Prolonged Waitlisting is Associated with Mortality in ECMO-Supported Heart Transplantation Candidates

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**METHODS**

- 246 ECMO-supported candidates listed from 10/18/2018 to 03/21/2021 identified in the SRTR database
- Stratified based on waitlist time (≤7 days vs. ≥8 days)
- Primary outcome: 90-day post-listing survival

**RESULTS**

*Waitlisting for ≥8 days is associated with poor 90-day post-listing survival compared to those who undergo HTx within 7 days of listing (HR 5.59, 95% CI 2.59–12.1).*

**IMPLICATIONS**

- Obtaining a heart within one week of listing may improve survival.

CI, confidence intervals; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio; HTx, heart transplantation; SRTR, Scientific Registry of Transplant Recipients.
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Glossary of Abbreviations:
- ECMO, extracorporeal membrane oxygenation.
- HTx, heart transplantation.
- IABP, intraaortic balloon pump.
- LVAD, left ventricular assist device.
- SRTR, Scientific Registry of Transplant Recipients.
Central Picture

Prolonged listing is associated with worse 90-day post-listing survival.

Central Message

In heart transplant candidates supported by ECMO, undergoing transplant within the first week of listing may improve overall survival.

Perspective Statement:

The new donor heart allocation system places ECMO-supported candidates at highest status 1. A substantial portion, however, wait for more than one week, which predisposes candidates to deconditioning and ECMO-related complications. These candidates face a 5-fold increase in
hazard of 90-day post-listing mortality. Every effort should be made to obtain a transplant within one week of listing.

Structured Abstract (249 words)

Objective

Heart transplantation (HTx) candidates supported by venoarterial extracorporeal membrane oxygenation (ECMO) may be listed at highest status 1 but are at inherent risk for ECMO-related complications. The effect of waitlist time on post-listing survival remains unclear in candidates listed on ECMO under the new allocation system.

Methods

Adult candidates listed with ECMO for a first-time, single-organ HTx from 10/18/2018 to 03/21/2021 in the SRTR database were included and stratified by waitlist time (≤7 vs. ≥8 days). Post-listing outcomes were compared between cohorts.

Results

Among 175 candidates waitlisted for ≤7 days, 162 (92.6%) underwent HTx while 13 (7.4%) died/deteriorated compared to 41 (57.8%) and 21 (29.6%) of the 71 candidates waitlisted for ≥8 days, respectively (P<0.01). Blood type O candidates (odds ratio (OR) 2.94, 95% confidence interval (CI) 1.54–5.61) were more likely to wait ≥8 days while candidates with concurrent intraaortic balloon pump were less likely (OR 0.30, 95% CI 0.10–0.89). Obesity was additionally associated among those listed at status 1 (OR 2.04, 95% CI 1.00–4.17). Waitlisting for ≥8 days was independently associated with 90-day post-listing mortality conditional on survival to day 8 post-listing (hazard ratio (HR) 5.59, 95% confidence interval (CI) 2.59–12.1).
Candidates listed at status 1 demonstrated similar trends (HR 5.49, 95% CI 2.39–12.6). There was no significant difference in 90-day post-HTx survival depending on whether a candidate waited for ≥8 days versus ≤7 days (92.7 vs. 92.0%, log-rank \( P=0.87 \)).

Conclusions

Among ECMO-supported candidates, obtaining HTx within one week of listing may improve overall survival.

Keywords: Heart transplantation, Allocation system, Prolonged waitlisting

Graphical Abstract:

- Methods
  - 246 ECMO-supported candidates listed from 10/18/2018 to 03/21/2021 identified in the SRTR database
  - Stratified based on waitlist time (≤7 days vs. ≥8 days)
  - Primary outcome: 90-day post-listing survival

- Results
  - Waitlisting for ≥8 days is associated with poor 90-day post-listing survival compared to those who undergo HTx within 7 days of listing (HR 5.59, 95% CI 2.59–12.1).

- Implications
  - Obtaining a heart within one week of listing may improve survival.

CI, confidence intervals; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio; HTx, heart transplantation; SRTR, Scientific Registry of Transplant Recipients.
In October 2018, the Organ Procurement and Transplantation Network updated its donor heart allocation policy to permit candidates in florid biventricular failure, supported by either veno-arterial extracorporeal membrane oxygenation (ECMO) or surgical biventricular assist device, uncontended placement atop the waitlist with wider access to donor organs. This change was prompted by data demonstrating disproportionate waitlist mortality in this cohort under old allocation systems that permitted hemodynamically stable candidates to be listed at the same status. During discussion of the new donor heart allocation system in 2016, the decision to restrict the initial qualifying period to 7 days for those supported by ECMO sought to balance equitable access to donor organs while ensuring device use in appropriate patients. However, modeling studies demonstrated that approximately 15% of candidates would be supported for ≥8 days, leading to the decision to allow reapproval for status 1 candidacy following application to the regional review board.

