

Time to Lung Transplantation: Lung Allocation Score and Other Factors

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Lung transplantation is a therapeutic option for selected patients with severe pulmonary disease who are refractory to medical therapy and continue to have progressive clinical deterioration. 38,119 lung transplants have been performed worldwide till June 30, 2010 [1]. In the United States, waitlist time is overseen by the Organ Procurement and Transplantation Network (OPTN), which is operated by the United Network of Organ Sharing (UNOS). Currently, there are 1,665 patients on the waitlist for a lung transplant [2].

As of May 2005, each lung transplant candidate is assigned a Lung Allocation Score (LAS). The LAS is a calculated score (from 0 to 100) derived for each patient over the age of 12 years which is utilized to predict waitlist survival probability with and without a lung transplant [3]. Patients with either cystic fibrosis (CF) or idiopathic pulmonary fibrosis (IPF) had documented higher waitlist mortality compared to patients with chronic obstructive pulmonary disease [4,5]. The creation of the LAS was intended to facilitate allocation of the short supply of available donor lungs to individuals with more urgent need. The implementation of the LAS has reduced mortality for IPF, COPD and CF, but not idiopathic pulmonary arterial hypertension (IPAH) [6].

Patients commonly ask, "what is my score and when am I having my transplant?" Since 2005, there has been a 58% increase in patients with LAS of 35 or higher, but 68.7% of patients still have LAS under 40. The overall median waitlist time for lung transplantation is less than 6 months. Candidates with LAS greater than 50 have a median wait time of 1 month. Despite the shorter waitlist time with higher LAS score, some patients may remain on the waitlist for longer periods of time. There are a number of factors that may explain this reason. First, there continues to be a shortage in organ donor availability has not kept pace with the increase in the number of recipients in need of lung transplantation. On an annual basis, up to 20% of lung transplant candidates will be either inactivated or die before an adequate lung donor becomes available [7].

Second, the fragility of the lungs makes overall donation challenging. Predetermined selection criteria are used to assess the viability of potential lung donors. The evaluation includes information regarding 1) chest radiograph images, 2) arterial blood gas values, particularly the PaO₂:FiO₂, on standard ventilator settings, 3) bronchoscopic findings and gram stain/cultures, and 4) examination of the lung at the time of procurement [8].

Wait time for lung transplantation have geographic variation in the United States. Patients in the northern and northwest regions experience longer wait times. Some proposed factors include geographical variations in homicide or motor vehicle accident rates. Depending on the acuity of the patient, the volume and experience, some transplant centers will also increase donor pool by performing transplantation using extended donor criteria, thereby making waitlist times shorter [8]. Extended donor criteria includes any of the following elements: 1) donor age > 55 years, 2) PaO₂:FiO₂ < 300 mmHg, 3) abnormal chest radiograph, 4) donor tobacco use for > 20 years, 5) evidence of aspiration, 6) presence of purulent secretions on bronchoscopy or a positive gram stain on lavage, and 7) chest trauma or history of cardiopulmonary surgery.

Some lung donors may have only unilateral disease, so recipient underlying lung disease greatly matters in the type of transplant

procedure required. Patients with either CF or IPAH will require bilateral lung transplantation, compared to patients with IPF or COPD who can undergo single lung transplantation [9].

Irrespective of the LAS, donor and recipient lung size match is essential for adequate function of the allograft and survival [10]. Shorter patients may require lung donors from pediatric patients. However, lungs offered from pediatric donors (age < 18 years) will first be offered to potential candidates under the age of 18 years.

Additional factors include donors and recipients ABO blood type and human leukocyte antigen (HLA) compatibility. Although most patients will have 0% panel reactive antibodies (PRA), since 2009 only 69.8% had 0% PRA. Patients with a higher PRA, particularly PRA greater than 25%, have a higher 30-day and overall mortality [11]. This makes the waitlist time for an appropriate cross match significantly longer and can potentially exclude the patient from transplantation.

More recently, it has been noted that a having a higher LAS without exemptions may not always represent greater urgency for all candidates. Patients with IPAH have a cumulative 20% mortality at 12 months after initial listing compared to 10% for patients with IPF [6]. A recent modification allows application for UNOS exemption for patients with IPAH who demonstrate hemodynamic compromise (mean right atrial pressure greater than 15 mmHg or cardiac index less than 1.8 L/min/m²) and clinical deterioration. The Lung review Board will determine if sufficient clinical data supports the request for the candidate to be at the 90th percentile.

Even if a candidate with high LAS undergoes transplantation a short time after listing, this may be offset by overall survival [12,13]. Lung transplant candidates having LAS > 60 (20-44 days) have been compared to candidates with LAS < 60 (55-98 days) [13]. Lung transplant candidates with LAS > 60 had all of the following post lung transplantation: 1) a greater need for post-operative mechanical ventilation, 2) higher rate of ICU admission, 3) longer immediate hospital course, 4) higher incidence of graft failure (13% vs. 3%) and 5) worse 1-year survival (83.7% for LAS < 46 and 68-75% for LAS > 60).

In summary, the advent of the LAS has shortened time to undergoing lung transplantation and decreased risk of death while on the waitlist for the majority of patients. LAS may not be the sole determinant for an early or delayed time to lung transplantation. A number of considerations, as outlined within this text may still delay the time to proceeding to transplantation. Additionally, patients with higher LAS may have worse morbidity and mortality following lung transplantation. In order to increase the odds of a candidate receiving

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a lung transplant, the transplant community has made concerted efforts to refine LAS algorithms, desensitization protocols, utilize transplantation of marginal donors, perform cadaveric or living lobar lung transplantation, use of donation after circulatory death, and recondition extra-marginal donor lungs with ex-vivo lung perfusion techniques.

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