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Geographic Variation in the Treatment of U.S. Adult Heart Transplant Candidates

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Abstract

BACKGROUND—The current U.S. priority ranking for heart candidates is based on treatment intensity, not objective markers of severity of illness. This system may encourage centers to overtreat candidates.

OBJECTIVES—This study sought to describe national variation in the intensity of treatment of adult heart transplantation candidates and identify center-level predictors of potential overtreatment.

METHODS—The registrations of all U.S. adult heart transplantation candidates from 2010 to 2015 were collected from the SRTR (Scientific Registry of Transplant Recipients). "Potential overtreatment" was defined as treatment of a candidate who did not meet American Heart Association cardiogenic shock criteria with either high-dose inotropes or an intra-aortic balloon pump. Multilevel logistic regression and propensity score models were used to adjust for candidate variability at each center. Center-level variables associated with potential overtreatment were identified.

RESULTS—From 2010 to 2015, 108 centers listed 12,762 adult candidates who were not in cardiogenic shock for heart transplantation. Of these, 1,471 (11.6%) were potentially overtreated with high-dose inotropes or intra-aortic balloon pumps. In the bottom quartile of centers, only 2.1% of candidates were potentially overtreated compared with 27.6% at top quartile centers, an interquartile difference of 25.5% (95% confidence interval: 21% to 30%). Adjusting for candidate differences did not significantly alter the interquartile difference. Local competition with 2 or more centers increased the odds of potential overtreatment by 50% (adjusted odds ratio: 1.50; 95% confidence interval: 1.07 to 2.11).

CONCLUSIONS—There is wide variation in the treatment practices of adult heart transplantation centers. Competition for transplantable donor hearts is associated with the potential

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overtreatment of hemodynamically stable candidates. Overtreatment may compromise the fair and efficient allocation of scarce deceased donor hearts.

Keywords

ethics; heart transplantation; organ allocation

Heart transplantation is a definitive, life-saving treatment for end-stage heart failure, a devastating disease that kills >250,000 Americans each year (1). Unfortunately, the supply of deceased donor hearts cannot meet the demand for transplantation. In the United States, more than one-third of candidates will die or be delisted without transplant (2,3). Under the current allocation system, candidates are given priority for scarce deceased donor hearts based on "status," a 3-tiered ranking system intended to prioritize medically urgent candidates (4,5). Status is determined by treatment intensity, based on the premise that candidates nearer death will require escalation of life-sustaining therapies.

There were expected to be relatively few patients waiting at the highest priority "Status 1A," as these candidates who are receiving the most intense forms of cardiac life-support therapy should have short life expectancies without heart transplantation (4). However, the proportion of Status 1A candidates has doubled in the past 10 years and now >40% of candidates wait at this highest priority designation, decreasing the likelihood that lower priority candidates are allocated a donor heart (2). Because status is based on therapy and not objective markers of illness, it has been suggested that this trend could be explained in part by transplantation centers "gaming the waitlist" by overtreating less urgent candidates with medically unnecessary therapy to elevate their statuses to the level needed to receive a transplant (6–8). In response to these concerns, the Organ Procurement and Transplant Network (OPTN) has proposed a new requirement that high-priority candidates meet American Heart Association (AHA) hemodynamic criteria for cardiogenic shock, "rather than qualifying [for status] based on the presence of the therapy alone" (9,10). With these criteria, the OPTN is specifically targeting the use of intense Status 1A qualifying therapy on candidates who do not physiologically require it. Recently, it has been shown that many candidates listed at Status 1A with high-dose inotropes and intra-aortic balloon pumps (IABP) are not in cardiogenic shock by AHA criteria and therefore are potentially overtreated (11,12).

However, heart transplantation centers may have legitimate nonhemodynamic reasons to treat candidates with intensive support therapies, such as severely impaired functional status or impending end-organ damage from heart failure. Analysis of the geographic variation in the treatment practices of heart transplantation centers provides an opportunity to explore this potentially inappropriate practice more fully. Intercenter variation in transplantation practices could be explained by geographic variation in candidate characteristics, which would exonerate centers that use this practice frequently. Donor hearts are allocated first to local Status 1A candidates in the same geographic region (through an organ procurement organization [OPO]) as the donor (13). Therefore, some of the variation in transplantation center listing practices may be explainable by differences in competitive forces that transplantation centers experience, such as the number of competing centers in an OPO.

This study uses a complete national registry to describe the center-level variation in the treatment of adult heart transplantation candidates, accounting for differences in candidate characteristics with risk standardization and propensity score methods. Secondarily, this study identifies the center-level predictors of potential overtreatment of heart transplantation candidates.

METHODS

DATA SOURCE AND STUDY PERIOD

This study used data from the SRTR (Scientific Registry of Transplant Recipients). The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the OPTN. The Health Resources and Services Administration, U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors. Initial registration data of all U.S. adult heart transplantation candidates added to the waitlist between January 1, 2010, and December 31, 2015, the same time period as of this work, quantified the impact of the shock requirement on the contemporary U.S. heart candidate population (11). Initial registration is a standard reference point in the care of advanced heart failure patients when complete candidate information is collected.