As a result of these changes, candidates supported by ECMO have noticed a substantial decrease in waitlist time with an associated increase in survival to heart transplantation (HTx) and have, moreover, noticed an improvement in post-HTx survival. Although this improvement is an undoubted step in the right direction, candidates listed at status 1 continue to display waitlist mortality at a substantially higher rate than others, reflecting the tenuous condition of patients supported by ECMO in addition to its significant complication burden.
Previous studies of ECMO under the new allocation system have analyzed waitlist outcomes and post-HTx survival separately, without demonstrating how undergoing HTx affects the post-listing survival course of a patient. In the present study, we aim to evaluate 1) how waitlisting for ≥8 days affects post-listing survival; and 2) candidate characteristics associated with waitlist time ≥8 days.

METHODS

Data Source

The Scientific Registry of Transplant Recipients (SRTR) database was utilized in this analysis. The SRTR has prospectively collected data on all solid-organ transplant candidates, recipients, and donors in the United States since October 1, 1987. Since the SRTR database is publicly available and deidentified, this study was deemed exempt from Institutional Review Board review.

Inclusion and Exclusion Criteria

Adults (≥18 years old) listed for a single-organ HTx between October 18, 2018 and March 31, 2021 supported by ECMO at the time of listing were identified. Candidates listed for a re-do HTx or multiple organ transplant were excluded.

Study Definitions
Candidates were stratified by waitlist time ($\leq$7 vs. $\geq$8 days) with comparison of characteristics at
the time of listing. The cutoff of one week was chosen as candidates supported by ECMO must
be reapproved by the regional review board every 7 days to remain at status 1.

The primary end point was composed of death (either post-HTx or waitlist) or waitlist removal
due to clinical deterioration, since nearly three-quarters of these patient die within one year of
delisting. Survival time from listing was calculated as the sum of waitlist time and post-HTx
survival time; candidates who did not undergo HTx were assigned a post-HTx survival time of
zero.

**Statistical Analysis**

Continuous variables are presented as median (interquartile range (IQR)) and categorical
variables are presented as number (percent). Following stratification by waitlist time, baseline
demographics were compared using the Wilcoxon rank-sum test for continuous variables and the
Chi-square test or Fisher’s exact test for categorical variables. The Kaplan-Meier method and
log-rank tests were used to determine survival differences between groups. Candidates who did
not experience the outcome of interest were censored at 90 days post-listing. Variables included
in logistic regression and Cox proportional hazards models were selected based on clinical
and/or biological relevance. Additionally, collinearity was examined in all models utilizing the
variance inflation factor. Results of multivariable analyses are presented as hazard ratio (HR) or
odds ratio (OR), where appropriate, with accompanying 95% confidence interval (CI). These
analyses included the following:
I) Cox proportional hazards models examining 90-day post-listing survival conditional on survival to 8 days post-listing, which was performed to determine difference in post-listing outcomes between those who were alive at this point following HTx versus those who were alive at this point on the waitlist;

II) Logistic regression to determine risk factors associated with waitlist time ≥8 days;

and

III) A subanalysis of post-HTx survival utilizing Cox proportional hazards models to determine 1) whether differences in post-listing survival were chiefly due to post-HTx or waitlist demise; and 2) if HTx remains a viable exit strategy for candidates waitlisted ≥8 days.

In analysis I, a landmarked analysis was performed to avoid immortal time bias, since, by definition, anyone who survives to ≥8 days of waitlisting has survived the first 7 days. We additionally examined characteristics of candidates who underwent HTx versus died or deteriorated on the waitlist if listed for ≥8 days. All analyses were repeated among candidates listed at status 1 to determine the robustness of observed results. Stata version 17 (College Station, TX) was used for all analyses.

RESULTS

Overall trends
A total of 246 candidates were included with a median waitlist time of 4 days (IQR: 2–9 days) (Figure 1A); patients listed as status 1 (N=210) had a median waitlist time of 4 days (IQR: 2–7 days) (Figure 1B). In 2018, 4/11 (36.4%) candidates were waitlisted for ≥8 days compared to 11/30 (36.7%) in 2021 (P for trend=0.46) (Figure 2A). Among status 1 candidates, 22.2% waited for ≥8 days in 2018 compared to 37.0% in 2021 (P for trend=0.15) (Figure 2B).

Baseline characteristics

Cohorts displayed similar distributions of age, gender, and body mass index (BMI). Candidates who waited for ≥8 days were more likely to be blood type O (56.3 vs. 34.9%, P<0.01) and have elevated creatinine (35.2 vs. 22.3%, P=0.04) while less likely to be concurrently supported by intraaortic balloon pump (IABP) (7.0 vs. 20.0%, P=0.01) or listed at status 1 (67.6 vs. 92.6%, P<0.01) (Table 1). Similar trends were observed among status 1 candidates, with significantly more blood type O (56.3 vs. 36.4%, P<0.01) and prior smokers (35.4 vs. 21.0%, P=0.04) among those waitlisted for ≥8 days with less concurrent intraaortic balloon pump (IABP) support (6.4 vs. 19.1%, P=0.03) (Table E1).

