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Demographic, social, economic and geographic factors associated with long-term outcomes in a cohort of cardiac arrest survivors

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Conflict of interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

We understand that the Corresponding Author, Dr. David J Wallace is the sole contact for the Editorial process (including Editorial Manager and direct communications with the office). He is responsible for communicating with the other authors about progress, submissions of revisions and final approval of proofs. We confirm that we have provided a current, correct email address that is accessible by the Corresponding Author.

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Abstract

Background—Demographic, social, economic and geographic factors are associated with increased short-term mortality after cardiac arrest. We sought to determine if these factors are additionally associated with long-term outcome differences using a detailed clinical database linked to state-wide administrative data.

Methods—We included cardiac arrest patients surviving to hospital discharge from five hospitals in the United States from 2005 to 2013, with follow-up through 2015. We obtained information on sex, race, arrest location, initial rhythm, median ZIP code income, post-arrest illness severity, cardiac catheterization, internal cardioverter-defibrillator insertion, rural residence and drive time from residence to the nearest acute care hospital. We used Cox proportional hazard models identify predictors of mortality.

Results—We included 891 patients followed for 2,081 patient-years. There were 340 deaths with median survival 6 years. In adjusted models we identified an interaction effect between median ZIP code income and cardiac catheterization. Among patients who had cardiac catheterization there was an attenuated benefit from cardiac catheterization at progressively lower neighborhood incomes (adjusted HR: 0.21 to 0.46 to 0.56). Residence more than 20 minutes from the nearest acute care hospital was associated with increased hazard of death (adjusted HR: 1.48; 95%CI: 1.35 to 1.62), after controlling for rural residence and residence in a Medically Underserved Area/Population. Female patients showed less benefit following ICD placement (male adjusted HR: 0.49; female adjusted HR: 0.66).

Conclusions—There are persistent long-term outcome differences in cardiac arrest survival based on sex, income, and geographic access acute care.

Introduction

Although overall survival after sudden cardiac arrest has improved over time^{1–3}, not all groups have experienced improved outcomes, with notable quality gaps associated with patient sex,⁴ race,⁵ socioeconomic status^{6–10} and rural residence.^{11, 12} It is not clear to what extent these effects arise from health system elements, underlying biological differences, geographic access to healthcare or an intersection of multiple factors. Health system factors are an important potentially modifiable aspect of cardiac arrest care and can serve as quality improvement targets. There is recent evidence that inpatient cardiac arrest clinical guidelines¹³ are applied variably across hospitals, and that women receive fewer guideline-recommended treatments in the prehospital setting.¹⁴ Patients living in rural and lower income areas face other potential challenges, such as lower rates of bystander-initiated cardiopulmonary arrest,^{6, 9} longer transit times to the hospital^{12, 15} less access to automated external defibrillators¹⁶ and poorer access to specialist care.¹⁷ Recognizing these continued threats, the National Academy of Medicine emphasized sex, race, socioeconomic, and rural health disparities as priorities for cardiac arrest research.^{18, 19, 20}

Using a highly detailed clinical registry with long-term outcome data in cohort of cardiac arrest survivors, our study sought to determine if there are persistent long-term outcome differences based on sex, race, income status, or health care access. We hypothesized that male sex, black race, lower income status, residence in a rural area, residence in an area with a shortage of primary care providers, and residence at greater distance to the nearest hospital would be associated with shorter duration of survival after hospital discharge.

Methods

Patient cohort, outpatient procedures and outcomes

We included adult patients resuscitated from in-hospital cardiac arrest or out-of-hospital cardiac arrest treated at one of five hospitals in Pennsylvania between 2005 and 2013.²¹ We included both in-patient and out-of-hospital cardiac arrest events as it was our objective to describe and better understand the long-term outcomes for these patients as a whole. Although the precipitating etiologies are frequently different for in-patient and out-of-hospital cardiac arrest, the post-hospital needs for these patients are probably similar. In order to address both of these concerns (i.e., differing etiologies and yet similar long-term management strategy) we planned *a priori* to control for arrest location in our multivariable model.