STUDY POPULATION AND OUTCOME VARIABLE: CANDIDATES AT RISK FOR POTENTIAL OVERTREATMENT

Hemodynamics on heart transplantation candidates are required to be recorded at the time of initial listing and note what supportive therapy the candidate was receiving at the time of measurement. Potentially overtreated candidates were defined as those candidates who were listed as Status 1A via treatment with high-dose inotropes with invasive hemodynamic monitoring or IABP in an intensive care setting, despite not meeting the hemodynamic requirements for cardiogenic shock. Cardiogenic shock was defined using the methodology published by the OPTN, which is based on AHA guidelines and minimum inotrope dose requirements (Figure 1, Online Table 1) (9–11). The study population was all heart transplantation candidates who were not in cardiogenic shock and therefore at risk for potential overtreatment. Candidates in cardiogenic shock were excluded from the principal analysis, as these candidates were not at risk for potential overtreatment. Similarly, candidates not subject to the shock requirement, specifically those with surgically placed mechanical circulatory support devices or a board-reviewed Status 1A exception, were excluded. Finally, candidates listed as Status 1A with veno-arterial extracorpeal membrane oxygenation, percutaneous ventricular assist devices, or who had missing hemodynamic data were conservatively considered to be in cardiogenic shock and excluded (Figure 2).

For candidates in the study population, all available nonhemodynamic data from the transplantation candidate registration was collected. Medical data included age, weight, height, sex, body mass index, cardiac diagnosis, blood type, renal function, history of diabetes, cerebrovascular disease, malignancy, cardiac surgery, smoking, and defibrillator placement. Functional status was recorded on the Karnofsky 11-point performance status scale, which has been validated in heart failure patients (14,15). Socioeconomic variables included citizenship, race, insurance type, education, and work history.

CENTER- AND OPO-LEVEL VARIABLES

For active heart transplantation centers during the study period, the yearly listing volume, transplantation volume, time to transplantation, and listing practices (initial status and therapy support) were calculated. To measure the local competition for transplantable hearts in each OPO area, the number of candidates listed, transplantations performed, supply of donor hearts, proportion of transplantations performed using local hearts, recipient status, and number of centers were calculated. The transplantation market share of each center and the OPO Herfindahl–Hirschman index (16) were also calculated. All variables were calculated individually for each candidate using data from the prior year's listing to account for variation over time. Centers with very low listing volume, defined as <5 adult listings per year, were excluded.

STATISTICAL ANALYSIS

Using unadjusted rates of potential overtreatment, we identified centers that fell in the top and bottom quartiles of potential overtreatment. The interquartile differences for all candidate, center-level, and OPO-level variables were compared. To account for correlations of candidates among centers, robust standard errors clustered by center were used. Time to transplantation and survival from time of candidate listing (including post-transplantation period for transplanted candidates) were estimated using Cox proportional hazard models with shared frailty by center.

ADJUSTMENT FOR CANDIDATE CHARACTERISTICS

There are legitimate nonhemodynamic reasons, such as very poor functional status, end-organ jeopardy, or the inability to use durable mechanical circulatory support, to treat a candidate with intensive therapies not strictly indicated by hemodynamic measurements. Therefore, we accounted for differences in nonhemodynamic candidate characteristics using 2 different methods.

First, because the data were clustered with candidates listed at centers located within OPO, we estimated a multivariate multilevel logistic regression model with random intercepts at the OPO and center levels (17,18). We used the model results to calculate risk-standardized potential overtreatment rates using methodology developed for public reporting of outcomes (19–23). This standardized rate provides an index to compare different centers, accounting for differences in candidate mix at each center.

Second, we performed a propensity score nearest-neighbor matching analysis to minimize bias from candidate-level differences, a recommended sensitivity analysis when performing risk-standardization (23). A propensity score was used to match candidates listed at top quartile centers to similar candidates listed in the bottom quartile based on all available candidate factors. After matching, recommended balancing diagnostics were performed to ensure adequate covariate balance in the propensity score–matched sample (24). The matched groups were compared to estimate the average effect of being listed at a top quartile center versus a bottom quartile center.

IDENTIFYING CENTER- AND OPO-LEVEL PREDICTORS OF POTENTIAL OVERTREATMENT

We then developed multilevel logistic regression models to identify OPO- and center-level variables associated with potential overtreatment. Because certain variables (e.g., OPO listing and transplantation volume) were highly collinear, we performed initial variable selection by calculating variance inflation factors and removing variables with variance inflation factors >10. For remaining variables with correlations of >0.7, we removed the variable(s) with the higher variance inflation factors. We then entered all remaining variables into the multilevel logistic regression model and performed backward selection with an exclusion criterion of p >0.1, forcing the retention of all controlling candidate-level variables. After OPO-level variable selection, we repeated the same process with center-level variables.

Analysis performed with Stata version 15 (StataCorp, College Station, Texas). A p value of <0.05 was considered significant and was calculated for all comparisons as a way to characterize the results even in situations where the entire population was included.

