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Impact of increased time at the highest urgency category on heart transplant outcomes for candidates with ventricular assist devices

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BACKGROUND: Ventricular assist devices (VADs) have improved survival among end-stage heart disease patients. Since 2002, heart transplant candidates with VADs have been afforded 30 days of elective time at the highest urgency category (Status 1A) under Organ Procurement and Transplantation Network (OPTN) policy. We aimed to determine the effect of increasing elective time at the highest urgency category for heart transplant candidates with VADs. This analysis was requested by OPTN during its evaluation of heart allocation policy.

METHODS: We simulated several allocation schemes wherein elective Status 1A time was increased to 45, 60, and 90 days; results were compared with a baseline simulation of 30 days and with the actual observed heart transplant waiting list cohort.

RESULTS: The simulations showed that increasing elective Status 1A time for candidates with VADs did not substantially change waiting list mortality overall or for sub-groups of concern, which were candidates with VADs listed at a lower-urgency category (Status 1B), those with with VAD complications, total artificial heart, or intraaortic balloon pump support; or those with extracorporeal membrane oxygenation. Across the different time allowances, the average post-transplant death rate remained stable. It also remained stable for recipients previously listed as Status 1A or 1B categories for VAD and for recipients with VAD complications or an intraaortic balloon pump at transplant, on extracorporeal membrane oxygenation, and those without devices.

CONCLUSIONS: Our results suggest that increasing time in the highest urgency category for candidates with VADs would not improve waiting list mortality or post-transplant outcomes for heart transplant candidates overall.

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Ventricular assist devices (VADs) can be used as bridges to transplant in patients with advanced heart failure and deteriorating clinical status. Third-generation continuous-flow VADs, which have fewer complications, improved durability, and broader application due to smaller size, have resulted in improved survival to transplant compared with

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prior devices.[1] For this reason, the management of advanced heart failure has shifted toward increased use of VADs among patients listed for heart transplant.[2]

VAD recipients may or may not be candidates for heart transplant.[3] The highest urgency category for heart transplant listing in the United States (U.S.) is Status 1A. Typically, candidates are listed at Status 1A for 7 to 14 days, at which point recertification is required. However, under the current allocation system in the U.S., which was significantly revised in 2002, all heart transplant candidates with VADs may accrue 30 days at Status 1A electively when the provider determines suitability for listing.[4] Under Organ Procurement and Transplantation Network (OPTN) Policy 3.7, this elective category for VADs is Status 1A(a)(i). We previously showed that less than 30% of candidates listed as Status1A for 30 days under this policy undergo transplant during this period. However, the proportion of new candidates with VADs on the heart transplant waiting list grew from 3% to 22% between 2007 and 2013,[5] suggesting that an increasing number of candidates with VADs will expend their Status 1A time and be required to undergo transplant under another urgency category. The question arises whether 30 days is an appropriate period of Status 1A time during which candidates with VADs can undergo heart transplant.

To continue allocating hearts to the sickest candidates, the allocation policy will need to address the appropriate duration of Status 1A time for VAD patients without VAD-related complications. The OPTN Heart Subcommittee, in its review of the heart allocation policy, considered whether increasing the current Status 1A allotment of 30 days for VAD patients would improve the transplant rate for this group and considered the effect of a proposed policy change on waiting list and post-transplant mortality for this group and other sub-groups of interest. The potential policy change would increase the 30 days at Status 1A to 45 days, 60 days, or 90 days. We evaluated the effect of this increase on waiting list mortality, access to transplant, and post-transplant mortality.

Methods

Study population

The analysis was performed using Scientific Registry of Transplant Recipients (SRTR) standard analysis files. The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the U.S., submitted by the members of OPTN, and has been described elsewhere.[6] The Health Resources and Services Administration, U.S. Department of Health and Human Services, provides oversight of the activities of the OPTN and SRTR contractors. Included were all heart transplant candidates on the heart, heart-lung, and lung waiting lists between July 1, 2009, and June 30, 2011, and any heart, lung, or heart-lung donors whose organs were offered for transplant during this period.

Modeling approach

We performed simulations using the thoracic simulated allocation modeling (TSAM) software, which is used by the OPTN committees to assess policy proposals.[7] The TSAM simulates the arrival of donated organs and new candidates on the waiting list over a 2-year period, checks compatibility of organs with candidates on the waiting list when an organ becomes available, creates ordered lists of compatible candidates based on the allocation rules being tested, predicts candidate acceptance or refusal of organ offers using a logistic regression model based on historic organ acceptance behavior, calculates the number of transplants and of organs recovered but not transplanted, and assigns an estimated post-transplant death date for each patient.

We simulated 4 policy scenarios: 30, 45, 60, and 90 days of Status 1A time allotted to patients with VADs. The TSAM repeated each simulation 10 times. Several elements of variability were introduced across the repetitions, including a random reordering of donor organ arrivals and the use of a random number in the organ acceptance process such that if a candidate were to receive an identical offer in 2 different repetitions of the same simulation, the candidate could not make the same acceptance decision both times. Because the same donors and candidates were used in each of the simulations and were the actual donors and candidates from July 1, 2009, to June 30, 2011, and hence not independent samples from a larger population, statistical tests of significance are not possible. Instead, the minimum-maximum range and average of results for the 10 repetitions are described for each simulation. This range reflects the variability of the simulation modeling but the not variability in actual organ allocations.

