Chapter 3

Donor Heart Allocation

Louis H. Stein, Mohammad Choudhary and
Scott C. Silvestry

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.74819

Abstract

The limited number of donor hearts is one of the greatest and persistent challenges to heart transplantation. Allocation of this precious resource requires the integration of objective data, clinical intuition, and moral fairness. Institution of an allocation system by UNOS has provided important structure to the allocation methodology. The system must be periodically reviewed and reorganized to ensure it is reflective of current patient disease and clinical practice and builds upon the previous knowledge paradigms. Since the establishment of the 2006 allocation system, not only has there been a dramatic increase in the number of heart transplant candidates, but also a dramatic increase in the number of patients qualifying as high-priority candidates. To address these changes, UNOS Thoracic Organ Transplantation Committee was tasked with providing a revised allocation system. The resulting system aims to improve waitlist mortality and post-transplant outcomes by better prioritizing the highest acuity patients while improving the geographic distribution of organ offers.

Keywords: allocation, adult congenital heart disease, donor service area (DSA), exception rule, mechanical circulatory support (MCS), LVAD, scientific registry of transplant recipients, status, thoracic organ transplantation committee, thoracic surgery allocation modeling, UNOS

1. Introduction

Orthotropic heart transplantation (OHT) has become the gold standard of therapy for end stage congestive heart failure (CHF). Among patients with advanced heart failure treated medically, the *mortality* at 1 year ranges from 75 to 94% [1–4]. In contrast, survival for OHT is 82% at 1 year, 69% at 5 years, with a median survival of 10.7 years [5]. The most profound limitation to OHT is the rarity of donor organs [6].

Deciding which donor graft should be offered to which recipient requires a balancing act of important clinical and ethical issues. One must balance those at highest risk of dying while waiting, who also have the highest risk of post-transplant death, compared with those with improved likelihood of post-transplant survival. The mortality associated with different subgroups evolves over time. For example, Morality following MCS implantation has significantly decreased over the last decade; while the use of MCS and ECMO have simultaneously burgeoned. A similar issue is the compromise for geographic equity. Cold ischemia should be minimized. Local donors of the highest acuity are first offered donor hearts. Compromises must be made when deciding if a less acute patient should be offered a heart over a farther patient of higher acuity.

The goal of heart allocation policy has remained to provide appropriate organs to those patients who were the "best" candidates with the shortest expected survival given geographic constraints. Fundamental rules of current practice were initially formed from small US heart transplant centers. Such rules were entertained without any clinical or physiological basis, simply "because they sounded good" [7]. The United States Heart Allocation system has evolved from its formal inception as a basic two tiered, local plus three zone system in 1989 to a three-tiered urgency based heart allocation system in 1998 [8–10]. Further modification occurred in 2006, integrating pediatric allocation and refining geographic ordering of heart offers.

2. The creation of the 2006 system

In the 1990s, UNOS classified heart transplant recipients using a two tiered system [8]. Those patients who necessitated either ICU care with inotropic infusions, support with MCS, or an IABP were given the highest priority, Status 1. The remaining patients were listed as Status 2. In 1999, the system was reappraised to include a Status 1A, 1B, and 2. In that era, mortality following LVAD implant reaches 5–10% per week [9]. Therefore, patients could be listed as 1A with ≤30 days of LVAD support. Alternatively, patients with >30 days of support and a device related complication could also be listed as 1A. This policy was subsequently revised in 2002 to permit listing any LVAD patient for 30 days once the treating physician determined they were "clinically stable." Criteria for listing patients as 1A just prior to the most recent change are listed in **Table 1**.

Status 1B was created for waiting list candidates with less urgent need for cardiac transplantation such as candidates stably waiting at home or in the hospital requiring intravenous inotrope or LVAD support. Active patients who were stable at home on oral medications were listed as Status 2 (**Table 1**).

