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Editorial

Research and Innovation in the Deceased Donor

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Advances in solid organ transplantation have transcended the expectations of the pioneering clinicians who initiated these endeavors for patients with end-stage organ disease. Beginning with renal transplantation and evolving to other organs, we have witnessed a steady increase in transplantation as an effective therapy for end-stage organ failure. Unfortunately deceased donation has stagnated over the past several years even as the number of waitlisted patients continues to increase. While most advances in clinical transplantation have been recipient-centric, future growth in transplantation will likely come from donor-focused innovations that increase the number and viability of organs donated for transplantation. Despite this pressing clinical need, clinical science surrounding donor management or *ex vivo* organ interventions remains in its infancy. The landscape of deceased donor research studies is dominated by low-risk studies that have involved different preservation solutions or static versus perfusion storage for kidneys. A limited number of studies have evaluated hormonal therapy, fluid resuscitation or ischemic preconditioning strategies (1–3). The veritable paucity of high quality, prospective randomized controlled trials in brain dead deceased donors is in part due to the significant regulatory and logistical challenges to performing transformative research in donation and transplantation (4). The lack of scientific research has hampered evidence-based progress for the field.

In this issue of the *American Journal of Transplantation*, Ware et al present a double-blind, placebo-controlled clinical trial of aerosolized albuterol designed to primarily study the change in PaO_2/FiO_2 ratio with multiple secondary clinical outcomes including: the change in static compliance of the respiratory system, change in chest radiographic score and donor lung utilization rate (5). Data analysis demonstrated that the intervention did not impact oxygenation as measured by change in the PaO_2/FiO_2 ratio from enrollment to procurement. No differences were identified in other lung-based clinical outcomes or in donor lung utilization. This study largely supports the results of two previous multi-center studies that similarly demonstrate no benefit of aerosolized albuterol or intravenous salbutamol in patients with acute lung injury.

Beyond the primary and secondary endpoints of the intervention under study, the authors should be commended for additionally looking at utilization and outcomes of other transplantable organs. It is important to remember that systemic administration of a drug to a deceased donor exposes multiple organs simultaneously. The authors reported a decrease in utilization of kidneys from donors treated with albuterol that could not be easily explained by the quality of donor kidney function. Beyond organ utilization, one can also readily envision that interventions other than the administration of aerosolized albuterol might affect organ function after transplantation. These collateral considerations that extend beyond the context of clinical science and are unique to donor intervention studies compel the establishment of a broad oversight mechanism capable of comprehensive assessment.

It is important for the donation and transplant community to consider and appreciate what this study has accomplished rather than focus on the unproven clinical hypothesis. The trial was well designed and well executed as a single organ procurement organization, multi-donor hospital, randomized, blinded and placebo-controlled trial driven by a power calculation. The sheer magnitude of this endeavor cannot be minimized as the regulatory and operational challenges associated with conducting large-scale donor management and/or intervention trials have been considered a barrier for other investigators. This study's current success may well be attributable, at least in part, to the intervention under study—aerosolized albuterol, a widely used therapy for a variety of common conditions. The low and known risk profile of the study drug likely facilitated the ability to carry out this study involving a myriad of donor hospitals and organ recipients. However, it is easy to envision the ethical, logistical and regulatory challenges that would be posed by unfamiliar interventions with undefined toxicity profiles. Arguably, it is these novel agents rather than the commonplace clinical workhorses that are most likely to exert a transformative impact on the number and/or the quality of deceased donor organs. Leaders of the organ

donation and transplantation communities have recently convened a multi-disciplinary conference to seek clarification and establish consensus with respect to the optimal infrastructure necessary to support the design, execution and oversight of large-scale, multi-institutional donor intervention trials (6). It is hoped that the initiation of dialog and cooperation among the innumerable stakeholders inclusive of governmental and regulatory bodies will identify algorithmic solutions that will invigorate the clinical science ultimately yielding more and better organs for transplantation.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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