Candidate and recipient demographics and outcomes (waiting list mortality, transplant rates, and post-transplant mortality) are reported for actual waiting list candidates observed under current policy, as simulated under current policy (30 days of Status 1A VAD allotment), and as simulated under proposed policies that extend the Status 1A time for VADs to 45, 60, and 90 days. To extend the Status 1A time allotments under the alternate policy scenarios, we altered candidates' status histories according to the following predetermined algorithm:

We assumed that extending the Status 1A time for VAD candidates would not change the start date of the elective period of 1A time, so the first observed period of 1A time for a VAD candidate was extended to 45, 60, or 90 days by converting actual periods of Status 1B time. Periods of Status 1A time for other reasons, Status 2 time, and inactive time were not changed. For simplicity and because only 18% of observed candidates used their elective 30 days of Status 1A VAD time in more than 1 period, VAD candidates in the simulation were assumed to use all of their Status 1A time consecutively, except as interrupted by Status 1A time for other reasons, Status 2 time, or inactive time. For these reasons, and due to the general limitations of the TSAM, results of the simulated 30-day policy differ from actual results observed under the current 30-day policy. Therefore, the effects of changing the policy are best understood by comparing the 45-day, 60-day, and 90-day simulations to the baseline 30-day simulation rather than to actual waiting list outcomes.

Waiting list mortality rates and transplant rates were defined as the number of deaths and the number of transplants per 100 patient-years on the waiting list, respectively. For device-specific rate calculations, exposure time was initiated at the earliest record of device use (i.e., any VAD) or status-specific device use (i.e., Status 1A VAD) and continued until death, transplant, removal from the waiting list, or June 30, 2011. Post-transplant mortality rates were defined as the number of deaths per 100 patient-years of follow-up within the first 2 years after transplant.

Recipients were categorized into device-specific groups by cumulative device use until the time of transplant. Because candidates may have used more than 1 device or experienced

more than 1 status upgrade associated with each device, they could contribute time to more than 1 rate calculation and be included in the counts for more than 1 device group.

Results

Between July 1, 2009, and June 30, 2011, 9,727 candidates were on the heart transplant waiting lists (Table 1). Of these, 4,442 underwent transplant during the observed analysis period, and simulations resulted in a range of 4,629 to 4,657 transplants for the various Status 1A allowances (Table 2). Of the observed candidates, 719 (7.4%) died while waiting (Figure 1).

Waiting list mortality and transplant rates

Observed outcomes

Waiting list mortality rates among observed candidates were highest for those with a history of intraaortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) use, both of which confer automatic Status 1A(a)(iii) and Status 1A(a)(iv) upgrades (Table 3). These 2 groups represented 21% of all deaths. Transplant numbers and transplant rates for observed candidates are shown in Figure 2 and reported in Table 4, respectively. The transplant rate was highest for candidates with a history of total artificial heart (TAH) use, which confers an automatic Status 1A(a)(ii) upgrade (Table 4), although this group underwent the smallest proportion (1.1%) of transplants (Figure 2). The transplant rate was higher for candidates with a history of VAD use or use of any device than for candidates with no history of device use (Table 4).

Simulated outcomes

The overall waiting list mortality rate remained stable, at an average of 5.1 deaths per 100 patient-years across the simulations (Table 3). The waiting list mortality rates for candidates at Status 1A for stable VAD ranged from 9.7 to 10.3 per 100 patient-years across the various allocation policies simulated (Figure 1). Because all minimum-maximum ranges overlapped, there was no evidence for a change in waiting list death rates with increased VAD Status 1A time. The waiting list death rate for candidates with no device use did not change, remaining at 4.1 deaths per 100 patients-years across the proposed policy variations.

There was no evidence that increasing the Status 1A(a)(i) time to 45, 60, or 90 days for VAD candidates would negatively affect transplant rates for the other device groups. However, transplant rates for VAD candidates listed as Status 1A(a)(i) increased 20%, from 154.0 to 185.1 transplants per 100 patient-years, when the Status 1A listing time was increased from 30 to 90 days (Table 4). The average number of transplants performed in candidates with no devices declined slightly, from 2,585.3 to 2,570.9, but this did not result in an appreciable decline in the transplant rate or the relative proportion of transplants performed in this group (Figure 2). The rate is unlikely to decrease appreciably due to the size of the group.

