

REGISTRY EDITORIAL

# Increasing complexity of thoracic transplantation and the rise of multiorgan transplantation around the world: Insights from the International Society for Heart and Lung Transplantation Registry



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The International Society for Heart and Lung Transplantation International Thoracic Organ Transplant Registry Report, now in its 35th annual iteration,<sup>1-4</sup> provides insight into the qualitative and quantitative advances in the application of thoracic transplantation around the world. This year, the Transplant Registry Steering Committee selected multiorgan transplantation as the focus theme for the reports. The last decade has seen a gradual but considerable rise in multiorgan transplants, although their absolute rates remain low. Multiorgan transplant recipients present new challenges for the transplant team, increasing demands on the infrastructure, need for generation of standardized protocols for post-operative care across organs, including immunosuppressive treatment and anti-microbial prophylaxis. The registry outcomes suggest that when selected carefully, multiorgan transplants (heart-kidney, heart-liver, heart-lung) demonstrate favorable short-term and long-term survival compared with isolated heart or lung transplantation. Curiously, recipients of combined organ transplants have a lower incidence of immune-related complications, including acute rejection, cardiac allograft vasculopathy, and bronchiolitis obliterans syndrome.<sup>1,2</sup>

The increasing performance of multiorgan transplants is one aspect pointing to the increased complexity of thoracic

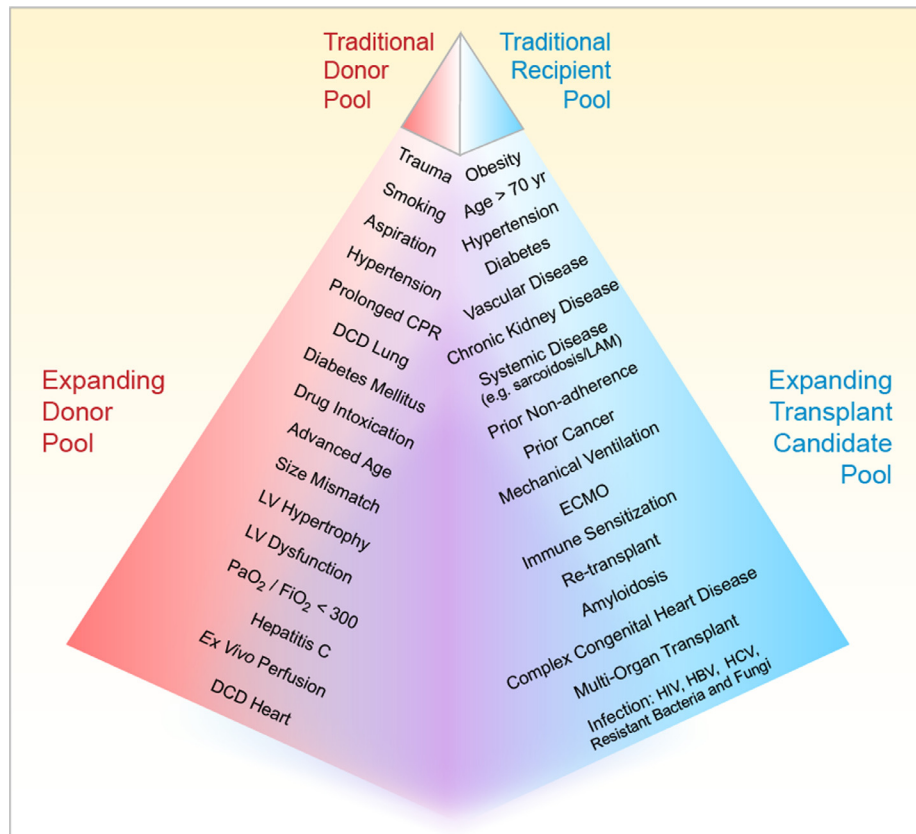
transplantation in the current era. The recipient now presents with multiple complexities, and there is increasing acceptance to tolerate these conditions, a reflection of the changing epidemiology of transplantation. In heart transplantation, age has increased significantly during the past 2 decades, with an ever-increasing proportion of recipients older than 60 years (24% of all recipients in 2006 up to 29% in 2016). Similarly, patients with complex congenital heart disease (CHD) and those with underlying chronic infections and conditions, such as cardiac amyloidosis, are now acceptable candidates for transplantation.<sup>5</sup>

