLT, but long-term outcomes for SLT and BLT in this group are poor.

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Lung transplantation has become the treatment of choice for eligible patients with progressive end-stage lung disease. However, due to pressures such as limited donor supply and issues of perioperative and long-term risk, factors such as age have historically been used to determine which patients are acceptable candidates for lung transplantation. Accordingly, international guidelines include recipient age older than 65 as a relative contraindication for lung transplantation [1]. Despite this warning, lung transplantation in patients older than 65 has become increasingly common [2–4]. The median recipient age has increased by 10 years during the past two decades [2]. Older individuals comprise the fastest-growing segment of our population, and as the average life expectancy continues to rise, the question of an age cutoff for lung transplant recipients becomes increasingly salient.

In the last decade, short-term lung transplant survival rates drastically improved across all ages [2–6], with comparable 3-month survival rates reported across all age groups. Reported 5-year survival rates in patients 65 or

older have been significantly lower [2, 7–9]. Several studies have examined this older group of lung transplant recipients in the broader perspective [4, 7, 8, 10, 11], but we aimed to more closely examine the short-term and long-term transplant outcomes across the age range of 65 to 79 years compared with the standard recipient age group of 12 to 64 years.

Determining the type of lung transplantation procedure (single [SLT] vs bilateral [BLT]) in patients 65 or older is subject to significant institutional and regional variability and, to some extent, is dictated by the underlying disease and pretransplant functional status of the candidate. The general tendency has been to opt for SLT in older recipients because it is believed to be a lower-risk procedure [7, 8, 11–14]; however, the justification is still not unanimous, and further objective evidence is needed.

Material and Methods

Patient Population

Before this study was initiated, written approval with waiver of informed consent was obtained from the Institutional Review Board for Human Research at St. Joseph's Hospital and Medical Center in Phoenix, Arizona. The Standard Transplant Analysis and Research Dataset for lung transplant recipients was obtained from the United Network for Organ Sharing (UNOS) for patients who underwent lung transplantation between May 2005 and

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December 2012. Data for 11,778 lung transplants were retrospectively reviewed. The study excluded 2 patients, ages 81 and 86. Recipients were allocated into one of four age groups: 12 to 64, 65 to 69, 70 to 74, and 75 to 79 years. The four age groups were compared for demographic and pretransplant variables, including sex, procedure, underlying lung disease, lung allocation score (LAS), mean pulmonary artery pressure (mPAP), ventilator dependency, and cause of death.

Statistical Analysis

Short-term survival (30 days, 90 days, and 1 year) and long-term survival (3 and 5 years) were estimated using the Kaplan-Meier approach. Survival distributions were then compared using log-rank tests. The χ^2 test was used to compare categoric variables, and the Student t test was used to compare continuous variables. Pairwise comparisons were used to identify the age groups that were significantly different for LAS and mPAP. The Bonferroni correction was applied to adjust for multiple comparisons. A Z test was used to compare column proportions for each cause of death. P values of less than 0.05 were considered significant. All analyses were performed with SPSS 21 software (IBM Corp, Armonk, NY).