Multivariable logistic regression demonstrated blood type O (OR 2.94, 95% CI 1.54–5.61) to be independently associated with increased likelihood of waitlist time ≥8 days; concurrent IABP support (OR 0.30, 95% CI 0.10–0.89) and status 1 listing (OR 0.12, 95% CI 0.05–0.30) were associated with decreased likelihood of waitlist time ≥8 days (Table 2). Among status 1 candidates, blood type O (OR 2.15, 95% CI 1.08–4.24) and obesity (OR 2.04, 95% CI 1.00–4.17) remained independently associated with prolonged waitlisting (Table E2).
Among candidates waitlisted for ≥8 days, 57.8% were ultimately transplanted, while 29.6% died or deteriorated on the waitlist. On the other hand, 92.6% of candidates waitlisted ≤7 days were transplanted while only 7.4% died or deteriorated (P<0.01) (Figure 3A). 93.8% of status 1 candidates waitlisted for ≤7 days were transplanted while 6.2% died or deteriorated; 56.3% of those who waited for ≥8 days were transplanted and 29.2% died or deteriorated (P<0.01) (Figure 3B). Overall, nine (3.7%) candidates were removed due to recovery or other causes; all of these candidates were listed for ≥8 days. The percentage of candidates removed from the waitlist due to HTx was highest when listed for ≤4 days at 97.6% (Figure E1).

Two out of 162 (1.2%) candidates who were transplanted within 7 days of listing died shortly after HTx. 90-day post-listing survival was estimated to be 70.4% (95% CI 58.3–79.6%) if a candidate remained waitlisted at 8 days compared to 93.7% (95% CI 88.7–96.6%) if the candidate was transplanted (Figure 4A). Multivariable Cox proportional hazards analysis demonstrated an independent association between waitlisting ≥8 days and 90-day mortality (HR 5.59, 95% CI 2.59–12.1) (Table 3). These results were replicated on analysis of status 1 candidates alone (HR 5.49, 95% CI 2.39–12.6) (Table E3; Figure 4B).

Recipient Characteristics

Forty-one recipients underwent HTx after listing for ≥8 days compared to 162 at ≤7 days. Recipients transplanted at ≥8 days were younger (44 vs. 53 years, P=0.04) and less likely to be supported by ECMO at HTx (63.4 vs. 95.7%, P<0.01) or mechanically ventilated (7.3 vs. 29.0%, P<0.01) while more often blood type O (53.7 vs. 35.2%, P=0.03) and more likely to be
supported by durable left ventricular assist device (LVAD) (12.2 vs. 0.6%, \(P<0.01\)) (Table E4).

Donors were similarly likely to be blood type O and otherwise displayed similar characteristics. There were no significant differences in ischemic time or distance from recipient to donor. At 90 days post-HTx, 92.0% of recipients listed for \(\leq 7\) days were alive compared to 92.7% if listed for \(\geq 8\) days (log-rank \(P=0.87\); Figure E2A).

Among those listed at status 1, those who underwent HTx at \(\geq 8\) days of listing were younger (39 vs. 53 years, \(P=0.04\)) and less likely to be mechanically ventilated (7.4 vs. 29.6%, \(P=0.02\)) or supported by ECMO (70.4 vs. 96.7%, \(P<0.01\)) but more likely to be supported by durable LVAD (7.4 vs. 0%, \(P=0.02\)) at the time of transplantation (Table E5). There was no significant difference in donor or operative characteristics. For patients listed as status 1, 90-day post-HTx survival was 92.6% among those who waited for \(\geq 8\) days compared to 91.4% among those who waited for \(\leq 7\) days (log-rank \(P=0.83\)) (Figure E2B).

Compared to candidates who were waitlisted for \(\geq 8\) days and underwent HTx, those who died or deteriorated were older (58 vs. 44 years, \(P<0.01\)) and demonstrated greater atherosclerotic burden, demonstrated by higher prevalence of ischemic heart disease (57.1 vs 19.5%, \(P<0.01\)), diabetes (47.6 vs. 17.1%, \(P=0.01\)), and cerebrovascular accident (23.8 vs 2.4%, \(P=0.01\)) (Table E6). Among those listed at status 1, a larger proportion of those who died demonstrated ischemic heart failure etiology (57.1 vs. 25.9%, \(P=0.049\)). The study design and findings are represented in Figure 5.
DISCUSSION

The present study examined the relationship between prolonged waitlist time and post-listing survival and had four key findings. First, waitlist time over one week while listed on ECMO is independently associated with worse post-listing survival. Second, blood type O, a non-modifiable risk factor, is associated with prolonged waitlist time. Third, waitlist time over one week does not compromise the efficacy of HTx as an exit strategy. Fourth, once waitlisted for more than one week, candidates who then die or deteriorate demonstrate characteristics associated with acquired heart disease. Moreover, the relationship between waitlist time and post-listing survival remained present on examination of status 1 candidates alone. Taken together, these data suggest that undergoing prompt HTx is of high importance in candidates listed with ECMO, although young candidates without a large chronic disease burden who are clinically stable can be maintained on the waitlist if they cannot be transplanted within in the first week.

