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County socioeconomic characteristics and heart transplant outcomes in the United States

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Abstract

Background—Geographic disparities in survival after heart transplantation have received mixed support in prior studies, and specific geographic characteristics that might be responsible for these differences are unclear. We tested for differences in heart transplant outcomes across United States (US) counties after adjustment for individual-level covariates. Our secondary aim was to evaluate whether specific county-level socioeconomic characteristics explained geographic disparities in survival.

Methods—Data on patients aged ≥18 years undergoing a first-time heart transplant between July 2006 and December 2014 were obtained from the United Network for Organ Sharing. Residents of counties represented by <5 patients were excluded. Patient survival (censored in March 2016) was analyzed using multivariable Cox regression. Shared frailty models were used to test for residual differences in overall all-cause mortality across counties after adjusting for recipient and donor characteristics. Measures of county economic disadvantage, inequality, and racial segregation were

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obtained from US Census data and coded into quintiles. A likelihood ratio test determined whether adjusting for each county measure improved the fit of the Cox model.

Results—Multivariable analysis of 10,879 heart transplant recipients found that, adjusting for individual-level characteristics, there remained statistically significant variation in mortality hazard across US counties ($P = .004$). Adjusting for quintiles of community disadvantage, economic inequality, or racial segregation did not significantly improve model fit (likelihood ratio test $P = .092$, $P = .273$, and $P = .107$, respectively) and did not explain residual differences in patient survival across counties.

Conclusions—Heart transplantation outcomes vary by county, but this difference is not attributable to county-level socioeconomic disadvantage.

Risk-adjusted patient survival is a key quality metric used for evaluating heart transplant programs in the United States (US).^{1,2} However, established methods of risk adjustment do not take into account geographic characteristics that may improve prediction of patient survival.³ This may be an important omission, as surgical outcomes have been shown to vary geographically across the US.^{4,5} Community socioeconomic disadvantage may limit access to care and social support available to transplant recipients, whereas individual socioeconomic status may influence patients' morbidity burden and likelihood of treatment nonadherence. Despite evidence suggesting that geographic disparities may exist in some groups of patients undergoing heart transplantation,^{6,7} it remains unclear at what geographic level (eg, US Census tract, ZIP code, or county) these disparities should be evaluated and which geographic characteristics accurately distinguish between locales with better or worse patient outcomes.

To overcome a lack of data on transplant recipients' individual socioeconomic status (SES), several studies have incorporated geographic measures of socioeconomic disadvantage in multivariable analysis of heart transplantation outcomes.^{8–11} Most commonly, the median household income (MHI) of patients' US Postal Service ZIP code has been used to supplement data available in the United Network for Organ Sharing (UNOS) patient registry, such as patient insurance status.^{8,11} Research in kidney and liver transplantation has demonstrated the value of this approach to improve prediction of posttransplant survival.^{12–14} However, analyses of US adult heart transplant recipients have found local MHI to be uncorrelated with survival or allograft rejection.^{9,14} Furthermore, adjusting surgical quality measures for socioeconomic characteristics may inadvertently adjust for differences in the quality of care provided at different institutions. Therefore, the rationale for adjusting models of heart transplant outcomes for local socioeconomic characteristics remains in question. To disambiguate the role of local socioeconomic characteristics in predicting heart transplant outcomes among US adults, we linked UNOS registry data to US Census Bureau data on county socioeconomic disadvantage, income inequality, and racial segregation. Our primary aim was to determine whether significant geographic variability in heart transplant recipients' survival existed after adjusting for individual characteristics. Our secondary aim was to determine which, if any, local socioeconomic characteristics adequately explained this geographic variation.