RESULTS

From 2010 to 2015, there were 19,919 adult heart-only candidate listings with 12,726 noncardiogenic shock candidates at risk for potential overtreatment listed at 108 centers within 51 OPO. Of at-risk candidates, 1,471 (11.6%) were potentially overtreated with high-dose inotropes or an IABP and listed as Status 1A, 5,369 (42.1%) were listed as Status 1B, and 5,922 (46.4%) were listed as Status 2 (Figure 2). The geographic variation in the unadjusted rate of potential overtreatment by OPO is displayed in the Central Illustration. There is substantial intraregional variation, with neighboring OPO often having dramatically different potential overtreatment rates. Of note, the 3 largest urban areas in the United States (New York, Chicago, and Los Angles) have high rates of potential overtreatment.

There was wide center-level variation in potential overtreatment, with center rates ranging from 0% to 68% (Figure 3). The distribution was right-skewed with the top quartile of centers responsible for 60% of all potentially overtreated candidates. In the bottom quartile, there were 27 centers who potentially overtreated only 2.1% (n = 50) of 2,345 at-risk candidates. In contrast, the 28 centers in the top quartile potentially overtreated 27.6% (n = 884) of 3,203 at-risk candidates, interquartile difference of 25.5% (95% confidence interval [CI]: 21% to 30%). The odds of potential overtreatment were 1,650% higher in the top quartile than in the bottom (odds ratio [OR]: 17.5; 95% CI: 13.1 to 23.4).

The top and bottom quartile centers were of similar size with no significant differences in transplantation volume and listed a similar proportion of noncardiogenic shock candidates at risk for overtreatment (64% vs. 64%; p = 0.951) (Table 1). Top quartile centers operated in more competitive OPO environments with more centers per OPO (3.5 vs. 2.4; p = 0.014) and a higher percentage of recipients who were Status 1A at transplantation (71% vs. 58%; p = 0.009). Top quartile centers had significantly different practice patterns than bottom quartile centers. Top quartile centers were more likely to initially list candidates as Status 1A (39% vs. 15%; $p < 0.001$) and use Status 1A–qualifying high-dose inotrope therapy (20% vs. 2%; $p < 0.001$). Top and bottom quartile centers listed similar proportions of candidates supported with durable left ventricular assist devices (28% vs. 23%; p = 0.218).

Noncardiogenic shock candidates at risk for potential overtreatment listed at top and bottom quartile centers had only a few clinically meaningful differences in characteristics (Table 2). Top quartile at-risk candidates had higher cardiac indices (2.25 vs. 2.12 ml/min/m^2, p = 0.014) despite worse functional status (37% vs. 26% with severe impairment requiring hospitalization, $p < 0.001$). Top quartile noncardiogenic shock candidates were transplanted faster (median days to transplantation: 146 vs. 412, p = 0.002) and had higher survival from listing (hazard ratio for death/deterioration: 0.78; 95% CI: 0.65 to 0.93) (Online Figure 1) compared with candidates listed at bottom quartile centers. The higher survival from listing at top quartile centers was similar for all initial listing statuses of non-cardiogenic shock candidates (test for a differential effect by status: p = 0.73) (Online Figure 1).

The geographic distribution of unadjusted and risk-standardized center rates was similar with a standardized interquartile difference of 23.2% (95% CI: 19.4% to 27.0%) (Figure 3, Online Figure 2, Online Table 2 for full model used during risk standardization). Of the 28 top quartile centers by unadjusted rate of potential overtreatment, 21 (75%) remained in the top quartile of standardized potential overtreatment rate (Online Table 3). In well-balanced propensity score matched candidate cohorts (Online Figure 3, Online Table 4 for balancing tests), the interquartile difference in potential overtreatment was 24.9% (95% CI: 22.9% to 26.8%) and was not significantly different from the unadjusted interquartile difference.

The OPO- and center-level variables with significant associations to potential overtreatment after adjusting for candidate level variables are displayed in Table 3 (Online Tables 5 and 6 for full models). For every 10% increase in the percentage of recipients who were Status 1A at transplant, the odds of potential overtreatment increased 6% (adjusted odds ratio [aOR]: 1.06; 95% CI: 1.00 to 1.14). If there were 3 or more centers in the OPO, the odds of potential overtreatment were 50% higher (aOR: 1.50; 95% CI: 1.07 to 2.11). Finally, the shortest quartile of median time from Status 1A listing to heart transplantation (<19 days) was associated with a 43% increase in odds of potential overtreatment (aOR: 1.43; 95% CI: 1.19 to 1.72) relative to the middle second and third quartiles (19 to 63 days). In the full model adjusting for candidate- and OPO-level differences, the significant center-level practice variables associated with potential overtreatment were the percentage of all candidates (not just those at risk for overtreatment) listed as Status 1A and the center's 30-day transplantation rate for all candidates. For every 10% increase in the percentage of candidates a center initially listed as Status 1A, the odds of potential overtreatment increased 20% (aOR: 1.20; 95% CI: 1.11 to 1.29). For every 10% increase in a center's 30-day transplantation rate (percentage of candidates transplanted within 30 days of listing), the odds of potential overtreatment increased 19% (aOR: 1.09 to 1.29).