Under prior allocation systems, it has been noted that inability to acquire a suitable heart for transplantation among ECMO-supported candidates in a timely fashion is associated with poor post-listing survival. Ivey-Miranda et al. analyzed 712 candidates supported by ECMO and demonstrated post-listing survival at 1 year to be 22.5% if the candidate did not undergo HTx compared to 73.4% if they did. In this same analysis, it was demonstrated that longer time on the waitlist is associated with worse post-HTx survival on the order of a 2% increase per day waitlisted. Despite higher rates of post-HTx mortality among ECMO-supported recipients, Singh et al. demonstrated that the survival benefit gained from HTx compared to continued
waitlisting increases among sicker candidates. In the present analysis, we were unable to detect a significant difference in post-HTx mortality among recipients with a prolonged waitlist time, with excellent post-HTx survival among those listed for ≤7 days (92.0%) and those listed for ≥8 days (92.7%). When interpreting this information, there is a caveat, however, in that selection bias may be present in considering candidates who survived to HTx after listing for ≥8 days. When examining the clinical characteristics of this population compared to those listed for ≤7 days, we notice these candidates were less likely to be ECMO dependent at HTx and more likely to be durable LVAD dependent, leading one to consider the role of durable LVAD as a feasible bridge from ECMO to HTx.

In a recent analysis of combined SRTR and INTERMACS databases, DeFillipis et al. investigated survival among candidates bridged with ECMO to LVAD versus HTx. They demonstrated post-ECMO to HTx survival of 70.7% at 1 year, 66.6% at 2 years, and 61.8% at 5 years compared to 69.2%, 62.6%, and 56.5% at 1, 2, and 5 years among those bridged to LVAD. However, this analysis did not separate post-HTx outcomes by allocation system. Published data demonstrate post-HTx survival rates of approximately 90% in those bridged directly to HTx and may thus obfuscate this equivalency in the current era. From this information, the question does then arise of whether temporary support candidates are currently transplanted too fast without consideration of transition to durable support. In a recent analysis of the SRTR database, Topkara et al. demonstrated a significant decrease in rate of waitlist recovery under the new system in this population, suggesting an inadequate period for improvement while on temporary support. It appears that candidates listed with durable LVAD also have shorter
waitlist time under the current allocation system, although their post-HTx outcomes may be suffering. Undoubtedly, further investigation is required in this area.

Among the total cohort, we noticed blood type O to be independently associated with prolonged waitlist time, while obesity emerged as an additional predictor among those listed at status 1. Regarding blood type, it has been recognized that type O candidates have longer waitlist time, at least in part due to the biology of donor organs they can accept. This phenomenon is intriguing when considering the population restricted to status 1 candidates, as per UNOS donor heart allocation policies, type O hearts are first offered to status 1 candidates of a primary blood type match within 500 nautical miles. Interestingly, there was no difference in the proportion of type O donors between those transplanted within 7 days versus ≥8 days without a notable difference in donor quality, although a larger proportion of candidates transplanted ≥8 days were blood type O. This likely indicates that several type O donor hearts were passed on by type O candidates. First, this could represent a subconscious bias in which type O candidates supported by ECMO tend to be listed earlier in their cardiogenic shock process given known difficulties obtaining HTx in this population. This may also be reflective of true differences in pathophysiology, as type O candidates are less likely to be afflicted by ischemic heart disease. Although listed for HTx, transplant teams may opt to monitor the patient’s status closely while still having the option of urgent HTx if needed as opposed to waiting for failure to recover and then listing. Regarding concurrent IABP use, Nishi et al. recently examined concurrent IABP use in ECMO in a large Japanese national database and demonstrated significant decreases in post-ECMO mortality. They demonstrated significantly higher rates of concurrent IABP use in large-scale
teaching institutions, although in the US, data documenting the correlation between center volume and advanced ECMO management strategies are sparse.

We additionally noticed an association between obesity and prolonged waitlist time among candidates listed at status 1. In a recently published study, Chouairi et al. examined the relationship between obesity and HTx outcomes. In this analysis, they demonstrated a dose-dependent decrease in the hazard of undergoing HTx as BMI increased, from 0.83 (95% CI 0.81–0.85) among those with BMI from 25-29.9 kg/m² to 0.42 (95% CI 0.36–0.49) among those with a BMI from 40-55 kg/m². This likely represents difficulty in procuring organs of appropriate size match, as donor BMI was noted to be a mean of 26.9 kg/m² in 2020. In our analysis, mean donor BMI was 28.2 kg/m², which points toward difficulty obtaining hearts from adequately sized donors as the likely etiology of the increased waitlist time.