Other important changes included in the 2006 revisions to the US allocation system included: (1) the integration of the allocation of pediatric hearts, (2) the institution of Geographic proximity in determining organ preference, and (3) utilizing ABO compatibility in determining generating priority. After initial offers to waiting list candidates in local or Donor Service Area (DSA) served by an organ procurement organization (OPO), offers then progressed to successive 500 mile geographic zones. Preference was given to ABO identical and then ABO compatible recipients within each status category and allocation proceeded to candidates eligible to receive a heart from any blood type donor after allocation to all compatible blood types.

Status	Criteria
1A	1. Continuous Hemodynamic monitoring in the setting of either ➢ infusion of a single high-dose intravenous inotrope ➢ multiple intravenous inotropes 2. Mechanical Circulatory Support with either: ➢ total artificial heart (TAH) , ➢ intra-aortic balloon pump (IABP) ➢ extracorporeal mechanical oxygenation (ECMO) ➢ mechanical ventilation 3. A ventricular assist device (VAD) for a discretionary 30 day period. 4. A Device related complication 5. An approved exception.
1B	1. VAD 2. Continuous infusion of inotropes
C	1. Patients stable on home oral medication

Table 1. Indications for listing status prior to 2017.

Patients with restrictive diseases such as amyloidosis or those adults with congenital heart disease relied on prioritization based on "exception criteria." For a given patient, a transplant center must elect to request for an exception from a given region through a review board. This mechanism created the potential for regional variability in patient status due to regional practices and organ availability with resultant unequal access to transplantation.

3. The changing land scape of heart failure and issues with the 2006 allocation

The management paradigm and spectrum of potential heart transplant recipients has changed dramatically. In 2006, 1203 patients were listed for transplant rising to 3008 by 2015 [8]. As would be expected in a system prioritizing the most urgent patients, Status 1A have received the majority of heart transplants on an annual basis since 1998. According to the Scientific Registry of Transplant Recipients (SRTR), the number (%) of Status 1A listed for transplant has gone from 660 (34.8% of the waitlist) to 1190 (58.4% of the weight list). In the same time period, the Status 1B has gone from 723 (38.8% of the waitlist) to 743 (3.5% of the waitlist), and Status 2 from 509 (26.9%) to 102 (5.0% of the wait list). (Scientific Registry of Transplant Recipients, 2016) In the same period, Status 1A patients increased from 5–13% of all patients listed. Sixty-seven percent of those who received transplants in 2015 were status 1A; however, those listed as 1A were three times more likely to die while on the transplant waiting list.

With refinement therapy for advanced heart failure the expected clinical course of patients listed as 1A have notably diverged. In particular, Mechanical circulatory support (MCS) technology has dramatically expanded driven by improved survival since prioritization was first established [11]. MCS supported patients now includes a wide spectrum ranging from deteriorating CHF to acute cardiogenic shock, while utilizing a larger range of percutaneous

and implantable devices. In 2006, 8.9% of candidates were registered with MCS criteria. By 2015, MCS patients increased to 24.4% [8]. MCS has concurrently expanded to distinct applications, with a wide range of expected mortality. Patients with RVAD support experience a log10 higher mortality on the wait list compared to those with LVAD. The increased use of MCS has also resulted in a similarly complex array of complications. Clearly, the MCS *per se* is no longer suitable as a dichotomous gage for acuity and transplant listing.

A criticism of the 2006 policy between patient prioritization and geographic proximity was that the allocation rule was inconsistent with the UNOS mandate that access to organs "shall not be based on the candidate's place of residence or place of listing …" [12]. By first offering hearts to waiting list candidates listed as Status 1A and 1B at transplant hospitals within the DSA and then broadened to waiting list candidates in status listed 1A or 1B in surrounding Zones (A and B), geographically close, high acuity patients may have very different access and outcomes. A patient with high acuity patient at a hospital designated as Zone A, although only 25 miles away from the donor institution, could be listed to receive an offer after less acute patients within the DSA [8].

