Defining and Refining Heart Failure Risk Stratification to Optimize Patient Selection for Cardiac Transplantation

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\[ \text{VO}_2 \text{, BNP, GFR, RAP, CI, LVEDP, EF, Na, BUN, MR, LVEDD, PCWP, PVCs, VT, QRS, LBBB, COPD, DM, Tpnl, alb, CAD, OSA, Hct, RDW, CRT, ICD, HRV—} \]

the complex alphabet soup of heart failure risk assessment used to inform clinical decision making, select patient cohorts for trials, and ensure that expensive and supply-limited treatments are utilized in the most effective and equitable manner. Despite the seeming complexity of this task, heart failure clinicians have become facile at integrating multiple distinct variables into a cohesive understanding of risk using baseline patient characteristics, measures of cardiac structure and function, biomarkers, and assessment of functional capacity. The prognostic significance of many risk-associated parameters, such as ejection fraction, ventricular size, and the pathogenesis of heart failure are firmly established. However, recognition of the importance of common comorbidities and the rapidly evolving field of novel biomarkers that represent perturbation of normal biological pathways or markers of early organ damage have reshaped and refined contemporary risk assessment.

More recently, larger datasets have facilitated the derivation of multivariable risk-prediction models, such as the Heart Failure Survival Score, the Seattle Heart Failure Model, and the ESCAPE Risk Score. The benefits of cardiac transplantation are time-limited with a median survival of 10 years. Thus, transplanting patients whose a priori mortality risk is not sufficiently high may actually shorten overall survival. The present study confirms that patients with left ventricular systolic dysfunction whose peak \( \text{VO}_2 \) exceeds 14 mL/kg per min do not routinely derive a mortality benefit from transplantation and suggests that serial risk assessment is appropriate. Conversely, patients with a peak \( \text{VO}_2 \) <10 mL/kg per min have a predicted short-term mortality that exceeds transplantation regardless of modifiers and should be considered for transplantation if eligible. It is the patient population with an intermediate peak \( \text{VO}_2 \) that requires additional testing to accurately assess mortality risk. Elevated plasma BNP seems to fill this void and provides incremental prognostic information. If validated, this approach could be applied broadly to improve selection of patients more likely to benefit from transplantation.

There is beauty in the simplicity of this observation. The authors have demonstrated that risk assessment can be refined using data elements currently available in centers with
experience in the diagnosis and management of advanced heart failure, and it is appealing to combine a functional parameter and a biomarker that reflects heart failure physiology, two fundamental principles that might be anticipated to predict heart failure outcomes. This approach would also be expected to enhance risk stratification for other advanced heart failure therapies such as mechanical circulatory support, particularly as this field begins investigation in a less moribund, ambulatory heart failure population.

The importance of accurate risk assessment in heart failure cannot be overstated. During the past decade, there has been no appreciable change in number of cardiac transplant procedures performed in the United States, despite a growing number of patients who might potentially benefit from the therapy. This combination of factors has led to a call for the Thoracic Committee of the United Network for Organ Sharing to examine issues of access and equity in heart allocation. Recent changes in heart allocation policies focused on enhanced risk assessment, and regionalized organ sharing have reduced waiting-list mortality and improved post-transplant survival. However, it is thought that there are opportunities for further risk stratification of patients awaiting cardiac transplantation. For example, allocation of 30 days at the highest priority (status 1A) on the heart transplant waiting list for stable patients supported on an LVAD has been questioned. It has been accurately argued that the risk of death in LVAD patients using elective status 1A time is quite low and is not equivalent to the risk of similarly listed patients utilizing other 1A criteria. However, once an LVAD patient develops a device-related complication that qualifies for 1A transplant listing, the pre-transplant mortality risks are higher than nearly any other patient cohort. Waiting-list mortality for other conditions, such as congenital heart disease and restrictive cardiomyopathies, may also be underestimated and result in inequitable access to donor hearts. These conditions often do not require the therapeutic interventions that qualify a potential recipient for transplant listing at the highest priority.

The Thoracic Committee is currently considering several options to improve waiting-list risk stratification that would allow expedited transplantation of high-risk patients. Strategies being considered include expansion and more granular definition of the current listing statuses and development of a heart allocation score similar to that used to allocate lungs in the United States. There seems to be consensus that waiting-list prioritization should be based on the risk associated with objective pathophysiologic parameters, rather than potentially arbitrary therapeutic interventions. In addition, waiting-list mortality and post-transplant survival are intimately linked in the determination of organ allocation effectiveness, and both must be considered in any attempt to enhance allocation policy. Optimal utilization of the limited supply of donor hearts each year will require us to define new and innovative risk-stratification methodology and to refine our existing tools so that the sickest patients will be afforded the timely opportunity for transplantation.

Disclosures
Dr Rogers serves as the Vice Chairman of the Thoracic Committee for the United Network for Organ Sharing (UNOS). The views expressed in this editorial do not necessarily reflect those of UNOS. Dr Rogers reports no other disclosures.

References

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