This study has several limitations inherent to its design. First, the study was retrospective in nature. Second, although the UNOS database contains over 500 variables, data are collected primarily at the time of listing and HTx, without update during listing. It has been demonstrated that a candidate’s risk can change rapidly. Moreover, important variables that may be indicative of a patient’s physiologic status, such as lactate, are not available. Third, the database does not contain granular information surrounding the reason to delist a candidate for other reasons or continue additional support, such as IABP, in those listed for a prolonged period, thus limiting conclusions regarding candidates listed for ≥8 days. Additionally, it should be noted that ECMO is primarily a therapy for those in biventricular failure as opposed to left heart failure, and the decision to pursue ECMO in these patients is highly individualized. Fourth, given the timepoints...
at which data are collected, we were unable to assess the situation surrounding the escalation to ECMO support, such as patients initiated on ECMO in the setting of cardiopulmonary arrest.

Fifth, non-status 1 candidates were included to represent the entirety of the candidate pool, with analyses then restricted to status 1 candidates, given the sample size of the current analysis.

Conclusions

Although candidates supported by ECMO are listed at status 1 under the new donor heart allocation system, a substantial portion are waitlisted for ≥8 days. Those who do not undergo HTx within the first week after listing are at increased risk of subsequent waitlist demise but demonstrate adequate post-HTx survival. Further investigation into optimal bridging strategies of candidates who cannot immediately undergo HTx is warranted.

REFERENCES


LEGENDS

**Figure 1.** Histograms demonstrating the distribution of waitlist time among (A) the entire cohort and (B) status 1 candidates. The vertical dashed line represents 7 days. Abbreviations: none.

**Figure 2.** Bar charts demonstrating the percent of candidates who waited for ≥8 days (A) cohort-wide and (B) when listed at status 1 by year of listing. Abbreviations: none.

**Figure 3.** Bar charts demonstrating the percentage of candidates removed from the waitlist due to HTx, death/deterioration, or other causes stratified by waitlist time. (A) represents the entire cohort and (B) represents status 1 candidates only. Chi-square $P$ is $<$0.01 in both figures. Abbreviations: HTx, heart transplantation.

**Figure 4.** Kaplan-Meier curves demonstrating a significant decrease in post-listing survival among candidates who waited for ≥8 days versus ≤7 days. (A) represents the entire cohort and (B) represents status 1 candidates only. Abbreviations: CI, confidence interval.

**Figure 5 (Graphical Abstract).** A summary of the study’s methodology, findings, and implications. Abbreviations: CI, confidence interval; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio; HTx, heart transplantation; SRTR, Scientific Registry of Transplant Recipients.
Figure E1. Bar charts demonstrating reasons for waitlist removal as days on the waitlist increase. (A) 1 vs. ≥2 days; (B) ≤2 vs. ≥3 days; (C) ≤3 vs. ≥4 days; (D) ≤4 vs. ≥5 days; (E) ≤5 vs. ≥6 days; and (F) ≤6 vs. ≥7 days. Abbreviations: HTx, heart transplantation.

Figure E2. Kaplan-Meier curves demonstrating post-HTx survival stratified by listing time (A) cohort-wide (adjusted HR 1.13, 95% CI 0.32–4.05) and (B) among candidates listed at status 1 (adjusted HR 1.08, 95% CI 0.24–4.87). Abbreviation: CI, confidence interval; HTx, heart transplantation; HR, hazard ratio.
Table 1. Candidate characteristics.

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<td>IABP</td>
<td>35 (20.0)</td>
<td>5 (7.0)</td>
<td>0.01</td>
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<tr>
<td>Microaxial LVAD</td>
<td>25 (14.3)</td>
<td>8 (11.3)</td>
<td>0.61</td>
</tr>
<tr>
<td>Durable LVAD</td>
<td>3 (1.7)</td>
<td>3 (4.2)</td>
<td>0.25</td>
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<td>Listing status</td>
<td></td>
<td></td>
<td>&lt;0.01</td>
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<td>162 (92.6)</td>
<td>48 (67.6)</td>
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<td>2</td>
<td>9 (5.1)</td>
<td>6 (8.5)</td>
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<td>3</td>
<td>1 (0.6)</td>
<td>4 (5.6)</td>
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<td>1 (0.6)</td>
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<td>7</td>
<td>2 (1.1)</td>
<td>4 (5.6)</td>
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*Northeast: UNOS regions 1, 2, 9; Southeast: UNOS regions 3, 4, 11; Midwest: UNOS regions 7, 8, 10; West: UNOS regions 5, 6.
Abbreviations: BMI, body mass index; CVA, cerebrovascular accident; IABP, intraaortic balloon pump; ICD, implantable cardioverter-defibrillator; LVAD, left ventricular assist device.
Table 2. Risk factors for prolonged waitlist time (≥8 days)