DISCUSSION

In this study of 12,762 adult heart transplant candidates listed in the United States between 2010 and 2015, we found wide center-level variation in treatment and listing practices that could not be explained by variation in candidate characteristics. The odds that a candidate was treated with high-dose inotropes or an IABP despite not being in cardiogenic shock was 17.5 × higher in the top quartile of centers than in the bottom quartile. Accounting for candidate-level differences with either risk standardization or propensity score matching did not reduce the magnitude of the center-level variation. Competitive local organ markets with more centers and higher percentages of top priority Status 1A candidates had higher rates of potential overtreatment.

Because the cardiogenic shock criteria are based on well-established major society guidelines (10), our null hypothesis for this study was that treatment of adult heart transplant candidates who were not in cardiogenic shock with high-dose inotropes or IABP would be rare. Furthermore, we hypothesized that what little overtreatment did occur could be explained by nonhemodynamic candidate variables. Instead, we found wide center-level variation in potential overtreatment with a more than 17-fold difference in the odds of potential overtreatment between the top and bottom quartile centers. After accounting for candidate variability with 2 different methods, the large variation in heart transplantation center treatment practices was unchanged.

The current U.S. geographic sharing system distributes donor hearts to local Status 1A candidates first. In this context, the center- and OPO-level variables associated with potential overtreatment have intuitive explanations. Centers located in more competitive OPO environments, with more Status 1A candidates and higher numbers of centers per OPO, were more likely to potentially overtreat candidates. In the pre-1999 heart transplant allocation system, which had only 2 status tiers, a similar relationship between competition and overtreatment was found (8). The relationship between median days from Status 1A listing to transplant with potential overtreatment can also be explained as a center response to the local transplantation environment. In OPO with good organ supply and very short Status 1A wait times (<19 days), admission to the intensive care unit (ICU) and treatment with IABP or high-dose inotropes may be used by centers with the goal of transplanting candidates quickly.

Overtreatment is not a new phenomenon in organ transplantation. Prior to the development of the Model for End-Stage Liver Disease (MELD) system in liver allocation, liver candidates with chronic liver disease who were physically in the ICU received higher priority for transplantation (25). After MELD was implemented and the ICU priority bump eliminated, the probability of ICU admission dropped 45% despite an increase in average recipient MELD score (26). This suggests that before MELD was implemented, unnecessary ICU admissions were frequent.

From the perspective of a heart transplantation physician, who is responsible for the care of an individual patient, potential overtreatment can be understood. There may be compelling subjective factors, such as severely impaired functional status, which make the use of high-dose inotropes or an IABP appropriate even if the patient is not technically in cardiogenic shock. Furthermore, for an individual patient, the risks of a long wait at lower status may outweigh the harms of overtreatment (6). In our study, we found that centers with top quartile rates of potential overtreatment transplanted their non-cardiogenic shock candidates much faster (median: 146 days vs. 412 days) and had better overall survival outcomes, regardless of initial listing status. These results imply that centers may be using escalation of medical therapies strategically to get their candidates transplanted earlier and achieve better overall results. These positive outcomes likely re-enforce aggressive treatment practices.

However, widespread overtreatment is problematic for multiple reasons. First, it could lead to excess cost and unnecessary risk of therapy-related complications. Chronic inotrope therapy increases mortality in stable advanced heart failure and high-dose inotrope therapy is only indicated in cardiogenic shock (27–29). More importantly, overtreatment in heart transplantation unfairly elevates the status of less urgent candidates while truly urgent candidates die waiting (or perhaps are never listed). The federal final rule governing U.S. organ transplantation states that candidates should be offered organs “from most to least medically urgent” (5). Because the median time from Status 1A listing to transplantation has ballooned to >3 months (2) and the sickest candidates benefit the most from heart transplantation (30), misallocation of hearts is ethically unacceptable. Further research is required to estimate how many of the >600 heart transplant candidates who die or become too sick to undergo transplantation each year could have been saved with a better allocation system (3).

It may be argued that the problem of overtreatment will be effectively solved by using the shock criteria to bar less urgent candidates from high priority listing status (31). However, as stated by the OPTN, the expected effect of the shock requirement is “based on current behavior and practices, and [this has raised concern] that the proposal would influence practitioners to behave differently than they currently do” (31). We believe it unlikely that transplantation programs that currently utilize IABP or multiple inotropes in aggressive treatment strategies will feel comfortable listing the majority of their candidates at low-priority status. Centers may be tempted to “game” hemodynamic measurements, perhaps by taking the lower of thermodilution or Fick cardiac indices. We also anticipate that centers will shift practices and use more surgically placed mechanical circulatory support devices, which would be exempt from the shock requirement (9). Finally, we believe therapy-based allocation systems will always be susceptible to manipulation and recommend the development of an objective scoring system for heart allocation analogous to MELD or the Lung Allocation System.

STUDY LIMITATIONS

We have been careful in this paper to use the term “potential” overtreatment to describe our principal outcome for a reason. Though based on major society guidelines, the criteria we used to define potential overtreatment were only announced in December 2016 and are not yet implemented as OPTN policy (9). Indeed, the criteria as written would penalize a center for using high levels of inotropic or mechanical support that ended up raising a candidate’s cardiac index above arbitrary cutoffs, even if the treatment team believed that strategy to be clinically necessary. Also, the AHA cardiogenic shock criteria have not been prospectively validated in the heart transplant candidate population and may not be the best way to risk stratify candidates (11,32,33). However, because the criteria are based on objective, audited hemodynamic measures that are routinely employed in the management of heart failure patients, we believe that the potential overtreatment outcome was adequate to measure variation in treatment practices.