Table 1 Observed Heart Transplant Waiting List Candidates and Recipients, July 1, 2009, to June 30, 2011

Characteristics	Waiting list No. (%)	Recipients No. (%)
Age, years		
< 18	1,293 (13.3)	712 (16.0)
18–34	985 (10.1)	407 (9.2)
35–49	1,861 (19.1)	779 (17.5)
50–64	4,320 (44.4)	1,948 (43.9)
≥ 65	1,268 (13.0)	596 (13.4)
Race/ethnicity		
White	6,581 (67.7)	2,991 (67.3)
Black	1,974 (20.3)	859 (19.3)
Hispanic	840 (8.6)	402 (9.0)
Asian	247 (2.5)	149 (3.4)
Other/unknown	85 (0.9)	41 (0.9)
Sex		
Male	6,995 (71.9)	3,169 (71.3)
Female	2,732 (28.1)	1,273 (28.7)
Primary diagnosis		
Coronary artery disease	3,234 (33.2)	1,510 (34.0)
Cardiomyopathy	4,896 (50.3)	2,392 (53.8)
Congenital heart disease	922 (9.5)	413 (9.3)
Valvular heart disease	158 (1.6)	67 (1.5)
Other/unknown	517 (5.3)	60 (1.4)
Blood type[a]		
A	3,528 (36.3)	1,787 (40.2)
B	1,159 (11.9)	627 (14.1)
AB	355 (3.7)	245 (5.5)
O	4,684 (48.2)	1,783 (40.1)
Device		
VAD		
Status 1A	1,638 (16.8)	1,064 (24.0)
Status 1B	2,340 (24.1)	1,160 (26.1)
Complications	780 (8.0)	498 (11.2)
IABP	799 (8.2)	388 (8.7)
TAH	62 (0.6)	49 (1.1)
ECMO	177 (1.8)	76 (1.7)
Any VAD	2,924 (30.1)	1,651 (37.2)
Any device	3,487 (35.8)	1,937 (43.6)
Status history		
Ever 1A	4,962 (51.0)	3,105 (69.9)
Ever 1B	5,527 (56.8)	2,922 (65.8)
Ever 2	4,451 (45.8)	1,421 (32.0)
Ever inactive	4,118 (42.3)	1,164 (26.2)
Status at transplant		
1A	…	2,654 (59.7)
1B	…	1,477 (33.3)
2	…	311 (7.0)
Donor locality		
Local	…	2,296 (51.7)
Zone A	…	1,792 (40.3)
Zone B	…	316 (7.1)
Zone C	…	35 (0.8)
Zone D	…	3 (0.1)
Zone E	…	0 (0)

ECMO, extracorporeal membrane oxygen; IABP, intraaortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

[a]Blood type was unknown for 1 candidate (in utero).