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<th></th>
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<th>MULTIVARIABLE</th>
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<tr>
<td></td>
<td>Univariable OR</td>
<td>P-value</td>
<td>Multivariable OR</td>
<td>P-value</td>
<td></td>
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<tr>
<td>Age, years</td>
<td>0.99 (0.97-1.01)</td>
<td>0.35</td>
<td>0.98 (0.96-1.00)</td>
<td>0.08</td>
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<tr>
<td>Female gender</td>
<td>1.26 (0.69-2.31)</td>
<td>0.46</td>
<td>1.46 (0.73-2.92)</td>
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<tr>
<td>Obese</td>
<td>1.45 (0.82-2.56)</td>
<td>0.20</td>
<td>1.93 (0.99-3.74)</td>
<td>0.052</td>
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<tr>
<td>Blood type O</td>
<td>2.41 (1.37-4.23)</td>
<td>&lt;0.01</td>
<td>2.94 (1.54-5.61)</td>
<td>&lt;0.01</td>
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<tr>
<td>Ethnicity, white</td>
<td>0.69 (0.39-1.23)</td>
<td>0.21</td>
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<td>Region</td>
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<td>Southeast</td>
<td>2.71 (1.29-5.72)</td>
<td>&lt;0.01</td>
<td>1.91 (0.82-4.42)</td>
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<td>Midwest</td>
<td>1.73 (0.77-3.91)</td>
<td>0.19</td>
<td>1.64 (0.68-4.00)</td>
<td>0.27</td>
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<tr>
<td>West</td>
<td>1.23 (0.49-3.09)</td>
<td>0.65</td>
<td>1.16 (0.43-3.16)</td>
<td>0.77</td>
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<tr>
<td>Private insurance</td>
<td>1.01 (0.58-1.77)</td>
<td>0.97</td>
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<tr>
<td>Ischemic HF etiology</td>
<td>1.19 (0.66-2.12)</td>
<td>0.57</td>
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<tr>
<td>Medical history</td>
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<tr>
<td>Diabetes</td>
<td>1.40 (0.73-2.69)</td>
<td>0.31</td>
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<tr>
<td>CVA</td>
<td>1.35 (0.48-3.81)</td>
<td>0.57</td>
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<tr>
<td>ICD</td>
<td>1.17 (0.65-2.07)</td>
<td>0.60</td>
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<tr>
<td>Smoking</td>
<td>1.72 (0.94-3.16)</td>
<td>0.08</td>
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<tr>
<td>Prior cardiac surgery</td>
<td>1.19 (0.64-2.24)</td>
<td>0.58</td>
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<tr>
<td>Inotrope dependent</td>
<td>0.85 (0.49-1.47)</td>
<td>0.55</td>
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<tr>
<td>Ventilator dependent</td>
<td>0.69 (0.37-1.27)</td>
<td>0.23</td>
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<tr>
<td>Creatinine ≥1.5 mg/dL</td>
<td>1.90 (1.04-3.46)</td>
<td>0.04</td>
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<tr>
<td>Concurrent MCS</td>
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<tr>
<td>IABP</td>
<td>0.30 (0.11-0.81)</td>
<td><strong>0.02</strong></td>
<td>0.30 (0.10-0.89)</td>
<td><strong>0.03</strong></td>
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<tr>
<td>Microaxial LVAD</td>
<td>0.80 (0.34-1.87)</td>
<td>0.61</td>
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<tr>
<td>Durable LVAD</td>
<td>2.53 (0.50-12.8)</td>
<td>0.55</td>
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<tr>
<td>Listing at status 1</td>
<td>0.17 (0.08-0.36)</td>
<td><strong>&lt;0.01</strong></td>
<td>0.12 (0.05-0.30)</td>
<td><strong>&lt;0.01</strong></td>
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</table>

*Northeast: UNOS regions 1, 2, 9; Southeast: UNOS regions 3, 4, 11; Midwest: UNOS regions 7, 8, 10; West: UNOS regions 5, 6.

Abbreviations: BMI, body mass index; CVA, cerebrovascular accident; HF, heart failure; IABP, intraaortic balloon pump; ICD, implantable cardioverter-defibrillator; LVAD, left ventricular assist device.
Table 3. Relationship between waitlist $\geq$8 days and post-listing death or deterioration, landmarked at 8 days.