Methods

Following Institutional Review Board approval, data were obtained from the UNOS registry, which tracks candidates and recipients of solid organ transplants in the US.¹⁵ Patients 18 years or older undergoing first-time heart transplantation since July 2006 (corresponding to the implementation of broader regional sharing of donor organs) were evaluated for inclusion if they had been transplanted no later than 2014, when the US Census Bureau released the most recent available data on socioeconomic characteristics of small geographic areas. Patients' residence was defined using ZIP codes, but there were too few patients in each ZIP code to evaluate clustering of transplant outcomes at that geographic level.¹⁶ Therefore, ZIP codes were linked to US counties according to the county that contained the majority of each ZIP code's population. Patients were excluded from the analysis if they were missing data on ZIP code of residence and if they were missing data on local socioeconomic measures, described below. Heart transplant recipients residing in counties represented by ≤ 5 patients (to assure a sufficient number of patients in each geographic unit for multilevel modeling) and with complete data on study covariates were included in the final multivariable analysis. Patients with incomplete data on 1 or more covariates were excluded from this group. The characteristics of this group were compared with 2 groups of excluded patients: those who were excluded because of residence in a county with <5 patients and those who were excluded solely because of missing data on covariates.

The primary outcome was overall, all-cause patient mortality (using all available follow-up data) ascertained from transplant center reports and linkage to the Social Security Death Master file. Whereas 1-year survival outcomes are currently used for transplant program evaluation,¹ we examined overall survival duration because of the potential for socioeconomic disparities in survival to emerge later than 1 year posttransplant.¹⁷ A secondary composite outcome was examined to account for possible disparities in nonfatal complications of heart transplant. The composite outcome was defined as experiencing death, graft failure, acute rejection, rehospitalization, or listing for retransplant; and the time elapsed until the earliest of these events was used for survival analysis. Results for this secondary outcome are presented in the Appendix. The primary exposure variables were measures of county characteristics obtained from US Census Bureau data and matched to patient records in the UNOS registry by the county of residence at the time of the transplant.

Data on county socioeconomic characteristics were obtained from the 2011–2014 5-year file of the American Community Survey.¹⁸ The first measure was a composite index of socioeconomic advantage indicators (MHI; median value of owner-occupied housing units; percentage of households with interest, dividend, or net rental income; percentage of workers employed in management, business, science, and arts occupations; and percentage of residents >25 years of age with a high school diploma [$\alpha = .81$]).¹⁹ Positive values indicated relative socioeconomic advantage, whereas negative values indicated disadvantage. The second measure was the Index of Concentration at the Extremes, measuring the local concentration of wealthy families (incomes $>\$75,000$) and poor families (incomes below the Federal poverty line).²⁰ Index of Concentration at the Extremes scores were expressed in the range of -1 to 1 , with -1 indicating that all families were poor and 1 indicating that all families were affluent. Lastly, we used the county index of dissimilarity to measure

residential racial segregation, indicating the percentage of white or black households that would have to change neighborhoods to achieve integration.²¹ The index of dissimilarity was calculated using Census tracts as the neighborhood unit, and scores ranged from 0 to 1, where 0 indicated that the county was completely integrated and 1 indicated that the county was completely segregated. Each of these 3 measures was recoded into quintiles among the counties represented in the analytic data set.

Study outcomes were analyzed using multivariable Cox proportional hazards regression. The primary model included individual-level covariates (described below) and a shared frailty parameter at the county level. “Shared frailty” refers to an unobserved county characteristic that increases or decreases mortality hazard by some factor for all residents of that county. The model estimated the variance of the shared frailty term, where a variance of zero meant the hazard did not vary by county (after adjusting for observed covariates), whereas a nonzero variance implied that transplant outcomes remained unequal across counties.²² The statistical significance of the shared frailty term was determined using a likelihood ratio (LR) test against a model where the variance was constrained at 0, and the *P* value of this test was our primary measure of county-level differences in outcomes (*P* < .05 implying statistically significant residual variability in transplant outcomes across counties).

