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Contemporary Issues in Lung Transplant Allocation Practices

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Abstract

Purpose of Review—To discuss the current state of donor lung allocation in the United States, and future opportunities to increase the efficiency of donor lung allocation.

Recent Findings—The current donor lung allocation system prioritizes clinical acuity by use of the Lung Allocation Score (LAS) which has reduced waitlist mortality since its implementation in 2005. Access to donor lungs can be further improved through policy changes using broader geographic sharing, and developing new technology such as ex vivo lung perfusion to recover marginal donor lungs.

Summary—The number of lung transplants in the U.S. continues to increase annually. However, the demand for donor lungs continues to be outpaced by an ever growing waitlist. Efficient allocation can be achieved through improved allocation policies and new technology.

Keywords

lung transplant; outcomes; donor allocation; geography

Introduction

Lung transplantation remains the definitive treatment for end-stage lung disease, with the number of lung transplants in the United States (U.S.) reaching an all-time high of 2,072 in 2015 [1•]. The main indications for transplant include pulmonary fibrosis, chronic obstructive pulmonary disease, cystic fibrosis, and pulmonary hypertension. Despite an annual increase in the number of lung transplants, the number of organ donors continues to be outpaced by the demand from an ever-growing U.S. waitlist [1•]. Therefore, continued research into and refinement of both allocation policies and new technologies are needed to provide careful stewardship of the limited donor lung supply.

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Compliance with Ethical Guidelines

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How donor lung allocation works in the United States

The geographic location of an organ donor is a major criterion for allocation. Donor lungs are first offered to nearby, or “local,” waitlisted patients prior to being offered to a wider region. “Local” is defined as within the geographic boundaries of a donation service area (DSA), which is administered by an organ procurement organization (OPO). There are 58 DSAs in the U.S. with boundaries that were determined in the early years of transplant mainly due to considerations of ischemic time. If no waitlisted patients within the boundaries of the DSA are identified using criteria such as blood type and thoracic size, the donor lungs are offered beyond the local DSA in 500 mile radius increments from the donor’s location until the organ is accepted [2•].

Another major criterion for donor lung distribution is donor age, which determines the priority of patient age groups eligible to receive the organs within each geographic area. Patient age groups are defined as: adults ≥ 18 years of age, adolescents 12 to 17 years, and children < 12 years. Adult donor lungs are first offered to adults or adolescents, and then children, within the local area. Adolescent donors are first offered to adolescents, and child donors are first offered to children before the other age groups are considered.

Only after using a donor’s geographic location and age to identify a cohort of waitlisted patients are additional clinical criteria used. These criteria include ABO blood type, thoracic size, immunologic compatibility, and the Lung Allocation Score (LAS). Current allocation policy prioritizes ABO identical matches over compatible matches, which is reflected in a recent national registry analysis showing that nearly 93% of double lung transplants were ABO identical matches, and the remaining 7% were ABO compatible matches. There was no significant difference in survival between the two cohorts at five years after transplant [3]. Thoracic size matching between donor and recipient is another important consideration, where oversized allografts are associated with better posttransplant pulmonary function testing and less occurrence of chronic rejection [4]. Finally, the LAS was implemented in May, 2005 and is a clinical acuity score that incorporates both medical urgency (predicted survival without transplantation) and net transplant benefit (difference between predicted survival with versus without transplant) [5]. The score ranges from 0 to 100 and the higher the score, the higher the priority for transplant. The LAS applies to adult and adolescent waitlisted patients; children on the waitlist are prioritized as status 1 or 2 depending on clinical data and time accrued on the waitlist. Since its implementation, the LAS has met its intended goal of reducing waitlist mortality by 40% from >500 annual waitlist deaths prior to LAS, down to an average 300 annual waitlist deaths starting the year after LAS implementation [6].

Ways to improve access to lung transplant

While the LAS has successfully prioritized the sickest waitlisted patients for lung transplant, there are many opportunities to further advance the allocation of donor lungs. Access to donor lungs can be pursued in several ways: 1) increase the supply of donor organs, 2) decrease the demand for donor organs, or 3) more efficiently allocate donor organs.

Efforts to increase the donor supply in lung transplantation have recently focused on optimizing organs previously deemed unsuitable for transplant through ex vivo lung perfusion (EVLP) [7]. On average, only 15% of lungs from organ donors are utilized [8], however EVLP enables transplant teams to procure and then preserve donor lungs to permit a window of time to re-evaluate and rehabilitate donor lungs to where they can safely be used for transplant. This has enabled one transplant center to perform twenty additional transplants using lungs originally deemed high risk [9].