Table 2 Comparison of Baseline Characteristics of Heart Recipients

	Observed	Simulated			
Variable	30-Day No. (%)	30-Day Mean No. (%)	45-Day Mean No. (%)	60-Day Mean No. (%)	90-Day Mean No. (%)
Blood type					
ABO: A	1,787 (40.2)	1,866.2 (40.2)	1,853.8 (40.0)	1,856.4 (40.0)	1,851.5 (39.9)
ABO: AB	245 (5.5)	265.1 (5.7)	264.3 (5.7)	263.9 (5.7)	265.3 (5.7)
ABO: B	627 (14.1)	679.3 (14.6)	679.1 (14.6)	678.6 (14.6)	674.1 (14.5)
ABO: O	1,783 (40.1)	1,833.1 (39.5)	1,838.5 (39.7)	1,843.7 (39.7)	1,852.1 (39.9)
Race/ethnicity					
Asian	149 (3.4)	149.8 (3.2)	149.9 (3.2)	149.0 (3.2)	150.4 (3.2)
Black	859 (19.3)	973.3 (21.0)	976.5 (21.1)	977.7 (21.1)	979.0 (21.1)
Hispanic	402 (9.0)	415.9 (9.0)	418.0 (9.0)	414.3 (8.9)	417.7 (9.0)
Other/unknown	41 (0.9)	42.2 (0.9)	40.0 (0.9)	41.9 (0.9)	39.9 (0.9)
White	2,991 (67.3)	3,062.6 (66.0)	3,051.3 (65.8)	3,059.7 (65.9)	3,056.0 (65.8)
Age, years					
<12	503 (11.3)	523.1 (11.3)	523.1 (11.3)	524.3 (11.3)	522.8 (11.3)
12–17	209 (4.7)	213.7 (4.6)	213.7 (4.6)	212.1 (4.6)	210.4 (4.5)
18–34	407 (9.2)	443.2 (9.6	443.2 (9.6)	444.9 (9.6)	443.5 (9.6)
35–49	779 (17.5)	857.3 (18.5)	857.3 (18.5)	858.3 (18.5)	857.9 (18.5)
50–64	1,948 (43.9)	2,033.9 (43.9)	2,033.9 (43.9)	2,042.4 (44.0)	2,043.4 (44.0)
≥ 65	596 (13.4)	564.5 (12.2)	564.5 (12.2)	560.6 (12.1)	565.0 (12.2)
Status at time of transplant					
1A	2,654 (59.7)	2,846.3 (61.3)	2,900.2 (62.6)	2,943.5 (63.4)	2,983.8 (64.3)
1B	1,477 (33.3)	1,538.9 (33.1)	1,477.9 (31.9)	1,443.8 (31.1)	1,406.3 (30.3)
2	310 (7.0)	258.6 (5.6)	257.6 (5.6)	255.3 (5.5)	252.9 (5.4)
Diagnosis group					
CAD	1,427 (32.1)	1,481.5 (31.9)	1,483.4 (32.0)	1,482.9 (31.9)	1,487.6 (32.0)
Cardiomyopathy	2,352 (52.9)	2,461.3 (53.0)	2,446.0 (52.8)	2,455.7 (52.9)	2,459.2 (53.0)
Congenital	385 (8.7)	411.4 (8.9)	412.9 (8.9)	413.3 (8.9)	408.0 (8.8)
Valvular disease	70 (1.6)	75.0 (1.6)	77.8 (1.7)	77.4 (1.7)	76.4 (1.6)
Other/unknown	156 (3.5)	214.6 (4.6)	215.6 (4.7)	213.3 (4.6)	211.8 (4.6)
Geographic zone where heart originated					
Local	2,296 (51.7)	2,578.9 (55.5)	2,578.4 (55.6)	2,591.3 (55.8)	2,593.9 (55.9)
Zone A	1,792 (40.3)	1,679.7 (36.2)	1,674.7 (36.1)	1,677.7 (36.1)	1,669.8 (36.0)
Zone B	316 (7.1)	318.2 (6.9)	315.6 (6.8)	310.4 (6.7)	314.8 (6.8)
Zone C	35 (0.8)	58.4 (1.3)	57.9 (1.2)	56.4 (1.2)	55.8 (1.2)
Zone D	3 (0.1)	8.4 (0.2)	8.8 (0.2)	6.5 (0.1)	8.4 (0.2)
Zone E	0	0.2 ($<$ 0.1)	0.3 ($<$ 0.1)	0.3 ($<$ 0.1)	0.3 ($<$ 0.1)
Cumulative device use at time of transplant					
VAD 1A	1,127 (25.5)	1,066.2 (23.0)	1,093.5 (23.6)	1,119.4 (24.1)	1,148.0 (24.7)
VAD 1B	1,117 (25.2)	1,134.7 (24.4)	1,152.5 (24.9)	1,172.1 (25.2)	1,193.8 (25.7)
VAD with complications	498 (11.3)	414.8 (8.9)	412.2 (8.9)	409.0 (8.8)	405.3 (8.7)
Any VAD	1,545 (34.9)	1,792.6 (38.6)	1,820.3 (39.3)	1,840.2 (39.6)	1,823.8 (39.3)
IABP	386 (8.7)	423.3 (9.1)	428.4 (9.2)	428.0 (9.2)	404.1 (8.7)
ECMO	71 (1.6)	84.8 (1.8)	86.2 (1.9)	86.8 (1.9)	71.4 (1.5)
TAH	47 (1.1)	48.4 (1.0)	48.9 (1.1)	49.4 (1.1)	47.7 (1.0)
Any device	1,815 (41.0)	2,059.5 (44.3)	2,087.8 (45.0)	2,108.1 (45.4)	2,073.1 (44.6)
No device	2,611 (59.0)	2,585.3 (55.7)	2,548.9 (55.0)	2,535.5 (54.6)	2,570.9 (55.4)

CAD, coronary artery disease; ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

Post-transplant mortality

Observed

Numbers of observed post-transplant deaths are shown in Figure 3. The post-transplant death rate within the first year after transplant was 10.9 per 100 patient-years and was lowest for recipients without devices, at 9.6 per 100 patient-years (Table 5).

Simulated

In general, the simulations for 45-day, 60-day, and 90-day time allotments for Status 1A(a)(i) did not negatively affect the post-transplant mortality rates of recipients with or without devices, and the overall rate remained stable across the simulations at approximately 15 per 100 patient-years (Table 5). There was a trend toward a slight increase in

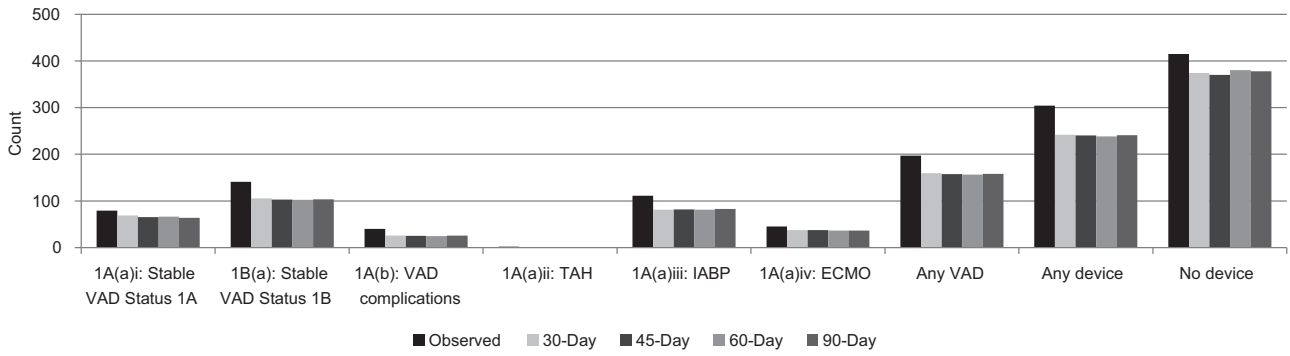

Figure 1 Observed and simulated average waiting list death counts by device use at 30, 45, 60, and 90 days. ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