The 2006 paradigm for heart allocation places significant emphasis on patients with MCS, and prioritizing them for eventual transplant. As a consequence of this, the system has an inbuilt bias in favor of patients with systolic dysfunction. A large component of patients, such as those with lethal arrhythmia or heart failure with preserved ejection fraction (HFpEF), does not fit within this clinical spectrum [13]. Patients requiring exceptions to the group requiring exceptions is a heterogeneous group. The most common exceptions for status 1A were: (1) candidate is experiencing ventricular tachycardia or ventricular fibrillation; (2) candidate does not have intravenous access for inotropes or cannot tolerate a pulmonary artery catheter; and (3) congenital heart, while the most common exceptions for listing as status 1B were: (1) candidate is experiencing ventricular tachycardia or ventricular fibrillation; (2) congenital heart disease diagnosis; and (3) candidate requires a re-transplant. These six criteria comprise over half of those listed for exception. These patients are inherently susceptible to regional variability as their institution must first elect to apply for exception, which must be approved by the regional. Therefore, they were considered to ensure they not become marginalized in a new system. To be listed for OHT, these patients necessitate applying administrative exception for listing represents a growing component of the transplant candidate cohort.

4. The 2018 system

In 2016 the UNOS Thoracic Organ Transplantation Committee proposed changes to this allocation system, which were subsequently ratified. One of the first strategies proposed was the design of a heart allocation scoring system [8]. This is an attractive method in that a scoring system could provide a more objective method based on patient related data. This method is not without precedence. The Lung Allocation Score (LAS), which weighs pre-transplant morality risk against post-transplant survival, has been used in the allocation of donor lung grafts [14]. While the concept of a Heart Allocation Score (HAS) was strongly advocated by many, The

Thoracic Organ Transplantation Committee determined there was too little data to provide an accurate reliable score. Therefore, the committee elected to proceed with a modification of the allocation system with plans for a HAS in a future iteration.

A new prioritization that could better reflect the clinical needs of patients in the present day was needed. Analysis demonstrated that patients supported with continuous flow LVAD (cfLVAD) demonstrated a mortality closer to Status 2 patients than those at Status 1A or B (such as those requiring inotropic therapy [9, 10, 15]. Conversely, mortality has remained high among patients with biventricular support or among patients with LVAD related complications [15]. Analysis of waitlist and post-transplant mortality data was used to construct a "straw man" model [10]. The SRTR utilized thoracic surgery allocation modeling (TSAM) to determine the effects of these changes on the newly proposed Status system, which did not suggest a change in waitlist or post-transplant deaths [10].

The resulting system contained six statuses. Much of Status 1 was partitioned to better reflect the candidate's relative urgency as reflected by waitlist mortality data. Status 1A candidates were re-stratified into Status 1–3. Status 4 is roughly equivalent to Status 1B, with the addition of patients who would require exception status to apply for transplantation. The new status policy is presented in **Table 2** with its equivalent 2006 status.

To provide higher acuity patients over a wider region, geographic distribution of organs was restructured. In the revised system, offers would be made to Status 1 patients with in the DSA and Zone followed by Zone B. Status 2 patients would then be extended the offer. These changes strike a balance between broadened access to a precious resource and availability to closer patients of lesser acuity [8].

5. Unmet challenges and future concerns

In spite of some substantial intrinsic changes to the heart donor allocation system, some important issues remain unaddressed. Some scenarios of concern were not addressed in the formulation of 2018 prioritization. Among this population of concern include highly sensitized recipients, those with adult congenital heart disease (ACHD), patients requiring multiple organ transplants. Similarly, potential issues regarding geographic redistribution remain.

Highly sensitized patients present a theoretically vulnerable cohort. Because of their high frequency of cross reactivity, they would presumably benefit require a broader donor pool. The 2006 allocation system provided some provisions for out of sequence prioritization of patients with high PRA. Few centers have reported complete PRA data; therefore, little data can be extrapolated to demonstrate the impact of sensitization on survival. Despite multiple attempts to provide appropriate priority for highly sensitized patients, sufficient data did not exist within the SRTR to develop appropriate offsets.

ACHD represents several challenges for allocation. The 2006 system necessitated application for an exception for optimal prioritization, which may be subject to inconsistent regional preferences and biases. The natural history of ACHD is a full spectrum of complex cardiac. There is still room to develop consistent criteria that are comparable to other cardiac diseases.