We identified patients from a detailed clinical registry maintained at the University of Pittsburgh.^{21–24} We obtained demographics (age, sex, race), arrest characteristics (location, presenting rhythm, and post-arrest illness severity modeled using Pittsburgh Cardiac Arrest Category),²⁴ hospital interventions (cardiac catheterization and implanted cardioverter-defibrillator (ICD) insertion), and functional status at hospital discharge (Cerebral Performance Category (CPC)) from this registry. We excluded patients who died before discharge, those who arrested secondary to trauma or neurologic catastrophe and sparsely represented demographic groups (defined as racial designations in fewer than 5% of the total cohort).

We linked registry records to data from the Pennsylvania Health Cost Containment Council (PHC-4) using social security number, date of birth, name, and sex. PHC4 is an independent state agency that collects information on inpatient hospitalizations, outpatient care and ambulatory surgery procedures. We performed this linkage, in addition to index hospitalization data collection, to identify cardiac catheterizations or ICD insertions that took place within six months after index hospitalization in the outpatient setting, as in some clinical contexts it may be medically appropriate to delay these procedures to await physiological or myocardial recovery.

We used three measures to evaluate patient health care access: patient residence in a rural area (a measure of health care *availability*), patient residence in an area with barriers to care or a scarcity of primary care providers (a separate measure of health care *availability*), and estimated drive time from patient residence to the nearest acute care hospital (a measure of health care *accessibility*). Availability and accessibility are complementary measures of health care access, with availability representing the relationship between volume of services and volume of patients, and accessibility representing the relationship between the location

of services and the location of patients. For our first measure of health care availability, we classified patients as living in a rural area if the geometric centroid of their home ZIP code was located in an area designated as rural by the United States Census Bureau.²⁵ We evaluated this exposure as rural health studies are a research priority outlined by the National Academy of Medicine. We additionally evaluated a second measure of availability using Medically Underserved Area or Population (MUA/P) designations. We obtained these locations from the Department of Health and Human Service's Health Resource & Services Administration (HRSA).²⁶ HRSA develops criteria for geographic shortages of primary care providers, in addition to dental and mental health. These regions are not limited to urban or rural areas, and can span single or contiguous groups of counties. Medically Underserved Populations include groups who face economic, cultural or linguistic barriers to care. We designated a patient's home address as being an MUA/P if the geometric center of the ZIP code was contained within one of the HRSA MUA/P regions. We evaluated this second measure of availability, as these regions are potential targets for post-acute care investment. For our measure of accessibility, we used patient drive time to the nearest acute care hospital, rather than from arrest location or drive time to the actual treating hospital. We estimated the drive time to the closest short-term acute care hospital using the geometric center of each patient's home ZIP code and hospital street addresses reported in the 2013 Centers for Medicare and Medicaid Healthcare Cost Report Information System national database using ArcGIS Desktop 10.4 (Redlands, CA). We evaluated total drive time as a continuous variable using fractionated polynomial analysis with STATA command `mfp` to identify possible nonlinear functional forms and to determine if there were natural time breakpoints associated with increased mortality.

We determined post-discharge survival by querying the National Death Index (NDI). The NDI is a comprehensive database of vital status obtained from state death records that has been used extensively to determine long-term mortality.²⁷ We linked registry records NDI data as previously described.²¹ The follow-up period extended to December 31st 2014, providing two to nine years of follow-up.

Statistical analysis

We summarized patient demographics, arrest characteristics, hospital treatments, and long-term outcomes using descriptive statistics. We performed unadjusted Cox proportional hazard regression to test the associations between long-term outcome and race, sex, estimated median income (defined as household income less than \$30,000, \$30,000 to \$60,000 and more than \$60,000), extended drive time to the nearest hospital (defined as more than 20 minutes), arrest characteristics (location, presenting rhythm and post-arrest illness severity), invasive cardiac procedures (cardiac catheterization and ICD insertion), and functional status at hospital discharge. We created median income and Charlson Comorbidity thresholds using natural breakpoints from lowess plots with mortality.