post-transplant mortality for stable VAD recipients, in that the average post-transplant mortality rates in the 90-day simulation were all higher than in the 30-day simulation. However, because all of the minimum-maximum ranges overlapped, the trends in the death rates did not correspond to substantial changes in the proportion of deaths (Figure 3). Overall, the simulations did not result in a noticeable redistribution or increase in waiting list deaths, transplants, or post-transplant deaths for heart transplant candidates (Figures 1–3).

A sensitivity analysis was conducted by limiting the results to adult transplant candidates and recipients. Results were similar (Supplementary Tables S1–S4 and Supplementary Figures S1–S3, available on the jhltonline.org Web site).

Discussion

Our study examined the effects of increasing elective time at the highest urgency category, Status 1A(a)(i), for heart transplant candidates with VADs from the current 30 days to 45, 60, and 90 days. We found that neither waiting list mortality nor post-transplant mortality improved for these candidates. A small increase occurred in the frequency and rate of transplants. The increased transplant rate was anticipated, because the longer time at a higher-urgency category likely resulted in more offers per candidate. More remarkably, there was no appreciable reduction in the overall transplant rate or increase in waiting list or post-transplant mortality for other high-urgency candidates across the simulations. In the sub-group analysis, we found a slight decline in transplant rates at 90 days for candidates with TAH, IABP, and no device, but with overlap in the ranges between the time points. Numbers of transplants also declined in the ECMO, TAH, IABP, and no-device groups. These changes did not correspond to consistently increasing waiting list death counts or rates for any of the groups.

The original intent of the current 30-day Status 1A policy for VAD candidates was to expedite transplants for them during the era of pulsatile devices to circumvent life-threatening complications, such as device failure, which occurred in up to 44% of candidates bridged with pulsatile devices.[8] Performing transplants in VAD candidates too early after implantation might have complicated outcomes and led to the elective 30-day listing instead of immediate listing. However, almost all VADs implanted today are continuous flow, which have a lower failure rate than pulsatile devices. Use of VADs in heart transplant candidates continues to grow; only 3% of newly listed candidates used a VAD at listing in 2007 compared with 22% in 2012, and

Table 3 Observed and Simulated Waiting List Death Rates per 100 Patient-Years by Specific Status and General Device Use

	Observed	30-Day		45-Day		60-Day		90-Day	
Variable	Rate	Rate	Range	Rate	Range	Rate	Range	Rate	Range
Status									
1A(a)(i): stable VAD Status 1A	10.1	9.9	9.3–10.5	9.7	8.8–10.5	10.3	8.9–11.0	10.3	9.5–10.9
1B(a): stable VAD Status 1B	8.6	7.3	6.8–7.6	7.1	6.8–7.6	7.2	6.4–7.7	7.4	7.1–7.8
1A(b): VAD complications	12.6	10.0	7.6–11.8	9.9	8.2–11.2	9.9	6.6–11.9	10.3	8.9–12.0
1A(a)(ii): TAH	10.9	5.1	0–7.1	3.8	0.0–6.6	4.0	0.0–7.0	5.7	0.0–6.9
1A(a)(iii): IABP	18.1	16.7	15.5–17.8	17.0	15.4–18.2	16.9	16.2–17.6	17.2	15.9–18.8
1A(a)(iv): ECMO	41.6	34.8	31.9–39.4	35.2	33.1–37.5	33.6	31.4–36.4	34.1	30.0–38.1
Overall	5.9	5.1	5.0–5.1	5.1	5.0–5.1	5.1	5.0–5.2	5.1	5.0–5.2
Device use regardless of status									
Any device	12.7	11.1	10.9–11.4	11.1	10.8–11.6	11.2	10.6–11.7	11.4	11.1–11.8
Any VAD	9.8	8.7	8.4–9.2	8.7	8.4–9.0	8.8	8.2–9.3	8.9	8.7–9.2
No device	4.6	4.1	4.0–4.2	4.1	4.0–4.1	4.1	4.1–4.2	4.1	4.0–4.2
Overall	5.9	5.1	5.0–5.1	5.1	5.0–5.1	5.1	5.0–5.2	5.1	5.0–5.2

ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

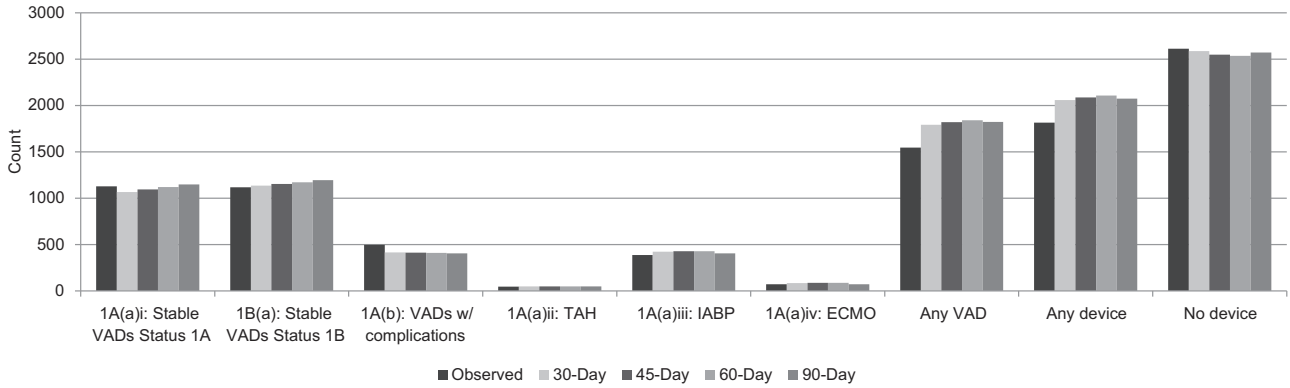

Figure 2 Observed and simulated average transplant counts by device use at 30, 45, 60, and 90 days. ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

41% of transplant recipients in 2012 used a VAD at the time of transplant compared with 23% in 2007.[9] The current allocation policy has not accounted for the transition to almost exclusive use of continuous-flow devices. Yet, most candidates with VADs who are listed as Status 1A(a)(i) for 30 days do not undergo transplant during this 1A time; in fact, only 22% do.[10] This raises the question of whether the current policy sufficiently addresses the needs of candidates on the heart transplant waiting list in the era of continuous-flow devices. One potential policy change considered by the OPTN Heart Subcommittee was to increase the duration of Status 1A time for VAD candidates, which would necessarily increase the likelihood of those patients undergoing transplant at Status 1A but might negatively affect other candidates. However, our simulations demonstrated that despite a modest increase in transplant rates for VAD candidates, there was no negative or positive effect on waiting list death or early post-transplant death.

For several reasons, increasing the time allocated to VAD candidates listed as Status 1A(a)(i) to 45, 60, or 90 days may not improve waiting list mortality. Waiting list mortality has already improved substantially for candidates with VADs and currently compares favorably to mortality rates for candidates without VADs due to improved durability of pumps and the transition to earlier and more frequent use of durable devices as bridges to transplant.[2] During the past decade, waiting list mortality among patients with VADs at the time of listing improved from 100.9 per 100 waiting list years in 2001 to 13.3 per 100 waiting list years in 2012.[9] Thus, demonstrating any change in survival among candidates who are electively listed for VAD may be difficult. Our analysis did not demonstrate a decrement in waiting list survival among candidates with VADs listed as Status 1A for complications; however, although transplants increased modestly in candidates with stable VADs, the transplant rate did not change for candidates with VADs with complications in the simulation, and waiting list and post-transplant deaths remained comparable. There was a theoretic concern that extending the Status 1A time for stable VAD candidates could result in a relative modest reduction in transplants in candidates with VADs with complications, arguably a higher urgency population, thereby attenuating the potential benefit of being listed in this category. However, the simulations do not support this concern.

The increase in VAD use has contributed to notable improvements in waiting list candidate survival. With this success, new challenges have arisen regarding allocation of

Table 4 Observed and Simulated Transplant Rates per 100 Patient-Years by Specific Status and General Device Use

	Observed	30-Day		45-Day		60-Day		90-Day	
Variable	Rate	Rate	Range	Rate	Range	Rate	Range	Rate	Range
Status									
1A(a)(i): stable VAD Status 1A	143.7	154.0	149.5–156.8	162.4	158.7–167.8	173.5	162.7–177.4	185.1	180.2–193.5
1B(a): stable VAD Status 1B	67.8	78.2	76.0–79.8	79.9	76.7–82.6	83.0	79.3–85.3	85.6	83.1–88.2
1A(b): VAD complication	156.5	162.6	146.8–170.2	162.4	153.6–168.8	162.8	152.9–179.1	164.6	165.0–171.4
1A(a)(ii): TAH	255.4	306.6	248.2–355.4	308.0	269.4–331.1	320.7	225.2–358.5	299.1	276.5–347.5
1A(a)(iii): IABP	62.9	82.1	79.8–86.0	83.9	78.7–87.5	84.1	81.0–87.3	83.9	81.3–86.3
1A(a)(iv): ECMO	65.6	63.8	57.5–71.5	64.1	57.5–70.8	64.7	58.9–70.2	66.5	61.3–73.2
Overall	36.3	38.3	38.1–38.4	38.2	38.1–38.3	38.3	38.1–38.5	38.3	38.2–38.5
Device use regardless of status									
Any device	76.0	92.9	91.4–94.6	94.6	91.8–97.2	96.8	93.8–97.8	98.6	97.1–100.2
Any VAD	77.1	96.7	95.4–98.7	98.7	95.7–101.9	101.5	97.6–103.4	103.8	102.2–105.8
No device	28.8	28.7	28.2–28.9	28.3	28.0–28.9	28.1	27.8–28.6	27.9	27.7–28.2
Overall	36.3	38.3	38.1–38.4	38.2	38.1–38.3	38.3	38.1–38.5	38.3	38.2–38.5

ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

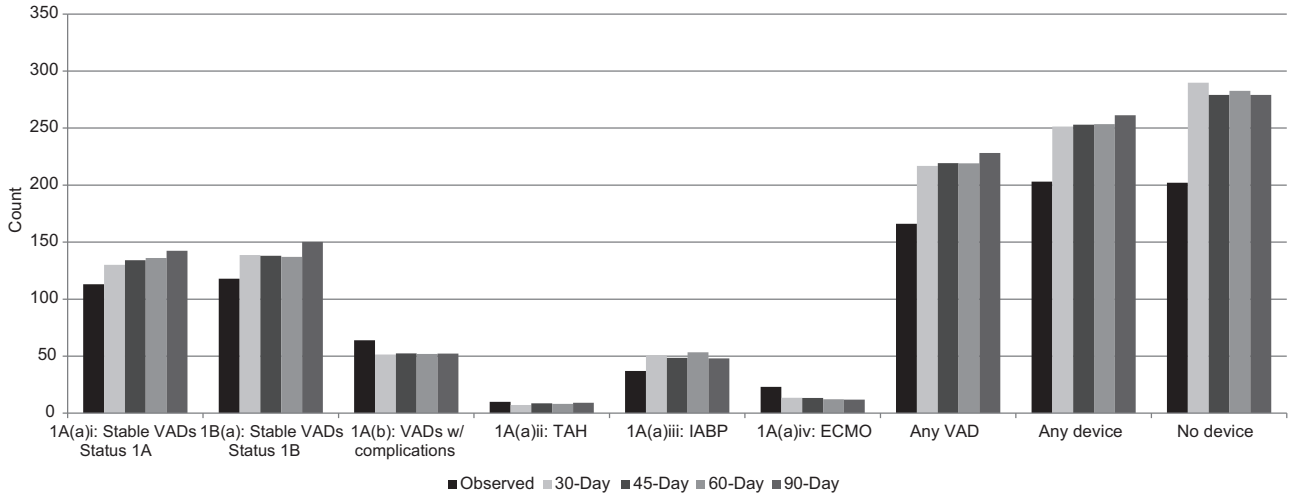

Figure 3 Observed and simulated average post-transplant death counts by device use at 30, 45, 60, and 90 days. ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

donor hearts. Our simulations failed to show an improvement in waiting list or post-transplant mortality, the former representing an important measure of the efficacy of allocation policies. Extension of elective Status 1A time for VAD candidates remains highly controversial.[11] Some view the current policy of 30 days' priority as unjust because VAD technologies and thereby VAD patient survival have improved, and they fear that the prioritization of all VAD candidates comes at the detriment of candidates without VADs. Even VAD thrombosis can be treated with VAD replacement in appropriate patients, with subsequent mortality similar to VAD patients without thrombosis.[12] Proponents of this viewpoint suggest that the Status 1A(a)(i) time should be eliminated.

Support for extension of Status 1A time stems from the fact that VAD complications persist. A recent study reported an almost 4-fold increase in VAD thrombosis since 2011 and an associated 6-month mortality of 48%.[12] Performing transplants after VAD complications have developed may compromise post-transplant outcomes and abrogate any potential benefit that may have been realized by having the VAD. In this setting, increasing Status 1A(a)(i) time may expedite transplant and avoid unnecessary and potentially fatal VAD complications.

Outcomes are worse for transplant candidates with VADs who have Interagency Registry for Mechanically Assisted Circulatory Support Profile 1, defined as critical cardiogenic shock,[13] and avoidance of implantation in this group has been recommended. As a result, some of these highly acute patients may be managed with IABP, ECMO, and non-durable devices, which under the current allocation policy are associated with the highest waiting list mortality (Table 3). For those in favor of a Status 1A extension for VAD candidates who are electively listed for heart transplant, the question is how such an extension would affect patients who do not qualify for durable mechanical circulatory support due to acuity of illness or anatomy. Delaying transplant in these candidates in favor

Table 5 Observed and Simulated Post-transplant Death Rates per 100 Patient-Years by Specific Pretransplant Status and General Pretransplant Device Use

