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ORIGINAL CLINICAL SCIENCE

Use of exception status listing and related outcomes during two heart allocation policy periods

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KEYWORDS:
heart transplant;
exception status;
heart allocation policy

BACKGROUND: The October 2018 update to the heart allocation policy was intended to decrease exception status requests, whereby candidates are listed at a specific status due to perceived need despite not meeting prespecified criteria of illness severity. We assessed the use of exception status and waitlist outcomes before and after the 2018 policy.
METHODS: We used data from the Scientific Registry of Transplant Recipients on adult heart transplant candidates listed from 2015 to 2021. We assessed (1) the use of exception status across patient characteristics between the two periods and (2) transplant rate and waitlist mortality or delisting due to deterioration in each period. Patients listed by exception versus standard criteria were compared with multivariable logistic regression, and waitlist outcomes were assessed using Cox proportional hazard models with medical urgency and exception status as time-dependent covariates.
RESULTS: During the study period (n = 19,213), heart transplants under exception status increased postpolicy from 10.0% to 32.3%, with 20.6% of transplants performed for patients at status 2 exception. Exception status candidates postpolicy were more frequently Black or Hispanic/Latino and less likely to have hypertrophic or restrictive cardiomyopathy and had worse hemodynamics. Exception status listing was associated with higher transplant rates in both periods. Postpolicy, candidates listed status 1 exception had a lower likelihood for waitlist mortality or delisting (hazard ratio, 0.60; 95% CI, 0.37-0.99; and p = 0.05).

Abbreviations: HCM, Hypertrophic cardiomyopathy; HRSA, Health Resources and Services Administration; IABP, Intra-aortic balloon pump; MCS, Mechanical circulatory support; OPTN, Organ Procurement and Transplantation Network; PA, Pulmonary artery; PCWP, Pulmonary capillary wedge pressure; RCM, Restrictive cardiomyopathy; VAD, Ventricular assist device

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CONCLUSIONS: Under the 2018 policy, exception status listings dramatically increased. The policy change shifted the population of patients listed by exception status and affected waitlist mortality, which suggests a need to further evaluate the policy's impact.
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In October 2018, the Organ Procurement and Transplantation Network (OPTN) modified the heart allocation policy to improve equitable access to and outcomes after heart transplantation.[1,2] The new policy expanded the number of listing statuses from 3 to 6 to improve discrimination among the highest urgency candidates, broadened geographic sharing of donor hearts, instituted hemodynamic criteria for listing candidates at the highest statuses, and required recertification of candidates' statuses after prespecified periods for most candidates. In addition, candidates with rarer phenotypes of cardiomyopathy and potential anatomical barriers to durable mechanical circulatory support (MCS) devices were given priority on the transplant list as status 4, and the review of exception requests shifted from an intraregional to an extraregional review board to limit competition for a shared donor pool. These series of changes were expected to decrease exception status listings, whereby candidates are listed at a particular status due to perceived illness severity despite not meeting standard criteria for a particular medical urgency status. Emerging literature, however, has suggested that the impact of these changes on exception status listings was not as intended and was associated with a marked increase in exception status listings after the policy change, contrary to the original intent.[3,4] We set out to describe the demographic and clinical characteristics of and waitlist outcomes for candidates listed by exception before and after the policy change.

Methods

Study cohort

This study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donors, waitlisted candidates, and transplant recipients in the United States submitted by the members of OPTN and has been described elsewhere.[5] 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.

The analysis was limited to adults (18 years or older) listed for heart transplantation in the United States, excluding Puerto Rico, though inclusive of retransplant candidates. Candidates listed for multiorgan transplantation or who started or remained inactive (status 7) throughout the study period were excluded. We included the first listing for each candidate listed for heart transplantation from November 1, 2015, to September 30, 2021. Candidates were then stratified based on whether they were listed for transplantation in the prepolicy (November 1, 2015, to October 17, 2018) or postpolicy (October 18, 2018, to September 30, 2021) periods. Medical urgency status and exception status listing (compared to listing by standard criteria) were treated as time-dependent covariates. Information for all other variables was obtained at the time of listing and included extensive data on demographic characteristics, clinical characteristics, and laboratory values. The study was submitted to the Institutional Review Board at the University of Michigan and was determined to be exempt from review. This work is in compliance with the International Society for Heart and Lung Transplantation (ISHLT) ethics statement.