While we used all of the available candidate characteristics and 2 different methods to account for candidate variability, it is possible that key unmeasured candidate variables could justify some of the center-level variation in treatment. However, it is exceedingly unlikely that additional candidate variables could explain the large interquartile difference observed.

CONCLUSIONS

There is meaningful variation in the treatment practices of adult heart transplantation centers. Heart transplantation centers that overtreat candidates have shorter waiting times and improved survival. Competition for transplantable hearts may drive overtreatment of hemodynamically stable heart transplant candidates. Overtreatment may compromise the fair and efficient allocation of scarce deceased donor hearts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX

For a supplemental Methods section as well as figures and tables, please see the online version of this paper.

ABBREVIATIONS AND ACRONYMS

AHA	American Heart Association
IABP	intra-aortic balloon pump
ICU	intensive care unit

MELD	Model for End-Stage Liver Disease
OPO	organ procurement organization(s)
OPTN	Organ Procurement and Transplant Network

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE

The current heart allocation system, which ranks candidates according to treatment intensity, has resulted in wide variation in transplantation center practice for similar candidates, and competition for available donor hearts is associated with overtreatment of hemodynamically stable transplant candidates.

TRANSLATIONAL OUTLOOK

An improved allocation system that is not based on intensity of treatment may reduce overtreatment, promote improve allocation of donor hearts, and save lives.

OPTN/UNOS Shock Requirement for Adult Heart Transplant Candidates*

Hemodynamic Requirement ← OR → **End-Organ Damage Requirement**

Hemodynamic Requirement

- Within 7 days prior to support all of the following in one 24-h period:
  - a. SBP <90 mm Hg
  - b. Low cardiac index
    - < 1.8 l/min/m^2 (no support)
    - < 2.0 l/min/m^2 (on support)†
  - c. Pulmonary capillary wedge pressure > 15 mm Hg

OR

End-Organ Damage Requirement

- Within 24 h prior to support one of the following:
  - CPR was performed on the candidate
  - SPB <70 mm Hg
  - Arterial lactate >4 mmol/l
  - AST or ALT >1,000 U/l

Minimum Inotrope Doses

Therapy	Dobutamine	Milrinone	Dopamine	Epinephrine
Single high dose	7.5 μg/kg/min	0.50 μg/kg/min	N/A	0.02 μg/kg/min
Multiple inotrope (at least 2 required)	3 μg/kg/min	0.25 μg/kg/min	3 μg/kg/min	0.01 μg/kg/min

FIGURE 1. Visual Summary of the New OPTN/UNOS Shock Criteria for Adult Heart Transplant Candidates

Under the new adult heart allocation system, candidates listed with veno-arterial extracorporeal membrane oxygenation, percutaneous ventricular assist devices, intra-aortic balloon pump, and high-dose inotropes will be subject to cardiogenic shock criteria (based on American Heart Association definitions) to qualify for high-priority listing. The criteria include either meeting hemodynamic requirements and minimum inotrope doses (left) or having evidence of poor end-organ perfusion (right). *Candidates supported with surgically placed mechanical circulatory support devices (such as continuous-flow left ventricular assist devices) are exempt from the requirement. †Candidates supported with high-dose inotropes are allowed to have a cardiac index up to 2.2 l/min/m^2 while in support. ALT = alanine transaminase; AST = aspartate transaminase; CPR = cardiopulmonary resuscitation; N/A = not available; OPTN = Organ Procurement and Transplant Network; SBP = systolic blood pressure; UNOS = United Network for Organ Sharing.

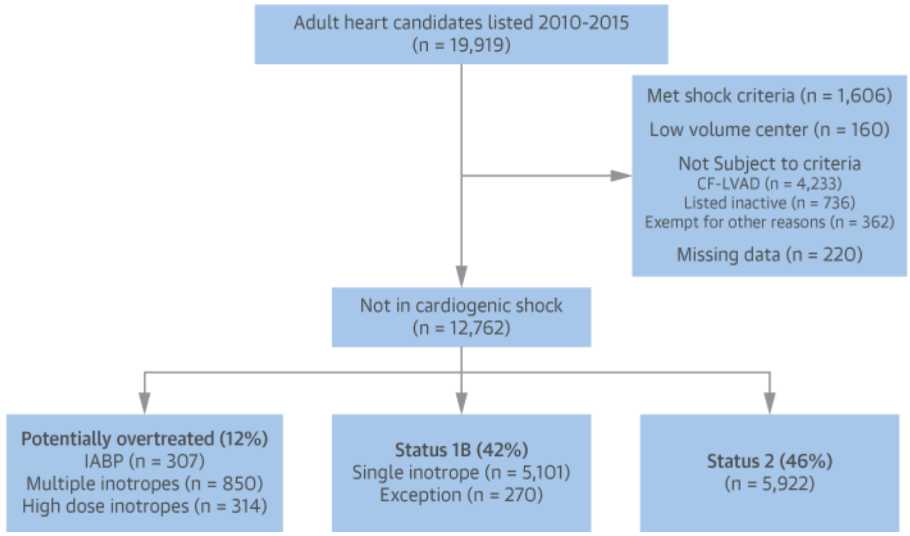


FIGURE 2. Flow Diagram Identifying Study Population From SRTR Dataset

Flow diagram constructed according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies. IABP = intra-aortic balloon pump; CF-LVAD = continuous-flow left ventricular assist device; SRTR = Scientific Registry of Transplant Recipients. Other reasons for exclusion include Status 1A exception or support with veno-arterial extracorpeal membrane oxygenation or percutaneous ventricular assist devices.