2006 Status	2018 Status	Indications
1A	1	ECMO[1] Non-dischargeable VAD[2] MVS with life threatening arrhythmia [2]
	2	Non-dischargeable LVAD[2] Percutaneous endovascular LVAD[2] IABP[2] VT/VF without MCS[2] MCS with mechanical failure[2] Dischargeable BiVAD/RVAD/TAH[2]
	3	Dischargeable LVAD[3] High Dose inotrope / multiple inotropes requiring monitoring[2] MCS with: • hemolysis[2] • pump thrombosis[2] • RV failure[2] • Infection[6] • mucosal bleeding[7] • aortic insufficiency[8] ECMO[4] Non-Dischargeable LVAD[5] Percutaneous Endovascular LVAD[5] IABP[5]
1B	4	Congenital heart disease[8] Hypertrophic cardiomyopathy[8] Restrictive cardiomyopathy[8] Dischargeable LVAD[8] Inotropes without monitoring[8] Intractable angina[8] Re-transplant[8]
	5	Multi -organ transplant[9]
2	6	All others[9]

Table 2. 2006 status with 2018 status and corresponding indications. The duration of listing varies by indication. 1: Renewable every 7 days. 2: Renewable every 14 days. 3: Discretionary 30-day period. 4: If Status 1 is not renewed. 5: If Status 2 is not renewed. 6: 14 days if clinical evidence of driveline infection, 42 days if bacteremia requiring antibiotic, 90 days if device pocket infection or recurrent bacteremia. 7: 14 days if two hospitalizations in 6 months, 90 days if 3 times in past 6 months. 8. Renewable every 90 days 9. 180 days.

The current practice of combined organ transplant involving Heart-Lung or Heart-other is inconsistent at best. Patients for combined organ would be listed at a minimum as status 5 but the majority of patients would qualify for higher status. The actual allocation of combined thoracic/thoracic-abdominal organs is inconsistently applied and varies from OPO to OPO despite policies aiming to clarify this practice. Current efforts within the transplant community seek to standardize these practices.

Although the geographic distribution of organ offers has been addressed in the 2018 paradigm, the exact unit of correction is unclear. Equal 500 mile circles do not yield equal access to potential organ offers. Should geography be indexed to population? Should the number of

transplant centers encompassed by these widening circles be factored into this algorithm? Further, all Organ Procurement Organizations do not perform equally, with regional, cultural, and religious differences contributing to willingness to donate as well as inherent differences in OPO practices and efficiencies. Should geography be indexed to create equal access in potential organ offers? Lastly organ acceptance varies greatly from program to program [16]. By offering wider circles of potential organ offers, is the new system incentivizing conservative acceptance practices instead of remedying geographic disparities in heart transplantation for acutely ill patients?

Therapeutic escalation has been a concern with the current system and will likely continue to be a concern with new allocation systems. Some have postulated that some centers will utilize temporary mechanical support in clinical scenarios that previously were treated with medical bridging (inotropes) or durable mechanical circulatory support in an effort to prioritize their patients. Despite stricter requirements for data and verification, no system will be able to prevent behavior aimed at simply improving the chances of heart transplantation by choosing one therapy over another. Further comparing the transplant needs of a patient on ECMO with a patient with a total artificial heart/durable biventricular support is difficult; given the initial condition may have been cardiogenic shock for both patients. Similar patients may be treated differently in centers with implications for transplant access that is the result of the center choices not patient acuity- a difference that is hard to incorporate into allocation policy.

6. Conclusion

The 2018 UNOS allocation system is rooted in the 2006 allocation reflects the evolution of the practice of heart failure since explosion of mechanical circulatory support. This next iteration of the allocation system focuses on present era mortality rates among like pools of candidates and seeks to improve regional sharing for more acute patients. It seeks to reduce waiting list mortality rates by allocating organs to the most critically ill candidates, rectify issues with specific patients groups, and incorporate broader geographic sharing to optimize access and limit regional disparities while keeping post-transplant survival (within each status) comparable to the current system. Future allocation systems will likely evolve toward a global heart allocation score.