In secondary models, each specific county-level socioeconomic measure was added to the model to evaluate whether each measure was significantly associated with patient survival and whether it accounted for county-level variability as expressed by the shared frailty term. Improvement in model fit after inclusion of specific geographic characteristics was evaluated using the LR test. Following our recent investigation of individual-level factors predicting survival after heart transplantation,¹⁴ covariates included patient age, gender, race, insurance status at the time of heart transplantation, and components of the Index for Mortality Prediction After Cardiac Transplantation score,²³ with the exception of pulmonary vascular resistance, which had significant missing data and was unrelated to survival after adjustment for other variables in the analysis. Donor characteristics in the analysis included age, gender, race, cause of death, cardiopulmonary resuscitation (CPR),²⁴ cytomegalovirus (CMV) and predicted heart mass (pHM)²⁵ matching with the recipient, and allograft ischemia time. Data analysis was performed in Stata/MP 13.1 (StataCorp, LP, College Station, TX), and *P* < .05 was considered statistically significant. No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

Results

There were 16,378 adult recipients of a first-time heart transplant between July 2006 and December 2014, of whom 323 were excluded because of unknown place of residence, 55 were excluded because of missing data on local socioeconomic characteristics, 2,606 were excluded because of residing in a county represented by <5 patients, and 2,515 were excluded because of missing data on covariates. Recipient, donor, and county characteristics of patients included in the multivariable analysis (*n* = 10,879) were compared with patients excluded because of residence in counties with <5 heart transplant recipients (*n* = 2,606) and patients excluded because of missing data (*n* = 2,515) in Table I. Patients excluded from the

analysis because of small subsample size in their county of residence were predominantly white and were more likely to live in small, rural counties. Patients excluded from the analysis because of missing data did not significantly differ in racial composition or educational attainment, and were slightly more likely to have private insurance, than patients included in the multivariable analysis.

The final analytic sample represented residents of 624 counties, of which 513 (82%) included 25 patients, 70 (11%) included 26–50 patients, 31 (5%) included 51–100 patients, and 10 (2%) included >100 patients. To characterize county differences in transplant outcomes, county-specific Kaplan-Meier estimates of 5-year survival are illustrated in Figure. In the median county, 5-year posttransplant survival was 75% (interquartile range 63%–86%). In 97 of the counties, 87 of which were represented by 10 or fewer patients, the estimated 5-year survival rate was >95% because of few or no deaths being observed within 5 years of transplant. The multivariable model of patient survival, adjusted for recipient and donor covariates and including a shared frailty term at the county level, is presented in Table II. There remained statistically significant residual differences in mortality hazard across counties, as indicated by the test of the shared frailty variance ($P = .004$). The estimated variance of the shared frailty term (0.037) implied that in one-fifth of counties, mortality hazard was at least 16% greater than the average county, whereas in another one-fifth of counties, mortality hazard was at least 16% smaller than in the average county. Recipient characteristics associated with increased mortality hazard included black race, public as opposed to private insurance, greater body mass index, higher bilirubin and creatinine, ischemic cardiomyopathy, prior dialysis, prior cardiac surgery, pretransplant infection requiring intravenous therapy, and pretransplant mechanical ventilation or extracorporeal membrane oxygenation. Donor characteristics associated with greater mortality hazard included older donor age, black donor race, and longer allograft ischemic time.

In subsequent analyses, specific county characteristics were added to the multivariable model. Adjusted hazard ratios (HRs) of county-level measures are summarized in Table III. Residents of counties with the highest concentration of rich households had a lower mortality hazard than residents of counties with the highest concentration of poor households (HR = 0.85, 95% CI 0.73–0.98, $P = .025$). Residents of the most segregated counties had a lower mortality hazard than residents of the least segregated counties (HR = 0.82, 95% CI 0.71–0.95, $P = .010$). Yet, county measures of SES, income inequality, and racial segregation did not explain residual variability in patient outcomes across counties (test of shared frailty variance $P = .010$, $P = .008$, and $P = .003$, respectively). Furthermore, county measures did not significantly improve model fit (LR test $P = .092$, $P = .273$, and $P = .107$, respectively). Consistent with these findings, the secondary composite outcome of posttransplant complications evinced significant variability across counties, which was not explained by adjusting for specific measures of county disadvantage (Appendix).