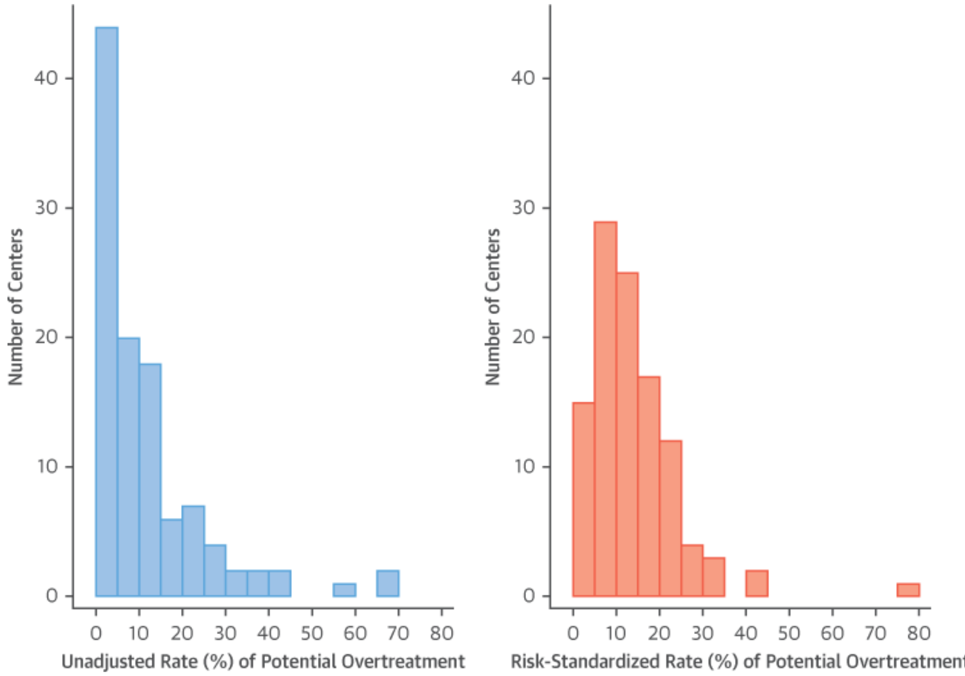
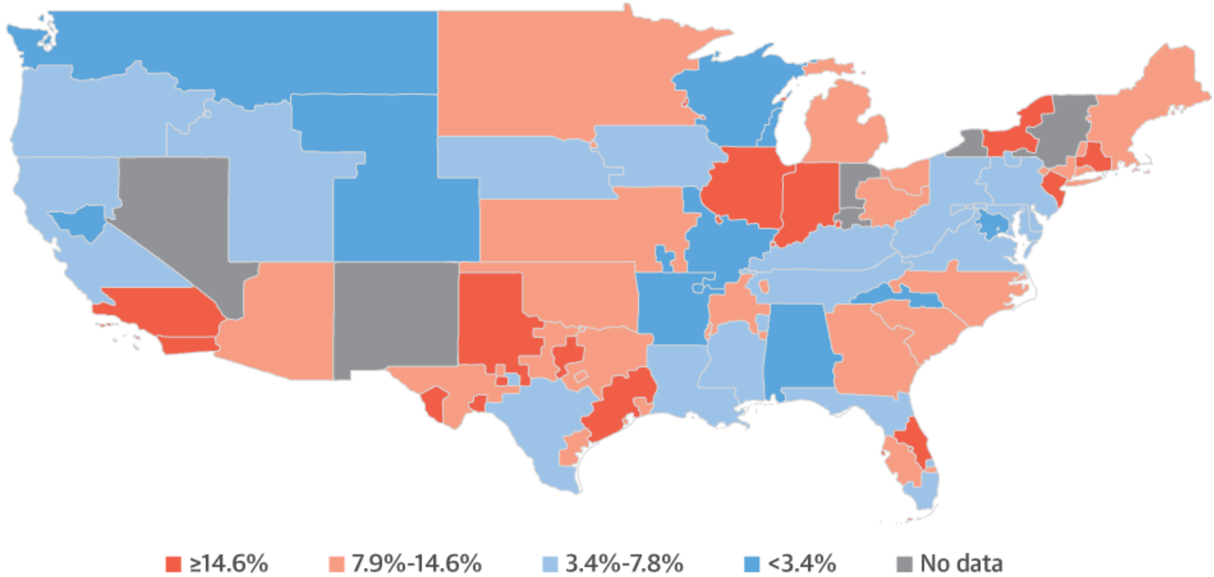


FIGURE 3. Unadjusted and Risk-Standardized Rates of Potential Overtreatment by Center

Rates are center averages during the 2010 to 2015 period. Adjusted rates calculated with multilevel regression results are shown in Online Table 2 using the methodology described in the Online Appendix. Only 7 centers had a >10% decrease in potential overtreatment rate after risk standardization. Ninety-four (87%) centers had a <10% change in overtreatment rate after risk standardization.



