HEART FAILURE AND TRANSPLANTATION
Journal Watch
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REVIEWS:

Meyer, D; et al. "The Future Direction of the Adult Heart Allocation System in the United States." *Am J Transplant* 2015; Jan 15(1): 44-54.

Reviewed by Rajeev Mohan

This article reviews the efforts of the OPTN/UNOS Heart Subcommittee of the Thoracic Committee in conjunction with the Scientific Registry of Transplant Recipients (SRTR) to evaluate the current heart allocation system in an effort to improve outcomes. The impetus to conduct a review of the current system was based on two factors. The waiting list mortality rate amongst the highest acuity patients remains high, and the prevalence of mechanical circulatory support has changed the demographics of the waiting list population. The stated goals of the subcommittee are to improve waiting list mortality as well as post-transplant survival.

The committee felt that the major limitation of the current three-tiered system is that it does not distinguish between candidates within a specific status. The committee identified several options to create a more equitable system based on urgency. These options were to change the qualifying criteria for entry into each status, expand the number of tiers, and/or develop a formal heart allocation scoring system. It was felt, however, that developing a formal scoring system would be time intensive and that it would not be easily modifiable in an era of rapidly changing MCS technology. Additionally, the data available to create such a scoring system is limited. Because of this, the committee has proposed prospectively collecting data that could be used for a future scoring system. Ultimately, an expansion of tiers was considered the best option.

Their analysis led to a "straw man" model that will be used by the SRTR in their thoracic simulation allocation model (TSAM). The TSAM is a program that has been used in the past by the SRTR to assess changes to allocation policy. It uses actual organ acceptance data in a given period of time to simulate organ donation, acceptance, and outcome based on inputted rules. These rules can then be altered to assess the effect of rule changes on organ allocation and outcome. Outcomes are projected using Cox proportional hazard models. This program will be used to develop multiple iterations of results based on incremental rule changes from the current system to the new "straw man" model.

The proposed model increases the number of candidacy tiers from 3 to 6. Tiers 1 through 3 correspond roughly to Status 1A in the current system. Tier 4 corresponds to Status 1B, while Tier 6 is equivalent to Status 2. The details of each tier are provided below.

Tier 1 is given the highest priority and consists of patients with any of the following:

1. ECMO
2. Mechanical ventilation

3. Non-dischargeable VAD
4. MCS with life-threatening ventricular arrhythmias

Tier 2 consists of patients with the following:

1. Intra-aortic balloon pump
2. Ventricular tachycardia or fibrillation without MCS
3. MCS with device malfunction or mechanical failure
4. Total artificial heart
5. Dischargeable BiVAD or RVAD

Tier 3 comprises:

1. Elective 30 day candidacy time for stable LVAD patients
2. Status 1A exception
3. Multiple inotropes or high-dose single inotrope with continuous hemodynamic monitoring
4. MCS with infection, thromboembolism or other complications

Tier 4 is assigned to patients with a variety of diagnoses including:

1. Complex congenital heart disease
2. Ischemic heart disease with intractable angina
3. Hypertrophic cardiomyopathy
4. Restrictive cardiomyopathy
5. Amyloidosis
6. Stable LVAD patients beyond 30 days
7. Inotropes without hemodynamic monitoring
8. Re-transplant
9. Status 1B exception.

Tier 5 consists of patients approved for combined organ transplants while tier 6 is for all remaining candidates. Tier 7 is designated for patients who are inactive or not candidates.

In their effort to consider the expansion of the number of tiers, the committee reviewed 6-month waiting list mortality and post-transplant survival. This was based on status as well as diagnosis for patients listed and transplanted between 2010 and 2011. The committee also reviewed all Status 1A and 1B exceptions requests between July 2009 and June 2011 to assess which patient populations required increased urgency in a modified allocation system.

With respect to modifying the allocation system to account for patients with VADs, several analyses were done. This included evaluating waitlist mortality of patients with stable LVAD function as well as those with device complications. The SRTR used the TSAM program to assess outcomes based on elective 30, 45, 60 and 90 day Status 1A time in stable LVAD patients. This showed no difference in the number of wait list deaths or transplant rates in the different time allowances and so this policy was not changed.

Another consideration in modifying the allocation system included options for improving distribution of organs by offering hearts to Status 1A patients over a broader geographic area prior to allocating them to Status 1B and 2, as well as eliminating local zone allocation altogether. Finally the committee recognized the need for a universal definition of the highly sensitized candidate and reviewed policies in other allocation systems including Canada. This will be further reviewed with the OPTN/UNOS Histocompatibility Committee to develop a more equitable solution.

Once the proposed model is reviewed by the Thoracic Committee, it will be open for public comment. After the commentary period closes, the committee will review these comments and finally send it to the OPTN/UNOS Board of Directors. If approved, the final phase of the project will be implementation.

The only limitation of this approach to the modification to the allocation system is the reliance on models to get an understanding of how rule changes will affect transplant rates and outcomes. It assumes acceptance behavior will not change in response to rule changes and is also based on historical acceptance behavior. The TSAM program, however, appears to be a good starting point in understanding broadly how policy changes may affect outcomes and has been used in the past to assess changes to allocation policy.