Discussion

Risk adjustment for socioeconomic characteristics has been proposed to improve the evaluation of hospitals on outcomes of complex surgery, including coronary artery bypass grafting and solid organ transplantation.^{3–5} A rich literature in social epidemiology has also

demonstrated that people's health is influenced by the socioeconomic circumstances of their communities.^{20,26–30} For example, disadvantaged communities may have lower investment in health care infrastructure, limited access to care, and fewer resources available to provide social support to patients requiring major surgery. Therefore, community characteristics may predict worse surgical outcomes independently of individual characteristics. In the setting of transplantation, this insight has led to recommendations that models predicting transplant outcomes should be adjusted for community or geographic characteristics.^{3,12} Whereas this approach might improve prediction of transplant outcomes, it may also create perverse incentives for transplant centers, such as “skimming” the healthiest patients from the least-disadvantaged communities, to demonstrate the best risk-adjusted outcomes. Further challenging this recommendation, the present study systematically demonstrates that key measures of county disadvantage do not explain variability in outcomes of heart transplantation across US counties.

Conceptually, socioeconomic disadvantage may predispose patients to comorbidities, treatment nonadherence, or risky behaviors that would predict worse surgical outcomes, holding constant the quality of care patients receive. In the case of heart transplantation, however, strict selection of eligible candidates on the basis of financial stability, compliance with treatment, and commitment to the transplant process may blunt the influence of socioeconomic disadvantage. Indeed, among prior studies of heart transplant outcomes, only studies including children had determined that geographic measures of socioeconomic disadvantage were associated with worse outcomes.^{6,8,31,32} By contrast, analyses of adult heart transplant recipients found no support for the influence of community MHI on either patient survival or allograft rejection.^{9,14} Together with the present analysis, these results suggest that socioeconomic disparities in adult heart transplant outcomes may be primarily related to characteristics immediately affecting access to care (eg, insurance coverage),¹⁴ whereas other differences in SES may exert a stronger influence on access to transplant among patients with end-stage heart failure rather than outcomes of transplant among patients undergoing this procedure. Therefore, further work to develop interventions addressing socioeconomic disparities in heart transplantation may require targeting barriers to transplant evaluation and wait listing rather than differences in outcomes among transplant recipients.

Geographic disparities in surgical outcomes are noted across a variety of procedures and patient populations.^{4,5,7,13} A significant barrier to reproducing these findings in the setting of heart transplantation arises from the rarity of this procedure. There are too few heart transplant recipients in small geographic units (eg, ZIP codes) to formally test whether transplant outcomes exhibit clustering at this geographical level.¹⁶ Whereas prior studies have evaluated specific geographical predictors of heart transplant outcomes, these studies did not provide a test for residual geographic variation in patient outcomes (not attributable to the explicitly measured ecological factor).^{7,32} Therefore, we examined shared frailty of heart transplant recipients at the county level. This approach confirmed that counties significantly differed in risk-adjusted outcomes of heart transplantation, without assuming which observed county characteristic was most predictive of patient outcomes. However, this finding may not be generalizable to sparsely populated counties that were not represented in our final analysis. We initially considered patients from 941 (30%) of the 3,141 US counties

for inclusion in the analysis. Sixteen percent (2,606/16,378) of patients evaluated for inclusion were excluded because of residing in a county represented by <5 adult heart transplant recipients. These patients were more likely to live in rural counties, so there may exist additional disparities in heart transplant outcomes between rural and urban counties beyond the county differences in outcomes documented in our analysis. Yet, in counties represented by few patients, it may be prohibitively difficult to disentangle county-level factors (eg, rural/urban status) from recipient and donor characteristics influencing transplant outcomes. Therefore, describing independent associations between county-level predictors and posttransplant mortality may only be plausible when analyzing patient outcomes in densely populated counties.