CENTRAL ILLUSTRATION. Geographic Variation in the Rate of Potential Overtreatment of U.S. Heart Transplant Candidates

National variation in the unadjusted rates of treatment of heart transplant candidates with balloon pumps or high-dose inotropes despite the absence of cardiogenic shock are displayed. Rates are aggregated at the organ procurement organization level, the first local level of organ allocation in the United States. **Colors** correspond to quartiles of potential overtreatment.

TABLE 1

Center-Level Differences by Rate of Potential Overtreatment

	All Centers 108 Centers (N = 19,539)	Bottom Quartile <3.4% Overtreatment 27 Centers (n = 3,658)	Top Quartile ≥14.6% Overtreatment 28 Centers (n = 5,020)	p Value
Candidates at risk	12,762 (65)	2,345 (64)	3,203 (64)	0.951
OPO-level variables				
OPO listing volume	101 ± 63	91 ± 68	149 ± 72	0.033
OPO transplant volume	63 ± 43	55 ± 42	97 ± 53	0.029
OPO Status 1A transplant proportion	0.62 ± 0.18	0.58 ± 0.20	0.71 ± 0.13	0.009
OPO Status 1B transplant proportion	0.34 ± 0.16	0.36 ± 0.18	0.23 ± 0.12	0.004
OPO donor heart supply	53 ± 29	40 ± 23	71 ± 35	0.004
OPO HHI	0.58 ± 0.26	0.63 ± 0.29	0.45 ± 0.20	0.041
Number of centers in OPO	2.7 ± 1.3	2.4 ± 1.3	3.5 ± 1.2	0.014
Center-level variables				
Center listing volume	47 ± 30	42 ± 30	52 ± 41	0.551
Center transplant volume	29 ± 23	24 ± 17	36 ± 33	0.313
Market share of center	0.57 ± 0.31	0.58 ± 0.34	0.40 ± 0.27	0.054
Proportion of center transplantations using OPO hearts	0.63 ± 0.20	0.60 ± 0.23	0.59 ± 0.18	0.792
Time to transplantation	189 ±249	246 ± 273	144 ± 214	<0.001
90-day transplantation rate	0.31 ± 0.17	0.21 ± 0.13	0.40 ± 0.18	<0.001
365-day transplantation rate	0.55 ± 0.18	0.47 ± 0.17	0.62 ± 0.16	<0.001
Listing status				<0.001
Status 1A	4,777 (24)	537 (15)	1,970 (39)	
Status 1B	8,110 (42)	1,815 (50)	1,629 (32)	
Status 2	5,922 (30)	1,184 (32)	1,320 (26)	
Inactive	730 (4)	122 (3)	101 (2)	
Listing therapy				<0.001
None	6,252 (32)	1,227 (34)	1,386 (28)	
High-dose inotropes	1,770 (9)	78 (2)	999 (20)	
IABP	647 (3)	60 (2)	239 (5)	
ECMO	212 (1)	28 (1)	60 (1)	
CF-LVAD	4,599 (24)	1,034 (28)	1,134 (23)	
Low-dose single IV inotropes	4,936 (25)	1,028 (28)	915 (18)	
Other	647 (3)	119 (3)	211 (4)	

Values are n (%) or mean±SD. All values calculated by year, excluding candidates with missing data or at low volume centers (n = 380). The p values for comparisons for between centers in the bottom and top quartile of overtreatment were calculated using generalized linear models with robust SE clustered by center.

CF-LVAD = continuous flow left ventricular assist device; ECMO = extracorporeal membrane oxygenation; HHI = Herfindahl-Hirschman index; IABP = intra-aortic balloon pump; IV = intravenous; OPO = organ procurement organization.

TABLE 2

Characteristics of Candidates at Risk for Potential Overtreatment by Center of Listing

