Lung transplantation in the most critically-ill: forging ahead

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Provenance: This is an invited Editorial commissioned by Executive Editor-in-Chief Jianxing He (The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, Guangdong, China) and the Section Editor Xue-Feng Leng (Department of Cardiothoracic Surgery, the Affiliated Hospital of Chengdu University, Chengdu, China).

Comment on: Crawford TC, Grimm JC, Magruder JT, *et al.* Lung Transplant Mortality Is Improving in Recipients With a Lung Allocation Score in the Upper Quartile. *Ann Thorac Surg* 2017;103:1607-13.

Abstract: Lung transplantation is the gold standard therapy for patients with end-stage lung disease. The use of the lung allocation score (LAS) has permitted improved allocation of scarce pulmonary allografts. Recently, Crawford *et al.* examined the experience in the United States in lung transplantation in candidates with the highest LAS, demonstrating that outcomes for candidates with the highest LAS scores have improved significantly. This editorial places these data in the broader context of thoracic transplantation, and highlights the critical need for ongoing examination of this critically-ill patient population

Keywords: Lung transplantation; lung allocation score (LAS)

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Lung transplantation is the gold-standard therapy for patients with end-stage lung disease. At present, suitable donor allografts are scarce, and not able to completely match demand. As such, organ allocation strategies are at required to best allocate this limited resource. The fundamental goal of organ allocation is to prioritize patients with the greatest medical urgency, while simultaneously maximizing the overall societal benefit from a limited donor pool.

In an effort to more appropriately meet this charge, in 2005 the United Network for Organ Sharing (UNOS), the agency responsible for the allocation of solid organ transplantation in the United States, replaced a prior allocation system in which priority for lung allocation was given to those with the longest time on the wait list with a new system referred to as the lung allocation score (LAS) (1).

The LAS represents a revolution in the allocation of lung donor organs, and has helped the lung transplant community remain ahead of the curve with respect to allocation strategies in solid-organ transplantation. The lung allocation system balances the likelihood of waitlist and

post-transplantation survival at 1 year. In this manner, the LAS attempts to meet the twin needs of medical urgency and expected post-transplantation benefit. This strategy then better meets the ethical principles for the allocation of scarce resources outlined by the American Medical Association's code of Medical Ethics, which recommends that allocation be based on “*likelihood of benefit, urgency of need, change in quality of life, duration of benefit, and, in some cases, the amount of resources required for successful treatment.*”

Now 10 years after the introduction of the LAS, the implementation of the LAS has resulted in substantial declines in the mean waitlist duration and improvements in waitlist mortality, but no concomitant improvement in post-transplant survival has yet been demonstrated (2). Notably, pre-transplantation LAS has risen, such that the fraction of candidates with an LAS greater than 50 has doubled since the introduction of the LAS.

Outcomes among this most ill cohort have been a source of concern in the lung transplant community. Those with the highest LAS scores have in previous literature been shown to be at higher risk for 1-year mortality,

for longer ICU stay, and higher rates of tracheostomy. When considering both wait list and post-transplantation mortality, those with LAS above 90 were shown to derive decreased overall benefit in comparison to those with a score at the time of transplantation closer to the mean. Further efforts have been made to ascertain if there exists a score that may serve as a ceiling for lung transplantation, a threshold proposed beyond which transplantation may be considered futile (3,4).

The study at hand interrogates this concept of an LAS ceiling. Specifically, Crawford *et al.* test the hypothesis that survival has improved over time in recipients who are the most critically ill at the time of lung transplantation, which might challenge the assertion that lung transplantation in the highest LAS quartiles is futile (5).

To test this hypothesis, the authors queried the UNOS Scientific Registry of Transplant Recipients (SRTR) database for adult patients who underwent isolated lung transplantation from May, 2005 (the introduction of the LAS) to March, 2014. A total of 14,170 recipients were then stratified by LAS at the time of transplantation, and then subsequently by era of transplantation.

With respect to the primary outcome, the authors found that across eras, survival of patients with LAS in the highest quartile at the time of transplantation improved significantly, from 77.9% in the earliest era, to 84.0% in the most recent era. This improvement in survival was likewise identified in the multivariable model, demonstrating that patients who underwent transplantation in more recent eras derived a survival benefit most pronounced in the third era (HR 0.54, $P < 0.001$).

The authors conclude that despite steady rise in LAS at the time of transplantation following the introduction of the LAS, both short term (30-day) and intermediate (1-year) survival are improving in patients who are the most critically-ill and physiologically-deranged. The authors also rightly note that in light of these data, this trend of improved lung transplantation outcomes might warrant further emphasis on the expansion of the thoracic donor organ pool, rather than a focus on restriction of access to those candidates most in need.

That outcomes continue to improve in this most critically-ill cohort is an important observation and has implications for the appropriate approach to the lung transplant candidate. These findings likely reflect steady improvement across the field with respect to the care of the critically ill lung transplant candidate, in particular with the use of ECMO as a bridge to transplantation (6). Crawford

and colleagues note that across eras, pre-operative ECMO support has increased. Improved technologies relevant to ECMO, as well as centralization at high-volume centers and improved care strategies all likely contribute to the community's improved familiarity with ECMO. Further study is still required to best ascertain patient selection for ECMO in the pre-transplant setting, but should now proceed in light of the fact that outcomes following lung transplantation are now improving in this patient population. Moving forward, we support the conclusion that these data suggest that lung transplantation may be appropriately extended to the most critically-ill candidates. Further consideration of the appropriate treatment of the use of ECMO in the LAS will also be required to better reflect both degree of urgency and post-transplant benefit in this population.

Thoracic transplantation rightly warrants intense scrutiny with respect to both transplant candidate selection and post-transplant outcomes both from the medical community and the larger national organizations that organize transplantation. Given the scarcity of the resource at hand and the significance of the gift of donation, constant re-assessment of the work at hand is necessary. Work such as this by Crawford *et al.* has the potential to both change clinical practice with respect to the management of the individual transplant candidate, as well as change policy at the national and international level through the guidance these data offer with respect to this favorable trend in long-term outcomes in the most critically-ill population.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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