The proposed model addresses the limitations of a three-tiered system and the increasing complexity of the waiting list population due to the increased use of MCS. By increasing the number of tiers, it distinguishes patients based on their acuity to a much more specific level such as giving patients on ECMO the highest priority. It prioritizes patients with MCS-related complications who are at risk for increased morbidity and mortality. It also prioritizes patients with total artificial hearts in whom there is no alternative besides transplant in the event of device complication. It establishes priority for several under-represented groups in the current allocation system including patients with congenital heart disease as well as restrictive cardiomyopathies that may not result in systolic dysfunction with the need for LVADs. Expanding the number of tiers and including more specific definitions for qualification into a specific tier will hopefully improve organ allocation to the sickest patients with the greatest need for transplant without negatively affecting post-transplant survival.

Jayarajan, S; et al. "Long-term outcomes in heart transplantation using donors with a history of past and present cocaine use." ***Eur J Cardiothorac Surg*** **2015; Jan 9. pii: ezu512. [Epub ahead of print]**

Reviewed by Burhan Mohamedali

Donor heart availability is a major bottleneck for orthotropic heart transplantation. As a result, there has been an increased need to review the pool of high-risk donor patients whose organs have conventionally been rejected for transplantation. This article examined long-term outcomes in heart transplantation from donors with a history of current or present cocaine use. This retrospective study analyzed UNOS registry data in excess of 19,500 patients over the ten year period between January 2000 and December 2010. In the above cohort, the authors identified 2274 donors (11.6%) with a history of cocaine use, of which 1008 donors were active cocaine users. Cox proportional hazard analysis using covariates associated with mortality was used to examine survival between donors with history of cocaine use [2274 (11.6%)], and donors with no such history [17362 (89.4%)].

Baseline demographic information revealed no significant baseline differences between the two groups except: cocaine users were older in age, more likely to be men, had a lower BMI, had higher proportion of tobacco use, and were more likely to show clinical signs of infection. Kaplan Meier survival analysis did not detect any statistically significant difference in survival between the two cohorts (median survival of 3843 days in cocaine users vs. 4165 days in patients without history of cocaine use, $p = 0.87$.) Similarly, there was no difference in survival between donors with active cocaine use compared to donors with a past history of cocaine use. Cox proportional hazard analysis examining risk of mortality at ten years revealed that overall cocaine use was not significantly associated with higher mortality (HR 0.95, 95% CI 0.87-1.03). Similarly, active cocaine use was not associated with increased mortality (HR: 0.97, 95% CI 0.89-1.05, $p= 0.42$).

The negative effect of cocaine on the heart is well known and often leads to the donor being labeled "high risk," leading to subsequent rejection of the donation. What was unique about this study is that it examined long term survival in patients who had received a heart from a donor with a history of either remote or active cocaine use. Although short-term outcomes in patients who have undergone heart transplantation from a cocaine user

donor have shown acceptable survival at 5 years, the current study extended the analysis to 10 years. Additionally they also demonstrated that such "high risk donor" hearts can be used safely even in older recipients, and in cases of prolonged ischemic time. They further demonstrated that acute rejection episodes at 1 year post-transplantation were not increased, nor was there a need for increased length of hospital stay in those patients.

Although this study has important implications in allowing for utilization of a larger pool of heart donors, the retrospective nature of the study warrants further investigation. Additionally, they included patients with active or history of cocaine use. The exact amount or method of use was not available. Finally duration since last cocaine use was not available. In conclusion, the study strongly suggests that cocaine user donors' hearts can be procured and successfully transplanted with comparable 10-year survival compared to donors who don't use cocaine.

ARTICLES OF INTEREST:

American Journal of Transplantation:

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Journal of Heart and Lung Transplantation:

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Takeda K, et al. Outcome of cardiac transplantation in patients requiring prolonged continuous-flow left ventricular assist device support. *J Heart Lung Transplant*. 2015 Jan;34(1):89-99.

Quader MA, et al. Heart transplantation outcomes in patients with continuous-flow left ventricular assist device-related complications. *J Heart Lung Transplant*. 2015 Jan;34(1):75-81.

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Alsoufi B, et al. Results of heart transplantation following failed staged palliation of hypoplastic left heart syndrome and related single ventricle anomalies. *Eur J Cardiothorac Surg*. 2015 Jan 18. pii: ezu547.

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Tang WH, et al. Comparative Assessment of Short-Term Adverse Events in Acute Heart Failure With Cystatin C and Other Estimates of Renal Function: Results From the ASCEND-HF Trial. *JACC Heart Fail*. 2015 Jan;3(1):40-9.

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Collins S, et al. for the SAEM/HFSA Acute Heart Failure Working Group. Early management of patients with acute heart failure: state of the art and future directions. A consensus document from the society for academic emergency medicine/heart failure society of america acute heart failure working group. *J Card Fail*. 2015 Jan;21(1):27-43.