Other opportunities to increase the donor lung supply in lung transplant include donation after cardiac death (DCD), which accounted for only 2.1% of lung donors in the U.S. between 2006–2014, but in an international registry between 2003–2013 utilization of DCDs was as high as 32% in some countries. In both the U.S. and international transplant registries DCD recipients have long term survival on par with deceased brain dead donors [10, 11]. Another mechanism by which the supply of donor lungs has increased is through the use of increased risk donors, which are organ donors the Centers for Disease Control (CDC) has designated based on social behaviors placing them at higher risk for human immunodeficiency virus (HIV). Between 2005 and 2013 increased risk donors accounted for 8% of U.S. lung transplants [12] with equivalent 5 year survival between patients receiving increased risk and non-increased risk donors. Finally, increased access to lung donors can be achieved through living donor lung transplant, which is limited by technical challenges and limited experience. The last living donor lung transplant in the U.S. occurred in 2013 [1•]. [Table 1]

Contrary to the idea of decreasing the demand for donors, the number of new patients added to the waitlist has risen annually for the past decade as the indications and acceptable comorbidities for lung transplant continue to increase. Despite a record number of U.S. lung transplants in 2015, there were still 1,637 patients on the waitlist at the end of the year [1•]. The increase can be attributed in part to more patients of advanced age being waitlisted and transplanted. Patients 65 years of age comprised 29% of U.S. lung transplant recipients in 2013, compared with 7% in 2003. When *Hayanga et al* reviewed the U.S. transplant registry between 2006 and 2012, there was no difference in patient survival between septuagenarians and sexagenarians at three months and one year posttransplant. However three and five year posttransplant survival was significantly lower in the septuagenarian group [13], indicating that lung transplants in patients of advanced age require more scrutiny and further research. Also increasing the demand for donor lungs are the rising number of patients bridged with mechanical ventilation or extracorporeal membranous oxygenation (ECMO), allowing the evaluation and waitlisting of patients previously too ill to wait for a lung transplant [14]. Finally, a new frontier in expanding patient access to lung transplant is the transplantation of patients with HIV [15]. In a limited case series, an increase in acute graft rejection was observed which will require closer monitoring in future cases. [Table 2]

Finally, access to lung transplant can be achieved through maximizing the efficient allocation of the existing donor lung supply. The most notable change has been the LAS system, which was implemented in 2005 to prioritize patients for transplant based on clinical acuity instead of a time based system, resulting in lower waitlist mortality and shorter waitlist times [6]. While this has resulted in patients being transplanted at a higher clinical

acuity, one year posttransplant survival has not significantly decreased. Though the LAS has helped direct donor lungs to patients of higher acuity, there are geographic allocation boundaries that were created in the 1980s which remain in place and limit the ability to increase allocation efficiency. As a result, donor lungs are still allocated to low acuity patients while high acuity patients remain on the waitlist [16]. Broader geographic sharing, which is the distribution of donor organs across a larger region, has the potential to further reduce waitlist mortality. [Table 1]

Disparities in allocation

The DSA boundaries are historical and were based on the preferences of the few early transplant centers in 1984 when the U.S. organ allocation system transitioned from a local to a national system. With the passage of time, an unintended consequence of these boundaries has resulted where the ratio of organ donors to waitlisted patients between DSAs is unequal and varies widely, creating a system where the geographic location of a transplant center determines a patient's likelihood of receiving a transplant [17].

Currently, the sickest, highest acuity patients, which comprise less than 10% of the lung transplant waitlist, account for 60% of waitlist deaths [18]. The majority of donor lungs (81%) are allocated within a DSA to a low-acuity, low priority patient even when a matched higher acuity patient exists just outside the boundaries in a separate DSA, resulting in an avoidable waitlist death [18, 19]. Thus, the current geographic boundaries may limit access for the sickest waitlisted patients to lung transplant.

There are also two populations of patients known to have limited access to donor lungs partially because of lack of *enough* appropriately matched donors but also because of lack of *access* to appropriately matched donors. First, patients of short stature (<162 centimeters) have been shown to have a lower rate of transplantation and a higher rate of waitlist death when compared to waitlisted patients of average height in a national registry [20]. Second, patients with a sensitized antibody profile have a longer waitlist time and are less likely to receive a lung transplant [21]. Therefore, improvements in donor lung allocation could improve access for high acuity waitlisted patients, and also those disadvantaged by short stature or a sensitized antibody profile.

Broader geographic sharing

Organ allocation utilizing broader geographic sharing has been implemented most notably in liver transplantation, as well as kidney and soon heart transplantation. In 2013, U.S. liver allocation was changed to a new policy called 'Share 35' such that deceased donor livers are offered regionally to waitlisted patients with Model for End stage Liver Disease (MELD) scores ≥ 35 before being offered locally to waitlisted patients with MELD scores <35. Prior to its implementation, the Liver Simulation Allocation Model (LSAM) software, developed by the Scientific Registry of Transplant Recipients (SRTR), was used to simulate broader geographic allocation boundaries, and when compared to the simulation using current liver allocation boundaries a reduction in waitlist deaths was predicted [22]. One year after implementation of the national algorithm that shared donor livers across a broader area, U.S.

liver waitlist mortality decreased by 30% without adversely impacting early posttransplant survival [23], confirming that in adult liver transplantation broader sharing of deceased donor livers can improve access to transplant for high acuity patients.