Author details

Louis H. Stein[1]*, Mohammad Choudhary[1] and Scott C. Silvestry[2]

*Address all correspondence to: louis.stein@downstate.edu

1 Downstate Medical Center, Division of Cardiothoracic Surgery, State University of New York, Brooklyn, New York, United States

2 Florida Hospital Transplant Institute, Orlando, Florida, United States

References

[1] Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, et al. Long-term use of a left ventricular assist device for end-stage heart failure. The New England Journal of Medicine. 2001;**345**(20): 1435-1443

[2] Tarichko IV, Sankar NM, Cherkasov I. Rupture of the posterior wall of the left ventricle after mitral valve prosthesis. Khirurgiia (Mosk). 1991;**6**:125-128

[3] Hershberger RE, Nauman D, Walker TL, Dutton D, Burgess D. Care processes and clinical outcomes of continuous outpatient support with inotropes (COSI) in patients with refractory endstage heart failure. Journal of Cardiac Failure. 2003;**9**(3):180-187

[4] Fang JC, Ewald GA, Allen LA, Butler J, Westlake Canary CA, Colvin-Adams M, Dickinson MG, Levy P, Stough WG, Sweitzer NK, et al. Advanced (stage D) heart failure: A statement from the Heart Failure Society of America Guidelines Committee. Journal of Cardiac Failure. 2015;**21**(6):519-534

[5] Lund LH, Edwards LB, Dipchand AI, Goldfarb S, Kucheryavaya AY, Levvey BJ, Meiser B, Rossano JW, Yusen RD, Stehlik J, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirty-third Adult Heart Transplantation Report-2016; Focus Theme: Primary diagnostic indications for transplant. The Journal of Heart and Lung Transplantation. 2016;**35**(10):1158-1169

[6] Colvin M, Smith JM, Skeans MA, Edwards LB, Uccellini K, Snyder JJ, Israni AK, Kasiske BL. OPTN/SRTR 2015 Annual Data Report: Heart. American Journal of Transplantation. 2017;**17**(Suppl. 1):286-356

[7] Frazier OH. Personal communication

[8] OPTN/UNOS Thoracic Organ Transplantation Committee. Proposal to Modify the Adult Heart Allocation System. In: OPTN/UNOS Briefing Paper; 2016

[9] Moazami N, Sun B, Feldman D. Stable patients on left ventricular assist device support have a disproportionate advantage: Time to re-evaluate the current UNOS policy. The Journal of Heart and Lung Transplantation. 2011;**30**(9):971-974

[10] Meyer DM, Rogers JG, Edwards LB, Callahan ER, Webber SA, Johnson MR, Vega JD, Zucker MJ, Cleveland JC Jr. The future direction of the adult heart allocation system in the United States. American Journal of Transplantation. 2015;**15**(1):44-54

[11] Coke M, Edwards LB. Current status of thoracic organ transplantation and allocation in the United States. Clinical Transplants. 2004:17-26

[12] 42 CFR 121.8. In: United States Code of Federal Regulations; 2011

[13] Reddy YN, Borlaug BA. Heart failure with preserved ejection fraction. Current Problems in Cardiology. 2016;**41**(4):145-188

[14] Lehr CJ, Zaas DW. Candidacy for lung transplant and lung allocation. Thoracic Surgery Clinics. 2015;**25**(1):1-15

[15] Wever-Pinzon O, Drakos SG, Kfoury AG, Nativi JN, Gilbert EM, Everitt M, Alharethi R, Brunisholz K, Bader FM, Li DY, et al. Morbidity and mortality in heart transplant candidates supported with mechanical circulatory support: Is reappraisal of the current United Network for Organ Sharing Thoracic Organ Allocation policy justified? Circulation. 2013; **127**(4):452-462

[16] Khush KK, Zaroff JG, Nguyen J, Menza R, Goldstein BA. National decline in donor heart utilization with regional variability: 1995–2010. American Journal of Transplantation. 2015;**15**(3):642-649