Secondarily, we have complemented earlier studies of MHI by comparing heart transplant outcomes according to measures of county socioeconomic disadvantage using a composite measure of SES developed by Diez-Roux et al.¹⁹ Composite measures of community SES have been used to provide a more nuanced comparison of geographical units with respect to transplantation outcomes,^{6,13,33} although important limitations of this approach are that different methodologies have been used to combine multiple socioeconomic indicators and the weights assigned to each indicator have varied across studies. The second characteristic examined in our study was the index of concentration at the extremes, a measure of county economic inequality. Recent studies have suggested that greater economic inequality contributes to worse individual health outcomes, although no previous research has evaluated the contribution of economic inequality to survival after transplantation.^{34–36} Neither the composite index of county SES nor the measure of county inequality explained residual variation in heart transplant outcomes across counties. This finding is consistent with an earlier analysis of adult heart transplant recipients in the UNOS registry,¹⁴ although a subanalysis of adults bridged to heart transplantation with a left ventricular assist device suggested that patients in highly disadvantaged communities had worse posttransplant survival.³³ In the overall cohort of adult heart transplant recipients, however, outcomes did not vary by measures of county disadvantage or inequality.

Finally, we examined the role of black-white segregation, defined using the dissimilarity index.²¹ In the US, segregation contributes to lower economic opportunities, greater perceived discrimination, and greater stress experienced by members of minority groups and culminates in worse health outcomes among people living in areas with greater segregation.^{21,37} In addition, segregation reinforces detrimental effects of other contextual factors, such as low neighborhood income, low community levels of educational attainment, and high levels of public program dependence.²⁶ Fifty-two US metro areas have been previously characterized as “hyper-segregated” and include one-third of black metropolitan residents.³⁸ Despite the clear role of segregation as a health risk in other contexts, our study did not find evidence that greater black-white segregation within counties was associated with worse outcomes after heart transplantation. This result may have been confounded by a higher level of segregation in more urban counties, where greater access to care could have favorably influenced heart transplant outcomes. Nevertheless, we demonstrated a black-white disparity in posttransplant survival according to individual patient’s race, which was not reducible to differences in individual or community SES. As discussed in a recent review, this racial disparity may be explained by individual-level psychosocial,

immunological, and genetic factors not reflected in conventional measurements of socioeconomic advantage.³⁹

Our conclusions are limited by data collection in the UNOS registry and some aspects of the analysis performed. First, with the lack of exact address data, we relied on matching ZIP codes to counties, which may have misclassified some patients' county of residence. Second, we did not account for geographic mobility after transplantation, especially mobility between dissimilar counties. In addition, individual-level data on some aspects of SES, including income and wealth, were not available. Inclusion of such data may have explained residual differences among counties in heart transplant outcomes and may have obviated the need to consider county-level characteristics. Furthermore, heterogeneity of patient outcomes within counties may fundamentally limit the utility of using county characteristics to predict posttransplant mortality or complications. As noted above, our exclusion of counties that contained <5 patients limited the generalizability of the findings to transplant recipients from rural counties. Lastly, the analysis was limited by missing data on some individual characteristics, although a comparison of included and excluded patients did not find evidence that our analytic sample was biased by inclusion of particularly well-off patients who might have been immune to adverse effects of community disadvantage.