	Observed	30-Day		45-Day		60-Day		90-Day	
Variable	Rate	Rate	Range	Rate	Range	Rate	Range	Rate	Range
Status									
1A(a)(i): stable VAD Status 1A	11.9	15.8	14.4–17.8	16.0	14.1–18.5	16.2	13.5–18.9	16.4	13.2–18.4
1B(a): stable VAD Status 1B	13.0	16.1	15.0–18.4	15.6	13.5–17.8	15.5	13.9–17.7	16.8	15.5–19.0
1A(b): VAD complications	14.4	16.6	14.5–20.5	16.9	11.2–22.8	17.5	14.2–21.5	17.2	15.2–21.2
1A(a)(ii): TAH	26.4	19.6	7.6–31.3	23.8	9.8–37.4	23.8	9.8–36.1	26.0	13.0–39.1
1A(a)(iii): IABP	11.7	16.2	13.2–20.5	14.9	11.8–18.6	16.9	13.1–20.7	15.6	13.1–19.1
1A(a)(iv): ECMO	44.6	25.5	17.5–35.6	22.8	12.8–35.4	22.2	17.1–30.8	22.0	13.3–29.8
Overall	10.9	15.2	14.2–16.1	14.8	13.7–16.2	15.0	13.6–16.2	15.1	14.2–16.0
Device use regardless of status									
Any device	12.8	16.1	15.0–17.5	15.9	14.7–18.2	16.0	14.4–17.5	16.5	15.4–18.0
Any VAD	12.2	15.7	14.6–17.6	15.7	14.6–18.3	15.8	13.8–17.4	16.5	15.3–17.8
No device	9.6	14.5	13.4–15.7	14.0	12.3–16.3	14.2	12.8–15.7	14.0	12.7–15.7
Overall	10.9	15.2	14.2–16.1	14.8	13.7–16.2	15.0	13.6–16.2	15.1	14.2–16.0

ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; TAH, total artificial heart; VAD, ventricular assist device.

of candidates with more stable devices could potentially increase waiting list mortality of these critically ill patients and worsen their post-transplant outcomes (Table 3). In addition, candidates with intractable angina, arrhythmias, cardiomyopathies with preserved left ventricular systolic function, and congenital heart disease may warrant higher urgency listing but do not fit the criteria; that is, they may not be candidates for inotropic agents or VADs and require listing as exceptions.

Prioritization of more "stable" candidates with VADs could potentially delay transplant for candidates who cannot be upgraded to a higher priority until their condition worsens and might increase their waiting list and post-transplant mortality and morbidity. Status 1A candidates on an ECMO or IABP had the highest mortality rates of all candidates and may have a survival disadvantage a priori. Percutaneous forms of support are limited due to inadequate left ventricular decompression, lack of durability, and local complications. Patients supported with temporary devices may already have a survival disadvantage, and prolonging the time to transplant could worsen their survival. Our simulation demonstrated the contrary, however; providing more time for Status 1A(a)(i) did not increase waiting list mortality for candidates with IABP, ECMO, or any device and did not result in reduction in transplant rates for these candidates. Only TAH candidates saw a decline in transplant rates from 60 to 90 days; however, from 30 to 45 to 60 days, the TAH transplant rate increased. TAH candidates were the smallest device group in the simulation and therefore the most difficult to accurately predict.

Our study has several limitations. Organ acceptance behavior in the TSAM is based on historic organ offers and acceptance, specifically from July 1, 2009, to June 30, 2011. Acceptance patterns are a function of the rules under which the organ was allocated. If allocation rules or status time allotments change, acceptance behavior may also change. The TSAM cannot account for such changes in organ acceptance behaviors.[7] However, given the limited supply of heart donors and the large number of candidates on the waiting list, the overall number of transplants is unlikely to increase. The TSAM simulates transplants, organs recovered but not transplanted, and removals from and deaths on the waiting list for a 2-year period.[7] Some effects of changes to organ allocation policy will endure beyond this time frame.

The TSAM was not designed to predict outcomes at the level of a transplant program or a donation service area because it assumes similar organ acceptance behavior across the country and assumes complete adherence to the national policy. As a result, determining the effect of the potential allocation policy on small geographic areas is not possible.

Finally, information regarding VAD types is limited, and as a result, broad VAD categories were used; however, these categories reflect the current policy under which hearts are allocated.

In conclusion, despite a substantial increase in Status 1A time from 30 to 90 days, transplant rates for candidates with a Status 1A stable VAD increased only 20%, and neither waiting list nor early post-transplant mortality was reduced. This insensitivity to change could suggest that the allocation system is constantly saturated with candidates at Status 1A and that adding more Status 1A time is not an efficient solution to the problem. Rather, different risk stratification of patients could better distinguish between types of Status 1A and prioritize those at higher risk of death[14]; not all VAD patients are at equal risk. Candidates with a history of ECMO or IABP have waiting list mortality rates higher than any VAD group, and candidates with VAD complications also die at a higher rate than candidates with stable VADs at either Status 1A or 1B. A better risk stratification could potentially positively affect multiple groups on multiple metrics, whereas the single revision would extend Status 1A time for stable VAD candidates, which we have shown to affect only the transplant rate of a single sub-group on the heart transplant waiting list.

Disclosure statement

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Supplementary materials

Supplementary material cited in this article is available online at www.jhltonline.org.

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