Not surprisingly, the burden of recipient comorbidities has increased in parallel, with increases in recipient weight, prior smoking history, hypertension, and diabetes. Indeed, the prevalence of recipient diabetes mellitus, which was initially considered a contraindication to transplantation, has increased from 15% in the 1992 to 2003 era to 27% in the most recent era of 2009 to June 2017.<sup>2</sup>

Adding to the complexity of finding an appropriate donor match and post-operative immunosuppression is the observation that the proportion of sensitized candidates (defined as panel reactive antibody > 10%) has increased from 8% 15 to 20 years ago to >20% today. This partly reflects the increasing use of mechanical circulatory support as a bridge to transplantation. Currently, more than 50% of patients are bridged with one or more forms of mechanical support, including percutaneous and durable ventricular assist devices (VADs), total artificial heart, and extracorporeal membrane oxygenation

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**Figure 1** Changing demographics of the thoracic transplant donor and recipient. CPR, cardiopulmonary resuscitation; DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LAM, lymphangioleiomyomatosis; LV, left ventricle; PaO<sub>2</sub>/FiO<sub>2</sub>, partial pressure of arterial oxygen/fraction of inspired oxygen ratio.

(ECMO), such that conducting heart transplantation in a patient without a previous sternotomy has become quite unusual.<sup>2</sup>

Advances in reparative surgery for CHD have resulted in a higher number of CHD patients who achieve better quality of life and longer survival, yet many progress to requiring transplantation (e.g., “failing” Fontan physiology). Despite the increased risk of peri-transplant complications and early post-transplant mortality, CHD transplant recipients tend to have a very good prognosis in the long-term. These patients, who often have concomitant liver disease, may be evaluated for combined heart-liver transplantation. The decision to perform such combined organ transplant procedures in patients with advanced CHD is never straightforward, and the indications, operative techniques, and post-operative care strategies are still being evaluated, debated, and revised.

Progress in cancer therapy provides lasting remission to many patients, yet the cardiotoxicity of chemotherapeutic agents may lead to the need for heart transplantation, with its specific challenges for perioperative and long-term care.<sup>5</sup> Increasingly, patients with prior cancer and a history of chest wall radiation present a unique complex group that requires better study for suitability.

In lung transplantation, patients with cystic fibrosis are living longer and are presenting to transplantation older and

with more comorbidities. More patients with idiopathic pulmonary fibrosis (IPF) than ever before are receiving transplants, significantly increasing the age of the average lung transplant recipient. IPF is a disease of older individuals—it is 5- to 10-times more common in those aged older than 65 than those younger than 55 years. These influences mean that disease of non-pulmonary organs in the transplant recipient is more common than before, which may be driving a change in the types of multiorgan procedures being offered (Figure 1).

Secular changes have also extended to the organ donor (Figure 1). The continued divergence between the rising number of transplant candidates added to the transplant waiting list and the number of suitable organ donors has increased pressure on clinicians to maximize the use of available thoracic organs for transplantation. Donor age at acceptance is increasing, as are underlying comorbidities. Median donor age in 2016 was 32 years in adult heart and 38 years in adult lung transplantation. Transplantation of heart and lung allografts from well-selected donors aged > 60 years is no longer uncommon. A recent analysis of data from the Spanish Heart Transplantation Registry was cautiously reassuring, demonstrating no survival disadvantage in recipients of donor hearts aged ≥ 50 years.<sup>6</sup> However, after multivariate adjustment, recipients of these older hearts did have

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