Outcomes

We assessed the characteristics of and waitlist outcomes for patients listed by exception status. Our first primary outcome was to describe the clinical characteristics of candidates listed by exception status postpolicy compared to prepolicy. The two primary waitlist outcomes were (1) waitlist mortality or delisting due to clinical deterioration and (2) transplant rate, both in each of the two policy periods. We additionally assessed the odds of being listed for heart transplantation by exception during each of the two policy periods.

Statistical analysis

Variables are reported as means with standard deviations for continuous variables and as counts and percentages for categorical variables. Comparisons between the two policy periods and between standard criteria listing and exception status listing were evaluated using the Fisher exact test for categorical variables and the *t*-test for continuous variables. Multivariable logistic regression was used to compare patients listed by exception versus standard criteria at the time of initial listing.

To determine the association of exception status listing with transplant rate, we fit separate Cox proportional hazard models for both the pre- and postpolicy periods where the outcome was removal from the waiting list for transplantation. Listings were right-censored upon removal from the waiting list for reasons other than transplantation, including death, or on either October 17, 2018 (prepolicy period) or September 30, 2021 (postpolicy period). Thus, models provided a cause-specific hazard ratio (HR). Models included medical urgency status (prepolicy status 1A, 1B, 2; postpolicy statuses 1-6) and exception status (yes/no) as time-dependent covariates and their interaction terms, which were updated each time a candidate requested a new status. Models were adjusted for additional clinical covariates known to affect transplant rate, including sex, blood type, and body surface area as fixed effects and the transplant center as a random effect. The postpolicy model was additionally adjusted for calculated panel-reactive antibodies although this was not included in the prepolicy model as this was not routinely collected at listing before 2018. Candidates were treated as not at risk for the outcome of transplantation when inactive at status 7 on the waiting list.

Separate multivariable Cox proportional hazard models were fit for each policy period to determine the association of exception status listing with the composite outcome of waitlist mortality or removal due to clinical deterioration. All candidates listed in the prepolicy period were right-censored upon removal from the waiting list or on October 17, 2018. Similarly, in the postpolicy period, all candidate listings were right-censored upon removal from the waiting list or on September 30, 2021. Because transplantation is a competing event for death while on the waiting list, candidates were censored at the time of transplantation to estimate a cause-specific HR.[6] Primary models were minimally adjusted in that they included only medical urgency status and exception status as time-dependent covariates and their interaction terms. Medical urgency status and exception status listing were carried forward when candidates moved to inactive status (i.e., status 7) as those candidates remained at risk for death or delisting due to clinical deterioration.

To evaluate the potential clinical factors responsible for differences in waitlist mortality between exception status listing and standard criteria listing, we also fit fully adjusted Cox proportional hazard models for each policy period. In these models, medical urgency status and exception status were similarly treated as time-dependent covariates, and their interactions were tested. The models were additionally adjusted for variables previously shown to be associated with waitlist mortality with demographic and clinical factors as fixed effects and the transplant center as a random effect. Data were complete for most variables; thus, a complete case analysis was performed. Extreme values were trimmed to the 1st or 99th percentile (Supplemental Methods). Across all primary models, diagnostic plots were inspected (i.e., Schoenfeld residual plots and restricted cubic spline plots) and did not demonstrate any severe violations of proportional hazards or nonlinearity of continuous terms. All analyses were performed using R version 4, and a two-tailed p value < 0.05 was considered statistically significant.

Results

Baseline characteristics of waitlisted patients

From November 1, 2015, to September 30, 2021, 19,213 adult patients were listed for heart transplantation. Of these, 9,624 (49.9%) candidates were listed during the prepolicy period and 9,589 (50.1%) during the postpolicy period. At the time of initial listing, 328 (3.4%) candidates were listed by exception status during the prepolicy period compared to 1,704 (17.8%) candidates listed by exception status during the postpolicy period, a more than 5-fold increase (Figure 1, Table 1). The increase in exception status listings postpolicy was driven predominantly by candidates being