Conclusions

Geographic characteristics have been theorized to influence patient outcomes in the setting of heart transplantation. Using shared frailty models, our study presents the first formal confirmation of county-level variability in risk-adjusted survival among heart transplant recipients. Nevertheless, we failed to find associations between patient survival and a range of specific county socioeconomic characteristics. Therefore, if transplant program evaluation were to move forward with adjustment for socioeconomic factors, our results suggest a clear need to validate geographic measures of community disadvantage specifically in the context of heart transplantation before they can be used for this purpose. Whereas additional work in this area could reveal geographic variables that improve prediction of transplant outcomes, the sum of evidence in our study and prior research suggests that only socioeconomic factors directly related to health care provision (eg, insurance coverage) consistently influence heart transplant outcomes. This finding implies a need to prioritize barriers occurring earlier in the transplant process (eg, socioeconomic factors limiting timely evaluation and wait listing) in further research and intervention efforts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Appendix. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ahj.2017.05.013>.

Figure.
Distribution of 5-year survival rates after heart transplantation across US counties (n = 624).

Table 1

Recipient, donor, and county characteristics by inclusion in multivariable analysis of patient survival after heart transplantation (n, %, or mean, SD)

Variable	(A) Included in multivariable analysis (n = 10,879)	(B) Excluded because of residence in small county* (n = 2606)	(C) Excluded because of missing data† (n = 2515)	A vs B	A vs C
Recipient characteristics					
Posttransplant mortality	2352 (22%)	573 (22%)	642 (26%)	.682	<.001
Survival time (d)‡	1334 (910)	1415 (948)	1582 (992)	<.001	<.001
Recipient age (y)‡	53 (13)	53 (12)	53 (12)	.531	.543
Male recipient	8104 (74%)	1986 (76%)	1890 (75%)	.070	.495
Recipient race	—	—	—	<.001	.901
White	7112 (65%)	2184 (84%)	1649 (66%)	—	—
Black	2382 (22%)	315 (12%)	541 (22%)	—	—
Other	1385 (13%)	107 (4%)	325 (13%)	—	—
Recipient educational attainment	—	—	—	<.001	.094
High school or less	4700 (43%)	1229 (53%)	443 (46%)	—	—
Some college	3039 (28%)	577 (25%)	239 (25%)	—	—
College degree	3140 (29%)	527 (23%)	274 (29%)	—	—
Recipient health insurance	—	—	—	<.001	<.001
Private	5658 (52%)	1252 (48%)	1405 (56%)	—	—
Medicaid	1304 (12%)	267 (10%)	330 (13%)	—	—
Medicare	3603 (33%)	991 (38%)	719 (29%)	—	—
Other	314 (3%)	96 (4%)	61 (2%)	—	—
Recipient BMI (kg/m ²)‡	27 (5)	28 (5)	27 (5)	<.001	.111
Serum creatinine (mg/dL)	1.3 (0.9)	1.3 (0.7)	1.4 (0.9)	.086	.136
Serum bilirubin (mg/dL)	1.1 (1.7)	1.1 (1.2)	1.2 (2.4)	.621	.139
Ischemic cardiomyopathy	3781 (35%)	997 (38%)	932 (37%)	.001	.029
Prior cardiac surgery	5511 (51%)	1342 (52%)	1191 (47%)	.441	.003
Pretransplant dialysis	353 (3%)	74 (3%)	85 (3%)	.306	.580
Pretransplant infection	1192 (11%)	285 (11%)	223 (10%)	.611	.207
LVAD	3647 (34%)	935 (36%)	680 (27%)	.023	<.001