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<thead>
<tr>
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<th>UNIVARIABLE</th>
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<th>MULTIVARIABLE</th>
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<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P-value</td>
<td>HR (95% CI)</td>
<td>P-value</td>
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<tr>
<td>Waitlist $\geq$8 days</td>
<td>5.47 (2.58-11.6)</td>
<td><strong>0.01</strong></td>
<td>5.59 (2.59-12.1)</td>
<td><strong>0.01</strong></td>
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<tr>
<td>Age, years</td>
<td>1.04 (1.01-1.07)</td>
<td><strong>0.01</strong></td>
<td>1.04 (1.01-1.08)</td>
<td><strong>0.01</strong></td>
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<tr>
<td>Female gender</td>
<td>1.45 (0.69-3.02)</td>
<td>0.33</td>
<td>1.83 (0.90-3.74)</td>
<td>0.10</td>
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<tr>
<td>Obese</td>
<td>2.32 (1.14-4.70)</td>
<td><strong>0.02</strong></td>
<td>1.83 (0.90-3.74)</td>
<td>0.10</td>
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<tr>
<td>Blood type O</td>
<td>2.29 (1.11-4.72)</td>
<td><strong>0.03</strong></td>
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<tr>
<td>Ethnicity, white</td>
<td>0.62 (0.30-1.28)</td>
<td>0.20</td>
<td>1.18 (0.55-2.52)</td>
<td>0.67</td>
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<td>Region*</td>
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<tr>
<td>Southeast</td>
<td>2.55 (0.90-7.23)</td>
<td>0.08</td>
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<tr>
<td>Midwest</td>
<td>2.14 (0.70-6.54)</td>
<td>0.18</td>
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<tr>
<td>West</td>
<td>2.15 (0.66-7.04)</td>
<td>0.21</td>
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<tr>
<td>Private insurance</td>
<td>0.68 (0.34-1.38)</td>
<td>0.29</td>
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<tr>
<td>Ischemic HF etiology</td>
<td>2.19 (1.08-4.44)</td>
<td><strong>0.03</strong></td>
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<td>Medical history</td>
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<tr>
<td>Diabetes</td>
<td>2.53 (1.21-5.29)</td>
<td><strong>0.01</strong></td>
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<tr>
<td>CVA</td>
<td>3.09 (1.18-8.08)</td>
<td><strong>0.02</strong></td>
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<td>ICD</td>
<td>1.41 (0.69-2.89)</td>
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<tr>
<td>Smoking</td>
<td>2.23 (1.09-4.56)</td>
<td><strong>0.03</strong></td>
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<tr>
<td>Prior cardiac surgery</td>
<td>1.79 (0.86-3.73)</td>
<td>0.12</td>
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<tr>
<td>Inotrope dependent</td>
<td>0.83 (0.41-1.68)</td>
<td>0.60</td>
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<tr>
<td>Ventilator dependent</td>
<td>1.13 (0.53-2.41)</td>
<td>0.74</td>
<td>1.18 (0.55-2.52)</td>
<td>0.67</td>
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<tr>
<td>Creatinine $\geq$1.5 mg/dL</td>
<td>1.97 (0.95-4.05)</td>
<td>0.07</td>
<td>1.33 (0.64-2.77)</td>
<td>0.45</td>
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<tr>
<td>Concurrent MCS</td>
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<tr>
<td>IABP</td>
<td>0.56 (0.17-1.83)</td>
<td>0.34</td>
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<tr>
<td>Microaxial LVAD</td>
<td>1.78 (0.73-4.35)</td>
<td>0.20</td>
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<td>Durable LVAD</td>
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<tr>
<td>Listing at status 1</td>
<td>0.67 (0.28-1.64)</td>
<td>0.38</td>
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Abbreviations: BMI, body mass index; CVA, cerebrovascular accident; HF, heart failure; IABP, intraaortic balloon pump; ICD, implantable cardioverter-defibrillator; LVAD, left ventricular assist device.
A

Number at risk
≤7 days 160
≥8 days 71

≤7 days 157
≥8 days 62

≤7 days 156
≥8 days 57

≤7 days 153
≥8 days 54

≤7 days 152
≥8 days 52

≤7 days 149
≥8 days 50

≤7 days 148
≥8 days 50

Log-rank P=0.01

Probability of survival (%)
Survival time (days)
0 15 30 45 60 75 90
0 25 50 75 100

B

Number at risk
≤7 days 150
≥8 days 48

≤7 days 147
≥8 days 41

≤7 days 146
≥8 days 37

≤7 days 143
≥8 days 36

≤7 days 142
≥8 days 34

≤7 days 139
≥8 days 33

≤7 days 138
≥8 days 33

Log-rank P=0.01

Probability of survival (%)
Survival time (days)
0 15 30 45 60 75 90
0 25 50 75 100
METHODS

• 246 ECMO-supported candidates listed from 10/18/2018 to 03/21/2021 identified in the SRTR database

• Stratified based on waitlist time (≤7 days vs. ≥8 days)

• Primary outcome: 90-day post-listing survival

RESULTS

• Waitlisting for ≥8 days is associated with poor 90-day post-listing survival compared to those who undergo HTx within 7 days of listing (HR 5.59, 95% CI 2.59–12.1).

IMPLICATIONS

• Obtaining a heart within one week of listing may improve survival.