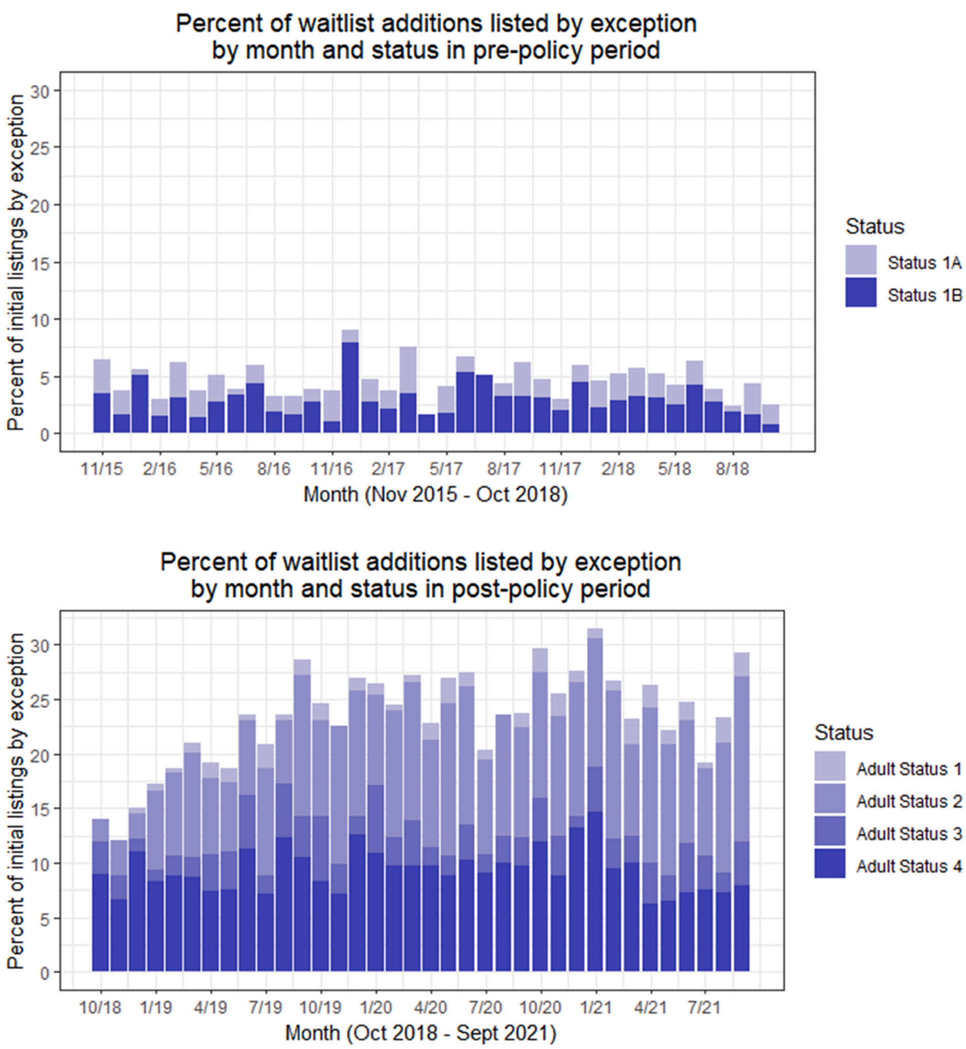

Figure 1 Percent of initial listing by exception by month and status in the (A) pre- and (B) postpolicy periods. Statuses not eligible for exception status (i.e., status 2 in the pre-policy periods and status 6 in the postpolicy period) were not included in the calculations. A test for linear trend confirmed an increase in statuses 1-4 exception listings during the postpolicy period (p < 0.001).

Table 1 Medical Urgency Status at Time of Listing and Transplant During the Pre- and PostPolicy Periods

		At listing	At transplant
Prepolicy period		n = 9,624	n = 5,627
1A	Standard	2,282 (23.7%)	3,474 (61.7%)
	Exception	122 (1.3%)	364 (6.5%)
1B	Standard	4,408 (45.8%)	1,435 (25.5%)
	Exception	206 (2.1%)	200 (3.6%)
2	Standard	2,606 (27.1%)	154 (2.7%)
Postpolicy period		n = 9,589	n = 6,480
1	Standard	334 (3.5%)	402 (6.2%)
	Exception	75 (0.8%)	184 (2.8%)
2	Standard	1,414 (14.7%)	1,901 (29.3%)
	Exception	731 (7.6%)	1,335 (20.6%)
3	Standard	877 (9.1%)	824 (12.7%)
	Exception	214 (2.2%)	293 (4.5%)
4	Standard	2,996 (31.2%)	903 (13.9%)
	Exception	684 (7.1%)	278 (4.3%)
6	Standard	2,264 (23.6%)	360 (5.6%)