Variable	(A) Included in multivariable analysis (n = 10,879)	(B) Excluded because of residence in small county* (n = 2606)	(C) Excluded because of missing data† (n = 2515)	P	
				A vs B	A vs C
ECMO	66 (0.6%)	18 (0.7%)	29 (1%)	.624	.003
Mechanical ventilation	152 (1%)	42 (2%)	91 (4%)	.409	<.001
IABP	601 (6%)	126 (5%)	159 (6%)	.162	.119
Donor characteristics	—	—	—	—	—
Donor age (y)‡	32 (12)	31 (12)	32 (12)	.050	.180
Male donor	7688 (71%)	1940 (74%)	1812 (72%)	<.001	.170
Donor race	—	—	—	<.001	.901
White	7112 (65%)	1874 (72%)	1649 (66%)	—	—
Black	2382 (22%)	423 (16%)	541 (22%)	—	—
Other	1385 (13%)	309 (12%)	325 (13%)	—	—
Donor cause of death	—	—	—	.066	.372
Anoxia	2151 (20%)	472 (18%)	461 (18%)	—	—
Stroke	2382 (22%)	540 (21%)	568 (23%)	—	—
Head trauma	6040 (56%)	1517 (58%)	1407 (56%)	—	—
Other	306 (3%)	7 (3%)	77 (3%)	—	—
Donor CPR	698 (6%)	152 (6%)	149 (6%)	.271	.361
Donor-recipient CMV matching	—	—	—	.165	.007
Donor– Recipient–	1714 (16%)	374 (15%)	282 (14%)	—	—
Donor– Recipient+	2442 (22%)	532 (22%)	496 (24%)	—	—
Donor+ Recipient–	2627 (24%)	649 (26%)	445 (22%)	—	—
Donor+ Recipient +	4096 (38%)	917 (37%)	804 (40%)	—	—
Donor-recipient pHM difference >10%	5737 (53%)	1376 (53%)	1341 (53%)	.951	.596
Allograft ischemic time (h)‡	3.2 (1.1)	3.1 (1.0)	3.3 (1.0)	.017	.368
County characteristics	—	—	—	—	—
Population (100,000s)‡	13.3 (20.0)	0.5 (0.4)	15.3 (22.8)	<.001	<.001
Rural county	114 (1%)	826 (32%)	21 (1%)	<.001	.335
Socioeconomic advantage index‡	0.17 (0.71)	–0.65 (0.33)	0.24 (0.76)	<.001	<.001
Economic inequality index‡	0.35 (0.15)	0.21 (0.14)	0.35 (0.15)	<.001	.069
Black-white segregation index‡	0.53 (0.14)	0.31 (0.20)	0.54 (0.13)	<.001	<.001

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BMI, Body mass index; *LVAD*, left ventricular assist device; *ECMO*, extracorporeal membrane oxygenation; *IABP*, intra-aortic balloon pump.

* Cases excluded from multivariable analysis because of residence in county represented by <5 heart transplant recipients.

[†] Cases excluded from multivariable analysis solely because of missing data on 1 or more covariates.

[‡] Mean and SD.

Table II

Multivariable Cox proportional hazards model of overall mortality after heart transplantation, with county-level shared frailty term (n = 10,879)

Covariate*	HR	95% CI	P
<i>Recipient characteristics</i>	–	–	–
Recipient age (y/10)	1.00	(0.96–1.04)	.925
Male recipient	0.95	(0.86–1.06)	.380
Recipient race	–	–	–
White	Ref.	–	–
Black	1.25	(1.13–1.40)	<.001
Other	0.92	(0.80–1.06)	.235
Recipient educational attainment	–	–	–
High school or less	Ref.	–	–
Some college	0.90	(0.81–0.99)	.031
College degree	0.85	(0.76–0.94)	.002
Recipient health insurance	–	–	–
Private	Ref.	–	–
Medicaid	1.35	(1.18–1.53)	<.001
Medicare	1.17	(1.07–1.29)	.001
Other	0.96	(0.74–1.25)	.759
Recipient BMI (kg/m ²)	1.02	(1.01–1.02)	<.001
Serum creatinine (mg/dL)	1.05	(1.01–1.09)	.013
Serum bilirubin (mg/dL)	1.03	(1.02–1.05)	<.001
Ischemic cardiomyopathy	1.13	(1.03–1.24)	.013
Prior cardiac surgery	1.21	(1.10–1.32)	<.001
Pretransplant dialysis	1.44	(1.16–1.80)	.001
Pretransplant infection	1.16	(1.02–1.31)	.019
LVAD	1.02	(0.93–1.13)	.628
ECMO	2.18	(1.42–3.33)	<.001
Mechanical ventilation	1.47	(1.10–1.97)	.009
IABP	1.14	(0.95–1.35)	.150
<i>Donor characteristics</i>	–	–	–
Donor age (y/10)	1.12	(1.08–1.16)	<.001
Male donor	0.92	(0.83–1.01)	.090
Donor race	–	–	–
White	Ref.	–	–
Black	1.15	(1.03–1.29)	.013
Other	1.08	(0.97–1.21)	.161
Donor cause of death	–	–	–
Anoxia	Ref.	–	–
Stroke	0.95	(0.83–1.09)	.437
Head trauma	0.95	(0.85–1.07)	.427