CI, confidence intervals; ECMO, extracorporeal membrane oxygenation; HR, hazard ratio; HTx, heart transplantation; SRTR, Scientific Registry of Transplant Recipients.
KM Curve: Post-listing 90-day Survival

Adjusted hazard ratio: 5.59 (95% CI 2.59–12.1)
Log-rank P<0.01
Prolonged Waitlisting is Associated with Mortality in Candidates Listed for Heart Transplantation on ECMO Support

Presenter: Dr. Masashi Kawabori
Invited Discussant: Dr. Leora Yarboro

Dr. Leora Yarboro (Charlottesville, VA):

Thank you very much and congratulations. That was an excellent presentation. I have received honoraria from Abbot and Medtronic, neither of which is related to my discussion today. The heart transplant allocation change in 2018 has dramatically impacted how we care for patients awaiting heart transplant. There's been a dramatic shift towards the increased use of temporary circulatory supports such as ECMO in these populations. In your talk today, you demonstrate a decrease in postlisting survival among those patients who were supported over eight days or longer with a high percentage of those patients not progressing to transplant. In this, I have three questions for you. The first is, in this data, you showed that a third of the transplant patients-- a third of the patients fall into the high-risk category of having to wait more than eight days from transplant. Do you foresee that this time will get longer as more patients are supported on ECMO pretransplant? And if so, what strategies do you think we can use to mitigate these complications?

Dr. Masashi Kawabori (Boston, MA):

Thank you for comments, Dr. Yarboro. To answer this question, I think, as shown in the slide, I think there's improvement room for these issues because, number one, there's more than one-third of patients, a lot of patients, is in the high-risk group. And we know what the issue is, prolonged waitlisting. And now, we know that if we could transplant the patient within seven days or if we could use balloon pump, which is protective factors, which will help transplant these patients earlier.

Dr. Yarboro:

Thank you. The second question is, your finding of increased wait time for those patients with the blood group O is consistent with our previous work showing the same thing, the durable LVAD population. Given that these patients are less likely to progress to transplant, do you think there needs to be a further change in how we allocate organs, or should we be managing these patients who are at disadvantaged from their blood group differently?
Dr. Kawabori:

Absolutely. In my research group, we do run multiple UNOS analysis. And then, one of the topics-- one of the other topics we have is blood type O transplantation under the new allocation system, which our surgical fellow, Dr. Eapen, will present today at rapid-fire oral today. I don't want to steal her thunder. However, long story short, there is-- so blood type O recipient could only receive type O donors. However, only 75% of donor O heart are allocated to O recipients. So, there's 25% of patient donor O hearts, which is leaking out to type A, 15%, and type B, 10%. So, if we could potentially make some allocation algorithm changes, that might help save some of the blood type O recipients.

Dr. Yarboro:

Thank you. And finally, we have found deconditioning to be a significant problem for our patients who are awaiting transplant on mechanical support. And were you able to identify any data that was related to cannulation strategy and success in terms of transitioning them to transplant?

Dr. Kawabori:

That is one of the limitations of our study, the UNOS database data of [inaudible]. So UNOS data doesn't have the cannulation strategy. So, I think the ELSO database, those have the cannulation site. So, I think those studies using ELSO database will help understand those clinical questions.

Dr. Yarboro:

Thank you.

Dr. Kawabori:

Thank you.

Dr. Yarboro:

And the follow-up to that is, what is your center-specific approach to cannulation for those patients who may be blood type O? Is it used any differently, or do you have any thoughts to that?

Dr. Kawabori:
In our centers, we basically do femoral cannulations. And if the patient does not look optimized enough for transplant, then either we use [inaudible] 55 or bridge with surgical bypass.

Dr. Yarboro:

Thank you.

Dr. Kawabori:

Thank you.

Dr. Yarboro:

Congratulations.

Dr. Kawabori:

Thank you.

Dr. Sylvester (Orlando, FL):

No disclosures for this. So, the question is-- two questions, short questions. First is, you need to look at whether this is acute ECMO or chronic ECMO. These patients who decompensate and then get transplanted or are these patients who are chronic, who slide into ECMO and ECMO is utilized, and you can get that by looking at the time from listing to actual ECMO. And the date is in the SRTR, so that you can tell patients who were listed who get ECMO as opposed to patients who were listed on ECMO, which is a very important difference. My question to you is we have these data-- and then I'll ask the question. So what? What do you do differently? What is the actionable item? Is it the patients-- the sick patients who don't get transplanted because they're not really ready for transplant or is it the doctors? They're picking and choosing the hearts that they want. They're not willing to take a 50-year-old heart for a 30-year-old who's on ECMO. What is the factor? And the reality is, it's probably variable in different places, but we wanted on the committee ECMO seven days only. And we didn't want to renew because at some point, as Donna Mancini said, "ECMO becomes a chronic choice because there's a game advantage of transplants."

Dr. Kawabori:
I think that's a very good point. In the UNOS database it doesn't have data how many days were there on ECMO prior to this date. So, there is acute and also chronic ECMO patients, which cannot be captured from this data. And I understand that the ECMO duration is one of the factors, so I totally agree with you that ECMO over seven days might be overused.