listed as either status 2 exception (7.6% of candidates) or status 4 exception (7.1% of candidates). In total, 95.7% of all exception requests for the initial listing at a given status were approved postpolicy, with regional approval rates ranging from 92.8% to 98.1%. Among the 184 initial exception requests that were declined, 22.8% of individuals underwent transplantation while at the requested status, 42.4% were downgraded to a less urgent or inactive status, 26.1% remained at the requested status with a newly submitted exception request, 3.8% stayed at the requested status by standard criteria, 2.7% upgraded to a more urgent status, and 2.2% were removed from the list due to deteriorated condition. Data on exception request approvals during the prepolicy period were unavailable.

During the prepolicy period, 5,627 (58.5%) candidates underwent heart transplantation, of whom 564 (10.0%) were listed by exception at the time of transplantation. In contrast, during the post-policy period, 6,480 (67.6%) candidates underwent heart transplantation, of whom 2,090 (32.3%) were listed by exception, a more than 3-fold increase in transplants while at exception status (Figure 1). This increase was driven predominantly by an increase in candidates undergoing transplantation while at status 2 exception, with 20.6% of all candidates undergoing transplantation while at status 2 exception postpolicy (Table 1). In both the pre- and postpolicy periods, candidates frequently required extension of their statuses before transplantation (Table S1).

Characteristics associated with exception status listing

During the pre- and postpolicy periods, there were significant differences between candidates listed by standard criteria compared with those listed by exception (Table 2; Tables S2-S9). In the prepolicy period, candidates listed by exception status compared to those listed by standard criteria were significantly younger and were less often Black and less often treated with temporary or durable MCS devices or with intravenous inotropes (Table S2). In contrast, in the postpolicy period, candidates listed by exception status were more often Black. They also were more often treated with temporary or intravenous inotropes (Table S3). Younger age, white race, nonuse of intravenous inotropes, and lower mean pulmonary artery pressures were independently associated with exception listing in the prepolicy period, while Black race, use of intravenous inotropes, and lower pulmonary capillary wedge pressure (PCWPs) were independently associated with exception listing in the postpolicy period (Table 3).

Comparing exception status patients before and after the policy change revealed important differences between the 2 eras in the types of patients listed by exception (Table 2). In the postpolicy period compared to the prepolicy period, exception status candidates were older, more frequently Black or Hispanic/Latino, and less likely to have hypertrophic or restrictive cardiomyopathy or congenital heart disease. Exception status candidates in the postpolicy period were also significantly more likely to have temporary MCS devices or to require intravenous inotropes and had lower cardiac outputs and higher PCWPs and mean pulmonary artery pressures. Use of exception status was infrequent in both policy periods for candidates with durable MCS devices. Results were largely similar at the time of transplantation though candidates listed by exception in the postpolicy period were more likely to have a durably implanted MCS device (Table S10).

Transplant rate

During the prepolicy period, 5,627 candidates underwent transplantation. There were significant differences in transplant rate for those listed by exception status compared to those listed by standard criteria, and the cause-specific HR varied by medical urgency status (p for interaction = 0.05 (Table 4, Table S11). After adjusting for clinical factors associated with transplant rate, there was a faster rate of transplantation among candidates listed status 1B exception compared with candidates listed status 1B by standard criteria (HR, 1.32; 95% CI, 1.14-1.54; $p = < 0.001$), and no significant difference in transplant rate for candidates listed status 1A exception compared with those listed status 1A by standard criteria (Table 4).

In the postpolicy period, 6,480 candidates underwent transplantation. There were significant differences in transplant rate by exception status, and the cause-specific HR varied by medical urgency status (p for interaction < 0.001) (Table 4). After multivariable adjustment, exception status listing was associated with a significantly faster transplant rate at nearly all statuses (Status 1: HR 1.21 [95% CI 1.00-1.47]; Status 3: HR, 1.26; 95% CI, 1.10-1.46; and $p = 0.001$; and Status 4: HR, 1.75; 95% CI, 1.52-2.03; and $p < 0.001$, respectively) (Table S11).