Results

Of the 11,776 patients reviewed (mean age, 53.6 ± 14.1 years), 9,317 (79%) were between the ages of 12 and 64, 1902 (16%) were 65 to 69, 486 (4%) were 70 to 74, and 71 (1%) were 75 to 79 (Fig 1). Table 1 reports recipient demographics across age groups. The four age groups were significantly dissimilar in all patient characteristics, including sex distribution, disease diagnostic group, LAS,
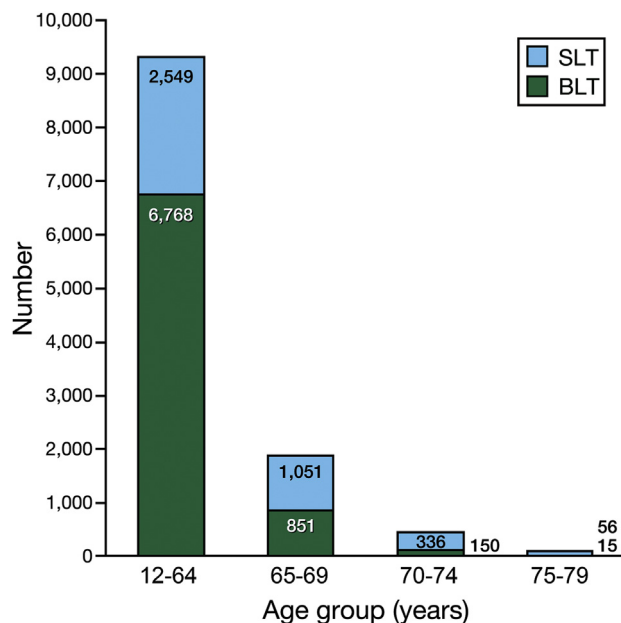

Fig 1. Age distribution according to single-lung transplant (SLT; turquoise) or bilateral-lung transplant (BLT; green).

mPAP, and procedure type (SLT vs BLT). The proportion of male recipients increased significantly by age group, comprising 56% in the 12 to 64 group, 66% in 65 to 69, 77% in 70 to 74, and 94% in 75 to 79 ($p < 0.001$). The older age groups had an increasingly higher proportion of recipients with restrictive lung disease ($p < 0.001$). Although the mean LAS score increased significantly across increasing age groups ($p < 0.001$), the mean mPAP and ventilator dependency at registration decreased significantly across increasing age groups ($p < 0.001$). Of the transplants in the 12 to 65 age group, 73% were BLTs, whereas all three senior age groups received fewer BLTs: 45% in 65 to 69, 31% in 70 to 74, and 21% in 75 to 79 ($p < 0.001$).

Table 2 demonstrates the cumulative short-term (30-day, 90-day, and 1-year) and long-term (3-year and 5-year) survival among the four age groups. Cumulative survival rates for SLT and BLT are depicted as Kaplan-Meier curves in Figure 2. The 30-day and 90-day survival across all age groups and procedure types was similar with the exception of BLT in recipients aged 75 to 79, who had inferior cumulative 30-day survival of 73% and 90-day survival of 60%. Recipients in the 12 to 64 group had a significantly higher cumulative survival rate than the older age groups, regardless of procedure type (Fig 2). Although 5-year data were not available, survival at 3 years was already significantly worse in the BLT 75 to 79 group compared with SLT in the same age group and with 3-year survival in the other age groups.

We also compared outcomes for SLT and BLT within each of the four age groups (Fig 3). For recipients aged 12 to 64, survival was significantly higher for BLT over SLT ($p < 0.0001$). For recipients aged 65 to 69 and 70 to 74, there was a trend toward higher survival for BLT that was not statistically significant ($p = 0.059$ for 65 to 69, and $p = 0.079$ for 70 to 74). For the 75 to 79 group, there was no relevant difference in cumulative survival between SLT and BLT ($p = 0.14$).

When we compared disease-specific cumulative survival for SLT and BLT in each age group (Fig 4, Table 3), the 12 to 64 group showed significantly higher survival for BLT over SLT in the obstructive ($p = 0.048$) and restrictive disease groups ($p < 0.001$). The older age groups showed no statistical difference in cumulative survival for BLT vs SLT in the obstructive or restrictive disease groups.

An analysis of cause of death by age group (Fig 5, Table 4) showed that the most common causes of death in all age groups were infection and pulmonary disease. Interestingly, there was no difference in the frequency of infection as cause of death among the different age groups. We noted that patients in the 12 to 64 group more commonly died of graft failure, whereas patients in the older age groups were more likely to succumb to malignancy (65 to 69 and 70 to 74) and cardiovascular disease (70 to 74).

Comment

Longer life expectancy has led to a shift in the age structure of our population, and many elderly people suffer from end-stage lung disease. However, current