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Improved waitlist and transplant outcomes for pediatric lung transplantation after implementation of the lung allocation score

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BACKGROUND: Although the lung allocation score (LAS) has not been considered valid for lung allocation to children, several additional policy changes for pediatric lung allocation have been adopted since its implementation. We compared changes in waitlist and transplant outcomes for pediatric and adult lung transplant candidates since LAS implementation.

METHODS: The United Network for Organ Sharing database was reviewed for all lung transplant listings during the period 1995 to June 2014. Outcomes were analyzed based on date of listing (pre-LAS vs post-LAS) and candidate age at listing (adults >18 years, adolescents 12 to 17 years, children 0 to 11 years).

RESULTS: Of the 39,962 total listings, 2,096 (5%) were for pediatric candidates. Median waiting time decreased after LAS implementation for all age groups (adults: 379 vs 83 days; adolescents: 414 vs 104 days; children: 211 vs 109 days; $p < 0.001$). The proportion of candidates reaching transplant increased after LAS (adults: 52.6% vs 71.6%, $p < 0.001$; adolescents: 40.3% vs 61.6%, $p < 0.001$; children: 42.4% vs 50.9%, $p = 0.014$), whereas deaths on the waitlist decreased (adults: 28.0% vs 14.4%, $p < 0.001$; adolescents: 33.1% vs 20.9%, $p < 0.001$; children: 32.2% vs 25.0%; $p = 0.025$), despite more critically ill candidates in all groups. Median recipient survival increased after LAS for adults and children (adults: 5.1 vs 5.5 years, $p < 0.001$; children: 6.5 vs 7.6 years, $p = 0.047$), but not for adolescents (3.6 vs 4.3 years, $p = 0.295$).

CONCLUSIONS: Improvements in waiting time, mortality and post-transplant survival have occurred in children after LAS implementation. Continued refinement of urgency-based allocation to children and broader sharing of pediatric donor lungs may help to maximize these benefits.

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The lung allocation score (LAS) was implemented in May 2005 for lung transplant candidates ≥12 years of age, with the purpose of shifting donor lung allocation policy from a system based on accumulated waiting time to a system based on medical urgency. To this end, the LAS is a composite score, based on 2 risk-prediction models, which prioritizes allocation to candidates with a high probability of waitlist mortality balanced with an acceptable probability of 1-year post-transplant survival.[1,2] In adolescents and adults, allocation based on the LAS has resulted in decreased waiting time and waitlist deaths and increased transplant

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rates, as well as increased transplantation of older candidates, those with fibrotic lung disease, and more critically ill candidates with higher LASs.[3–7] Despite prioritization of candidates with higher medical urgency for transplant, an improvement in overall 1-year post-transplant survival has been observed,[3] although others have reported inferior post-transplant survival in recipients with higher LASs.[4,7–9]

The LAS has not been considered valid for pediatric candidates <12 years of age, however, primarily because differences in diagnoses between children and older candidates made the mortality risk prediction model of the LAS inappropriate as a measure of medical urgency. In addition, the small numbers of lung transplant recipients in this age group have not allowed for the creation of a reliable post-transplant survival model for children.[1,10,11]

Although the LAS has not been used in children <12 years old, several other key changes have occurred in lung allocation policy for this age group since LAS inception. These include adoption of broader geographic sharing for prioritized allocation of child donor lungs to child candidates,[12] creation of a 2-tier priority system for stratification of child candidates based on medical urgency,[12] and approval of an adolescent exception policy to allow individual child candidates to participate in the LAS system under special circumstances.[13] The applicability of a medical urgency–based allocation policy to children has been debated widely,[10,14–21] but corollaries to the marked changes in adult allocation and transplant outcomes since LAS inception have not been thoroughly examined in the pediatric population. One study suggested that, although transplant rates rose similarly after LAS implementation in candidates aged <12 and ≥12 years, the rise in waitlist death rates may have been greater in candidates aged <12 years.[22] We therefore sought to examine the changes in waitlist and transplant outcomes for pediatric lung transplant candidates since implementation of the LAS.

Methods

Study population

This study was approved by the institutional review board of Washington University School of Medicine. Standard Transplant Analysis and Research (STAR) data files were reviewed for all waitlist entries for lung transplantation included in the Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) database from 1995 to June 31, 2014. Patients receiving heart–lung or living donor lung transplantation were excluded. To minimize the contribution of an "era effect" to differences in outcomes, candidates listed before 1995 were excluded.[23,24]

The LAS was implemented on May 4, 2005 and, accordingly, listings were divided into 2 cohorts based on date of listing: pre-LAS (January 1, 1995 to May 3, 2005) and post-LAS (May 4, 2005 to June 31, 2014). Based on candidate age at listing, the listings were then sub-divided into age groups consistent with those used in OPTN lung allocation policies: adults (≥18 years); adolescents (12 to 17 years); and children (0 to 11 years).[2]

Study outcomes

LASs for all candidates listed after May 4, 2005, including candidates <12 years of age, were used as provided from calculated fields in the STAR data files. Priority status data for child candidates listed after January 1, 2010 was obtained by special request from OPTN/UNOS.

A waitlist analysis was conducted, which included all waitlist entries for the study cohort and compared group characteristics at the time of listing and waitlist outcomes. Waitlist mortality and transplant rates were calculated as the number of deaths or transplants, respectively, per 100 patient-years on the waitlist, and are reported by year of candidate listing. A waitlist outcome of "too sick to transplant" was considered a mortality for this analysis.

A transplant analysis was also conducted, which included all deceased donor lung transplantations for the study cohort and compared group characteristics at the time of transplant, as well as long-term post-transplant survival. Survival data for this analysis were used as provided in the STAR data files and are current as of the end of the study period.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or as median with interquartile range, and were compared using either *t*-tests for 2-sample comparisons or 1-way analysis of variance with post-hoc analysis by Tukey's method for multiple comparisons. Categorical variables were expressed as frequencies and percentages, and were compared using chi-square analysis with Bonferroni's correction for multiple *a priori* comparisons. Kaplan–Meier survival curves for post-transplant survival were constructed, and were compared using the log-rank test. Data analyses were performed using SAS version 9 (SAS Institute, Cary, NC) and SPSS version 23.0 (IBM SPSS, Armonk, NY) statistical software.

Results

Waitlist analysis

A total of 39,962 listings were included in the waitlist analysis. Of these, 2,096 (5.2%) were for pediatric candidates <18 years of age. Mean LASs are presented for all candidates listed after May 4, 2005, although LAS was not used for allocation in children. Mean LASs were lower in children than adolescents and adults at both listing and waitlist removal, although a similar gradual rise was seen in all groups throughout the post-LAS time period (Figure 1A). Priority classification is presented for children listed after January 1, 2010 (Table 1).

Notable differences in diagnosis groupings included a higher prevalence of pulmonary vascular disease (Group B, includes most listings for congenital heart disease) and restrictive/interstitial lung disease (Group D), and a lower prevalence of cystic fibrosis/immunodeficiencies (Group C) in children compared with adolescents (see Table S1 in Supplementary Material, available online at www.jhltonline.org). There was little change in diagnosis groupings after LAS implementation for children and adolescents, as opposed to adults, in whom there was a decrease in the