Table 2 Clinical Characteristics of Candidates Listed by Standard Criteria or Exception During the Pre- and PostPolicy Periods

	Prepolicy period		Postpolicy period		*p* value pre versus post exception
	Standard (*n* = 9,296)	Exception (*n* = 328)	Standard (*n* = 7,885)	Exception (*n* = 1,704)	
Medical-urgency status					
Status 1A	2,282 (24.5%)	122 (37.2%)	-	-	
Status 1B	4,408 (47.4%)	206 (62.8%)	-	-	
Status 2	2,606 (28.0%)	0 (0.0%)	-	-	
Status 1	-	-	344 (4.2%)	75(4.4%)	
Status 2	-	-	1,414 (17.9%)	731 (42.9%)	
Status 3	-	-	877 (11.1%)	214 (12.6%)	
Status 4	-	-	2,996 (38.0%)	684 (40.1%)	
Status 6	-	-	2,264 (28.7%)	0 (0.0%)	
Age, mean (SD), y	53.4 (12.6)	48.2 (14.7)	53.0 (13.0)	53.3 (13.0)	< 0.001
Male sex	6,846 (73.6%)	227 (69.2%)	5,786 (73.4%)	1,230 (72.2%)	0.28
Race and ethnicity[a]					
Black	2,165 (23.3%)	31 (9.5%)	1,904 (24.1%)	468 (27.5%)	< 0.001
Hispanic/Latino	786 (8.5%)	24 (7.3%)	766 (9.7%)	176 (10.3%)	
White	5,934 (63.8%)	259 (79.0%)	4,845 (61.4%)	988 (58.0%)	
Other	411 (4.4%)	14 (4.3%)	370 (4.7%)	72 (4.2%)	
Body surface area, mean (SD), m^2	2.02 (0.26)	1.98 (0.27)	2.02 (0.26)	2.00 (0.26)	0.39
Blood type					
A	3,546 (38.1%)	130 (39.6%)	2,948 (37.4%)	631 (37.0%)	0.16
B	1317 (14.2%)	43 (13.1%)	1,147 (14.5%)	261 (15.3%)	
AB	456 (4.9%)	9 (2.7%)	340 (4.3%)	90 (5.3%)	
O	3,977 (42.8%)	146 (44.5%)	3,450 (43.8%)	722 (42.4%)	
Primary diagnosis					
Coronary artery disease	2,915 (31.4%)	60 (18.3%)	2,258 (28.6%)	459 (26.9%)	< 0.001
Dilated cardiomyopathy	5,191 (55.8%)	99 (30.2%)	4,371 (55.4%)	944 (55.4%)	
RCM	292 (3.1%)	22 (6.7%)	315 (4.0%)	78 (4.6%)	
HCM	230 (2.5%)	38 (11.6%)	280 (3.6%)	41 (2.4%)	
Congenital heart disease	248 (2.7%)	39 (11.9%)	256 (3.2%)	76 (4.5%)	
Valvular heart disease	98 (1.1%)	6 (1.8%)	73 (0.9%)	20 (1.2%)	
Other	322 (3.5%)	64 (19.5%)	332 (4.2%)	86 (5.0%)	
Serum creatinine, mean (SD), mg/dL	1.22 (0.53)	1.17 (0.38)	1.21 (0.41)	1.23 (0.43)	0.006
Temporary MCS[b]	1,187 (12.8%)	9 (2.7%)	1,523 (19.3%)	503 (29.5%)	< 0.001
ECMO	126 (1.4%)	2 (0.6%)	257 (3.3%)	56 (3.3%)	0.006
IABP	484 (5.2%)	4 (1.2%)	981 (12.4%)	365 (21.4%)	< 0.001
Temporary VAD	619 (6.7%)	4 (1.2%)	386 (4.9%)	109 (6.4%)	< 0.001
Durable MCS	2,515 (27.1%)	11 (3.4%)	2,123 (26.9%)	61 (3.6%)	1.00
Mechanical ventilation	127 (1.4%)	1 (0.3%)	130 (1.6%)	23 (1.3%)	0.16
Intravenous inotropes	2,979 (32.0%)	45 (13.7%)	2,064 (26.2%)	910 (53.4%)	< 0.001
Cardiac output, mean (SD), L/min	4.31 (1.31)	4.40 (1.30)	4.28 (1.34)	4.12 (1.31)	< 0.001
PCWP, mean (SD), mm Hg	18.3 (8.83)	15.6 (7.60)	18.1 (8.81)	19.3 (8.90)	< 0.001
PA pressure, mean (SD), mm Hg	27.9 (10.1)	23.9 (9.33)	27.3 (10.2)	28.8 (10.5)	< 0.001

The *p value refers to the comparison between candidates listed by exception during the pre- and postpolicy periods.*

Abbreviations: ECMO, extracorporeal membrane oxygenation; HCM, hypertrophic cardiomyopathy; IABP, intra-aortic balloon pump; MCS, mechanical circulatory support (device); PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure; RCM, restrictive cardiomyopathy; VAD, ventricular assist device.