In 2014, the U.S. Kidney Allocation System (KAS) was implemented which allowed patients with combined panel reactive antibodies (cPRA) of 99 and 100% to have the highest priority for deceased donor kidneys from regional and national levels, respectively. This highly sensitized population was recognized in the pre-KAS era to have disadvantaged access to transplant due to the limited number of matching donors. *Parajuli et al.* reviewed their single center experience since implementation of the new policy and found no statistically significant differences in kidney function and patient survival in highly sensitized patients when compared to control patients [24]. In addition, donor kidneys considered marginal by the Kidney Donor Profile Index (KDPI) will now be offered initially at the regional level instead of local to increase the likelihood of organ acceptance [25].

Finally, U.S. heart transplant allocation moved towards broader geographic sharing starting in 2006 by changing policy so that donor hearts were allocated to high priority patients both locally and regionally (within 500 miles) before considering lower priority patients locally. This policy change was thought to contribute, partly, to a reduction in waitlist mortality. And while this meant more high priority and therefore high acuity patients were transplanted, 1 year posttransplant survival was not adversely impacted [2]. Currently, heart allocation policy is undergoing additional review as the current geographic system used in heart allocation is recognized as a major limitation to ensuring the sickest patients are transplanted [26]. The new policy will have additional tiers to better capture the clinical acuity of a waitlisted patient, and incorporates broader geographic sharing of donor hearts [27, 28].

In lung transplant the principles of broader geographic sharing have been applied to the pediatric lung transplant population by modeling alternative geographic boundaries for organ allocation. For example, current allocation rules require that adolescent donor lungs are allocated locally first to adolescents, children and then adults. In Tsuang et al (2016), simulations showed that if the same adolescent donor lungs are offered more broadly first to waitlisted children and then adolescents within a 1,000 mile radius before local waitlisted adults are considered, both the child and adolescent transplant rate would potentially increase without adversely impacting the adult transplant rate [29••].

Donor organ ischemic times

With broader geographic sharing, it is anticipated that donor organ cold ischemic times increase due to increased travel distances between donor and recipient. As donor lungs are shared locally (within a DSA), regionally (outside the DSA but within a defined region), and nationally (outside the region), donor lung ischemic times have been shown to increase from an average of 4.6 hours, to 5.3 hours, and 6 hours, respectively [19]. The impact of ischemic time on post lung transplant survival is an area of active investigation, with recent work suggesting ischemic times beyond six hours are acceptable [30, 31]. With the use of EVLP technology, donor lung ischemic times beyond 12 hours do not impact hospital length of stay, primary graft function scores, and posttransplant survival [32]. A study using the SRTR

registry has shown that donor location relative to the waitlisted patient (local vs regional vs national) does not influence risk of death after lung transplant [33].

Conclusion

With any allocation policy change, the benefits of increasing access to donor lungs for the highest priority (and therefore highest acuity) waitlisted patients must be weighed against the survival benefit of undergoing transplant. Prioritizing the sickest patients can lower waitlist mortality, but if posttransplant mortality substantially increases, the overall net benefit is low. The LAS is assigned to each waitlisted patient at the time of listing, and estimates both waitlist and posttransplant survival in an attempt to avoid futile transplants [5]. Recent work using the U.S. transplant registry which leverages a structural nested accelerated failure time model shows that patients with a higher LAS at the time of transplant do indeed experience a survival benefit [34]. Thus, the LAS discerns priority and benefit among waitlisted patients. And to increase access to transplant for waitlisted patients: 1) Changes in allocation policy utilizing broader geographic sharing has the potential to increase access to the pool of available donor lungs. 2) Advances in technology such as EVLP and increasing experience with DCD can increase the supply of donor lungs. This multifaceted approach to improve allocation will advance lung transplantation towards the goal of providing access to all waitlisted patients.

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Table 1

Increasing Lung Transplant Access

1. Increase Donor Lung Supply
Ex Vivo Lung Perfusion (EVLP)
Donation after Cardiac Death (DCD)
Increased Risk Donors
Living Donor Transplant
2. Increase Allocation Efficiency
Lung Allocation Score (LAS)
Broader Geographic Sharing

Table 2

Increasing Indications for Waitlisting

Patients of advanced age at time of transplant
Mechanical ventilation used as bridge to transplant
Extracorporeal Membrane Oxygenation (ECMO) used as bridge to transplant
Patients with HIV evaluated for lung transplant

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