	All At-Risk Candidates 108 Centers (N = 12,762)	Bottom Quartile 27 Centers (n = 2,345)	Top Quartile 28 Centers (n = 3,203)	p Value
Potentially overtreated	1,471 (11.6)	50 (2.1)	884 (27.6)	<0.001
Median time to transplantation	260 [67–844]	412 [138–1,124]	146 [38–539]	0.002
Survival from listing				0.006
1 yr	84.5 (83.8–85.2)	82.6 (80.9–84.1)	85.5 (84.2–86.7)	
3 yrs	73.3 (72.4–74.2)	69.6 (67.3–71.8)	76.3 (74.4–78.0)	
Post-transplantation survival				0.083
1 yr	91.0 (90.2–91.6)	88.4 (86.3–90.2)	91.9 (90.6–93.0)	
3 yrs	84.7 (83.7–85.7)	82.7 (80.1–85.0)	86.5 (84.7–88.2)	
Age at listing, yrs	53±12	53±13	54±12	0.039
Height, cm	174±10	174±10	173±10	0.189
Weight, kg	83±18	84±18	81±18	0.098
Cardiac index, ml/kg/m^2	2.17±0.63	2.12±0.62	2.25±0.63	0.014
Mean PAP, mm Hg	30±10	31±10	30±10	0.221
Mean PCWP, mm Hg	20±8	20±8	20±9	0.333
Diagnosis				0.455
Dilated cardiomyopathy	5,174 (41)	960 (41)	1,340 (42)	
Ischemic cardiomyopathy	4,335 (34)	761 (32)	1,144 (36)	
Restrictive cardiomyopathy	1,579 (12)	265 (11)	321 (10)	
Other	1,674 (13)	359 (15)	398 (12)	
Blood type O	5,448 (43)	990 (42)	1,365 (43)	0.928
Female	3,550 (28)	621 (26)	906 (28)	0.275
Karnofsky performance status				
Limited impairment, 10%–30%	4,292 (34)	972 (41)	748 (23)	0.003
Moderate impairment, 40%–60%	4,905 (38)	741 (32)	1,135 (35)	
Severe impairment, 70%–100%	3,191 (25)	616 (26)	1,172 (37)	
Unknown/missing	374 (3)	16 (1)	148 (5)	
Working for income	1,696 (13)	312 (13)	325 (10)	0.073
Race				0.986
White	8,448 (66)	1,478 (63)	1,988 (62)	
Black	2,716 (21)	515 (22)	697 (22)	
Hispanic	1,058 (8)	233 (10)	337 (11)	

	All At-Risk Candidates 108 Centers (N = 12,762)	Bottom Quartile 27 Centers (n = 2,345)	Top Quartile 28 Centers (n = 3,203)	p Value
Other	540 (4)	119 (5)	181 (6)	
College or higher education	6,987 (55)	1,292 (55)	1,626 (51)	0.181
Insurance type				0.419
Private	6,733 (53)	1,083 (46)	1,675 (52)	
Medicaid	1,336 (10)	330 (14)	372 (12)	
Medicare	4,177 (33)	830 (35)	1,027 (32)	
Other	516 (4)	102 (4)	129 (4)	
BMI, kg/m^2				0.088
<25	3,812 (30)	689 (29)	1,061 (33)	
25–29	4,629 (36)	823 (35)	1,176 (37)	
30–34	3,289 (26)	617 (26)	731 (23)	
≥35	1,032 (8)	216 (9)	235 (7)	
Diabetes	3,653 (29)	667 (28)	949 (30)	0.619
Renal function				0.352
≥60 ml/min/1.73 m^2	6,693 (52)	1,215 (52)	1,699 (53)	
30–59 ml/min/1.73 m^2	5,118 (40)	971 (41)	1,247 (39)	
<30 ml/min/1.73 m^2	579 (5)	96 (4)	147 (5)	
On dialysis	372 (3)	63 (3)	110 (3)	
Smoking history	5,795 (45)	1,124 (48)	1,355 (42)	0.215
CVA history	688 (5)	112 (5)	142 (4)	0.713
History of malignancy	1,071 (8)	200 (9)	237 (7)	0.357
History of cardiac surgery	4,210 (33)	840 (36)	1,136 (35)	0.907
Defibrillator in place	10,137 (79)	1,950 (83)	2,459 (77)	0.016

Values n (%), median [interquartile range], % (95% CI), or mean±SD. Candidates not at risk of potential overtreatment or with missing data (n = 7,157) were excluded (see Figure 1). The p values for comparisons for between top and bottom quartiles of overtreatment were calculated with robust SE clustered by center.

BMI = body mass index; CI = confidence interval; CVA = cerebrovascular accident; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure.

TABLE 3

OPO- and Center-Level Predictors of Potential Overtreatment in a Multilevel Logistic Regression

	Model 2	Model 3
OPO competition variables		
Percentage of recipients who were Status 1A at transplant (per 10%)	1.06* (1.00–1.14)	1.02 (0.96–1.10)
3+ centers in OPO, base 1–2 centers	1.50* (1.07–2.11)	1.45* (1.07–1.97)
Median time from Status 1A listing to heart transplantation by quartile, base middle quartiles, 19–63 days		
<19 days	1.43* (1.19–1.72)	1.25* (1.04–1.51)
≥64 days	1.22† (0.98–1.52)	1.31* (1.05–1.63)
Center practice variables		
Percentage of candidates listed as Status 1A, per 10%		1.20* (1.11–1.29)
30-day transplantation rate, per 10%		1.19* (1.09–1.29)
Candidates	12,762	12,762
Centers	108	108

Values are odds ratios (95% CI) or n.

* $p < 0.05$.

† $p < 0.1$. Candidate-level variable coefficients and full model results can be found in Online Tables 5 and 6. Model 2: Adjusted for candidate and OPO-level competition variables. Model 3: Adjusted for candidate, OPO-level competition, and center practice variables. The "30-day transplantation rate" is the percentage of candidates transplanted within 30 days of listing at a particular center.

Abbreviations as in Tables 1 and 2.