[a]White = non-Hispanic White; Black = Black including Hispanic Black; Hispanic/Latino = Hispanic/Latino and White or no origin specified other than Hispanic/Latino; and Other = American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, or multiracial.

[b]Candidates may have multiple forms of temporary MCS.

Table 3 Odds of Being Listed by Exception Status During the Pre- and PostPolicy Periods From Multivariable Logistic Regression

	Prepolicy period, status 1A and 1B		Postpolicy period, status 1-4	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Age (per 10 years)	0.85 (0.75-0.96)	0.01	1.05 (1.00-1.11)	0.06
Male sex	0.83 (0.55-1.23)	0.35	0.92 (0.77-1.08)	0.30
Race and ethnicity (ref = White)				
Black	0.38 (0.24-0.60)	< 0.001	1.28 (1.09-1.50)	0.002
Hispanic/Latino	0.64 (0.36-1.13)		1.00 (0.80-1.25)	
Other	0.84 (0.38-1.85)		0.75 (0.53-1.04)	
Body surface area, m^2	1.49 (0.71-3.12)	0.29	1.51 (1.12-2.05)	0.01
Blood type (ref = A)				
B	1.10 (0.69-1.75)	0.18	0.94 (0.77-1.14)	0.77
AB	0.47 (0.20-1.11)		1.03 (0.76-1.39)	
O	1.13 (0.82-1.58)		1.04 (0.90-1.20)	
Primary diagnosis (ref = CAD)				< 0.001
Dilated cardiomyopathy	0.84 (0.56-1.25)	< 0.001	0.92 (0.78-1.08)	
Restrictive cardiomyopathy	4.02 (2.135-7.58)		0.51 (0.38-0.69)	
Hypertrophic cardiomyopathy	7.23 (3.86-13.57)		0.26 (0.18-0.39)	
Congenital heart disease	6.20 (2.90-13.24)		0.46 (0.32-0.67)	
Valvular heart disease	2.08 (0.71-6.08)		1.97 (0.99-3.92)	
Other	7.69 (4.43-13.37)		0.65 (0.47-0.90)	
Serum creatinine	1.22 (0.83-1.80)	0.30	1.03 (0.88-1.20)	0.69
Temporary MCS	0.04 (0.02-0.09)	< 0.001	0.61 (0.52-0.70)	< 0.001
Durable MCS	0.01 (0.00-0.02)	< 0.001	0.04 (0.03-0.05)	< 0.001
Mechanical ventilation	0.40 (0.05-3.25)	0.39	0.50 (0.27-0.89)	0.02
Intravenous inotropes	0.05 (0.03-0.08)	< 0.001	1.43 (1.25-1.64)	< 0.001
Cardiac output	1.19 (1.05-1.35)	0.01	1.00 (0.95-1.06)	0.96
PCWP	0.98 (0.95-1.02)	0.27	0.97 (0.96-0.98)	< 0.001
Mean PA pressure	0.95 (0.92-0.98)	< 0.001	1.00 (0.99-1.01)	0.98

Abbreviations: CAD, coronary artery disease; MCS, mechanical circulatory support (device); OR, odds ratio; PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure.

Table 4 Association of Exception Status Listing With Transplant Rate by Medical Urgency Status

Medical urgency	HR for exception versus standard (95% CI)	*p*-value for HR	*p* value for interaction
Prepolicy period			
Status 1A	1.09 (0.98-1.22)	0.12	0.05*
Status 1B	1.32 (1.14-1.54)	< 0.001	
Postpolicy period			
Status 1	1.21 (1.00-1.47)	0.05	< 0.001
Status 2	1.03 (0.95-1.11)	0.45	
Status 3	1.26 (1.10-1.46)	0.001	
Status 4	1.75 (1.52-2.03)	< 0.001	

Separate multivariable Cox regression models were fit for each policy period, with covariates for sex, blood type, body surface area, and calculated panel-reactive antibody at listing (postpolicy only) and a random effect for the center. Candidates were considered not at risk of transplantation when inactive on the waiting list. The *p* value for interaction was derived from a likelihood ratio test for all 2-way interaction terms between exception status and medical urgency status. *$p = 0.045$.