Covariate*	HR	95% CI	P
Other	1.10	(0.86–1.41)	.451
Donor CPR	0.94	(0.79–1.13)	.532
Donor-recipient CMV matching	–	–	–
Donor– Recipient–	Ref.	–	–
Donor– Recipient+	0.91	(0.79–1.05)	.188
Donor+ Recipient–	1.09	(0.95–1.25)	.210
Donor+ Recipient+	1.05	(0.92–1.20)	.468
Donor-recipient pHM difference >10%	1.08	(0.99–1.17)	.088
Allograft ischemic time (h)	1.11	(1.07–1.15)	<.001

* Variance of county-level shared frailty term adjusting for all observed covariates = 0.037 (standard error = 0.017; $P = .004$ by LR test).

Table III

Comparison of multivariable Cox proportional hazards models of overall mortality after heart transplantation, adjusted for recipient, donor, and county covariates (n = 10,879)

Estimate*	Model 0: recipient and donor covariates only	Model 1: model 0 + county socioeconomic advantage index	Model 2: model 0 + county economic inequality index	Model 3: model 0 + county black-white segregation index
<i>County-level covariate quintile[†]</i>				
Q1 (lowest) HR (95% CI; <i>P</i>)		Ref.	Ref.	Ref.
Q2 HR (95% CI; <i>P</i>)		1.05 (0.92–1.19; <i>P</i> = .501)	0.96 (0.83–1.10; <i>P</i> = .533)	0.95 (0.83–1.09; <i>P</i> = .461)
Q3 HR (95% CI; <i>P</i>)		0.91 (0.79–1.05; <i>P</i> = .181)	0.94 (0.82–1.09; <i>P</i> = .406)	0.98 (0.85–1.13; <i>P</i> = .778)
Q4 HR (95% CI; <i>P</i>)		0.89 (0.78–1.03; <i>P</i> = .122)	0.94 (0.81–1.08; <i>P</i> = .361)	0.95 (0.82–1.10; <i>P</i> = .477)
Q5 (highest) HR (95% CI; <i>P</i>)		0.88 (0.75–1.03; <i>P</i> = .119)	0.85 (0.73–0.98; <i>P</i> = .025)	0.82 (0.71–0.95; <i>P</i> = .010)
Variance of county-level shared frailty (SE; LR test <i>P</i>) [‡]	0.037 (0.017; <i>P</i> = .004)	0.032 (0.016; <i>P</i> = .010)	0.033 (0.017; <i>P</i> = .008)	0.036 (0.016; <i>P</i> = .003)
Improvement over model without county-level covariates (LR test <i>P</i>)		<i>P</i> = .092	<i>P</i> = .273	<i>P</i> = .107

* All models include a county-level shared frailty term representing residual variation in mortality hazard across US counties after adjustment for model covariates. Results for individual-level covariates are not shown. Full results of model 0 are presented in Table II.

[†] County-level covariates are socioeconomic advantage in model 1, economic inequality in model 2, and black-white segregation in model 3.

[‡] *P* < .05 indicates statistically significant residual difference in outcomes across counties.