Abbreviation: HR, hazard ratio.

Waitlist mortality

During the prepolicy period, 843 candidates died or were removed from the transplant waiting list due to clinical deterioration. Exception status listing was not significantly associated with waitlist mortality or delisting due to clinical deterioration, and there were no significant interactions between medical urgency status and exception status ($p = 0.22$; Table 5). Results were similar in a fully adjusted model (Table S12).

In the postpolicy period, 578 candidates died or were removed from the waiting list due to clinical deterioration. There were significant differences in waitlist mortality for those listed by exception status compared to those listed by standard criteria, and the cause-specific HR for mortality after exception status listing varied by medical urgency status (p for interaction $= 0.01$; Table 5). In the postpolicy period, candidates listed by exception status 1 had a significantly lower likelihood for waitlist mortality or clinical deterioration compared to candidates listed for status 1 by standard criteria (HR, 0.60; 95% CI, 0.37-0.99; and $p = 0.05$).

In a fully adjusted model for the postpolicy period, there were no significant differences in waitlist mortality between candidates listed by exception and those listed by standard criteria, across medical urgency statuses (Table S13). This finding may indicate that the difference in waitlist mortality risk between status 1 exception and status 1 standard criteria listings can be explained by patient characteristics that differed between the 2 groups and were included in the fully adjusted model. To explore this possibility, we computed the

Table 5 Association of Exception Status Listing With Waitlist Mortality by Medical Urgency From Minimally Adjusted Cox Models

Medical urgency	HR for exception versus standard (95% CI)	*p* value for HR	*p* value for interaction
Prepolicy period			
Status 1A	1.04 (0.71-1.52)	0.85	0.22
Status 1B	0.71 (0.44-1.14)	0.16	
Postpolicy period			
Status 1	0.60 (0.37-0.99)	0.05	0.01
Status 2	0.87 (0.62-1.22)	0.42	
Status 3	1.74 (0.96-3.17)	0.07	
Status 4	1.40 (0.99-2.00)	0.06	

Abbreviation: HR, hazard ratio.

HR for status 1 exception versus status 1 standard criteria adjusting for each risk factor individually in a separate Cox model (Fig. S1). The HR moved toward the null and became nonsignificant only when adjusting for functional status, serum creatinine, race, or pulmonary artery systolic pressure.

Discussion

The current study evaluates the impact of the October 2018 change to the heart allocation policy on exception status listings and waitlist outcomes for patients listed by exception. Unlike previous work, our analyses allowed medical urgency and exception statuses to change over time and estimated the effect of exception status listing at each level of medical urgency. We found a dramatic 5.2 times increase in exception status listings following the policy change, with 32.2% of all candidates undergoing transplantation while at exception status and 20.6% of all candidates undergoing transplantation while at status 2 exception. We also found important and novel differences in the types of patients listed by exception in the prepolicy versus the postpolicy period and differences in waitlist outcomes for candidates while listed by exception status, including lower waitlist mortality for candidates listed status 1 exception compared to standard criteria after the policy change, a novel and important finding with the potential to inform future revisions to the heart allocation policy. Although some of these changes were an anticipated consequence of the policy change, some were unexpected.

First, we found important differences in the types of patients initially listed and transplanted by exception between the 2 policy periods. Candidates in the postpolicy period listed by exception were less likely to have hypertrophic or restrictive cardiomyopathy or congenital heart disease. This was an anticipated change because these patient populations were prioritized on the list at status 4 under the new policy as their anatomy often precludes durable MCS device implantation. We also found that candidates in the postpolicy period listed by exception had greater use of temporary MCS devices and intravenous inotropes, lower cardiac outputs, and higher PCWPs and mean PA pressures than candidates listed by an exception under the prior policy. This suggests that the rise in exception status listings was not driven by an increase in listings for less sick candidates. Furthermore, candidates transplanted by exception were more likely to have a durable MCS device, consistent with prior work and reflecting the relative deprioritization of left ventricular assist device recipients under the 2018 policy.[4,7]

Second, we found similar waitlist mortality for candidates listed by exception and standard criteria in the prepolicy period. This supports the appropriate use of exception status listings during the prepolicy period, as candidates listed at the same medical urgency status would be expected to have similar waitlist mortality regardless of whether they received the status by exception or standard criteria. In contrast, we saw significantly lower waitlist mortality for candidates listed status 1 exception compared to status 1 standard criteria in the postpolicy period. This is a novel and important finding as previous analyses did not examine the impact of medical urgency status on waitlist outcomes in exception status candidates. This may be driven by the increased use of extracorporeal membrane oxygenation in standard criteria candidates, thereby placing them at risk for adverse outcomes while on the waiting list. An alternative explanation would be greater use of status 1 exception listings for less sick candidates. Notably, in our analysis, candidates retained their status (both medical urgency and exception vs standard criteria listing) while being inactive at status 7 on the waiting list.

Finally, we found higher transplant rates for candidates listed by exception in both the pre- and postpolicy periods. The increase in the transplant rate while listed at exception status in the postpolicy period has been previously reported though the analysis did not account for medical urgency status.[4] Uniquely, we found that this result persisted in our interaction model, which accounted for both exception status listing and medical urgency status and adjusted for clinical covariates known to affect the transplant rate by impacting the rate of organ offers. The higher transplant rate in exception status candidates may thus reflect unmeasured clinical covariates affecting the offer rate or differences in acceptance practices for candidates listed by exception compared with those listed by standard criteria.

Our work builds on the existing literature in several important ways. First, we performed a comparative analysis of exception status listings during 2 policy periods, while prior work focused on a single policy period. This allowed us to identify changes in the use of and outcomes for exception status candidates following changes to the heart allocation policy. Second, in our analysis of waitlist mortality, our primary model was minimally adjusted, accounting only for medical urgency status and exception status listing. We deliberately chose not to add additional candidate covariates into the model as medical urgency status should reflect overall illness severity inclusive of all clinical factors as determined by candidates' treating cardiologists. This, however, was in contrast to our model for the transplant rate, which was fully adjusted as both medical urgency status and candidate-level characteristics impacting upon the available donor pool are known to influence the rate of organ offers. Finally, we treated both medical urgency status and exception status listing as time-dependent covariates in our waitlist models, allowing us to isolate the hazards of death and transplantation, while a candidate holds a particular medical urgency and exception status. This differs methodologically from other studies that have historically categorized candidates' statuses at a single time point, most often at listing or at transplantation. A particular concern with other analyses is "immortal time bias," which can arise when candidates are categorized as exception status listing if they were ever listed by exception. Our analysis is not subject to this bias because of the use of time-dependent covariates.[8]

The present study does have limitations. First, the data were extracted from a large registry, presenting issues of missing data and inaccurate reporting. There was relatively low missingness for the most important variables, however, allowing us to perform a complete case analysis. Data were not available, however, for all candidates on clinical characteristics known to affect listing status and thereby exception status requests, such as systolic blood pressure. Second, given changes to reporting requirements with the 2018 policy update, patterns of missingness may differ between the periods, particularly candidate sensitization and resulting in it being excluded as a covariate in our prepolicy model of waitlist mortality. Third, we are unable to ascertain in this study why candidates were listed at exception status, which would require a review of the individual exception request narratives. Finally, the current analysis contains approximately 3 years of data from both the pre- and postpolicy periods. As the 2018 policy change is still relatively recent, it remains to be seen whether center and provider practice patterns and candidate outcomes will continue to evolve.

In conclusion, the 2018 heart allocation policy update led to a significant and dramatic increase in the use of exception status despite its goal of reducing exception status listings. While the policy decreased exception status requests for certain subgroups with advanced heart failure, exception status requests increased for other subgroups with heart failure, such as patients with temporary and durable MCS devices. There were also unexpected changes in waitlist mortality for candidates listed by exception at select statuses. Most notably, the lower hazard of death for candidates listed status 1 exception raises concern that standard criteria candidates may be sicker or greater use of extracorporeal membrane oxygenation in this group may place them at higher risk for adverse outcomes. Future studies to disentangle which of these hypotheses might be responsible for the observed differences in outcomes for status 1 candidates are necessary and have potential implications for future revisions to the heart allocation policy.

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All authors take responsibility for the content of the manuscript. All authors contributed to the conceptualization of the work and study design. Lyden and Ahn performed the analyses under the supervision of Israni and Zaun. The first draft of the manuscript was prepared by Golbus. It was reviewed and edited by all authors, all of whom made the decision to submit the manuscript.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.healun.2023.05.004.

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