We performed cross tabulations and evaluated correlations between our three measures of geographic access. We performed these steps as we expected they could represent at least partially overlapping exposures.

We evaluated interactions within demographic characteristics and between demographic characteristics and invasive procedures, to determine if there were nuanced relationships between health disparity risk factors and long-term outcome such that subgroups of patients benefited more than others. We then created a multivariable Cox model to evaluate the association between long-term survival and demographic factors and measures of health care access, controlling for all other covariates. We evaluated each geographic access measure separately in the multivariable model, and collectively. We included interactions that were significant below the $\alpha < 0.05$ level in the final multivariable model. We performed a sensitivity analyses using additional drive times of 10, 15, 25 and 35 minutes, to evaluate if the relationship had a clear threshold. We performed standard regression diagnostics on all models, including checks for variable collinearity. We controlled for center clustering effects in all models.

We performed analyses using Stata version 13.1 (College Station, Texas) and ArcGIS Desktop 10.4 (Redlands, California).

Patients were not involved in any aspect of the study design or analysis. The University of Pittsburgh Institutional Review Board approved all aspects of this study under a waiver of informed consent.

Results

A total of 987 patients survived to hospital discharge. Twenty patients had missing race information and 9 were classified as “other”, and were therefore excluded from analysis. Sixty-one patients did not reside in ZIP codes within Pennsylvania, making post-discharge record matching with PHC4 unreliable, and were also excluded. Six patients were treated at smaller hospitals that did not perform both cardiac catheterization and ICD insertion, making their potential post-arrest management different from the rest of the cohort, and were therefore excluded. The final analytic cohort had 891 patients. After linking the clinical cohort with PHC4 records, we reclassified one patient as having undergone cardiac catheterization and one patient as having ICD insertion after discharge, as both occurred within six months of discharge from the index hospitalization.

Patients were predominantly male ($n=529$, 59%), white ($n=726$, 81%), resided in rural ZIP codes ($n=307$, 34%), lived an median estimated 7.9 minutes from the nearest hospital and lived in a ZIP code with an median annual income of \$45,100 per year (IQR: 38,110 – 52,773; Table 1). Median survival was 6 years with mean follow-up time after discharge was 2.3 years (standard deviation ± 2.2).

During 2,081 person-years of observation, 340 deaths occurred and median survival was 6.0 years. In univariate analysis, most prespecified comparisons were statistically significant, with the exceptions of female sex and median ZIP code income strata (Figures 1A–C, Figure 2A–C & Table 2). Two interactions were statistically significant in multivariable modeling: sex and ICD placement, and cardiac catheterization and median ZIP code income.

Fractionated polynomial analysis of drive time showed a linear relationship between drive time and outcome (aHR: 1.01, 1.00 – 1.02; $p < 0.01$). For ease of interpretation, we

operationalized worse health care access as greater than 20 minutes versus 20 minutes or less. We found negligible correlations between rural areas and MUA/P areas (0.13; $p<0.01$) and between MUA/P areas and drive time more than 20 minutes (0.14; $p<0.01$). We found low correlation between rural area and drive time more than 20 minutes (0.40; $p<0.01$).

In separate multivariable models that included patient covariates, a term for drive time more than 20 minutes was associated with decreased survival (aHR: 1.35; 1.16 – 1.57; $p<0.01$), patient residence in a rural ZIP code was not associated with survival (aHR: 0.96; 0.83 – 1.10; $p=0.52$), and residence in an MUA/P area was not associated with survival (aHR: 1.01; 0.91 – 1.12; $p=0.87$). In a model that included all three measures of access (i.e., drive time, MUA/P area, and rural ZIP code), residence in a rural ZIP code was associated with increased survival (aHR: 0.86, 0.75 – 0.98, $p=0.02$), and drive time more than 20 minutes was associated with decreased survival (aHR: 1.48; 1.35 – 1.62; $p<0.01$), and MUA/P area was not associated with survival (aHR: 0.99, 0.91 – 1.08, $p=0.88$) (Table 3). This finding was robust to checks for collinearity between the health care access measures. Our sensitivity analysis of varying drive times from home to the nearest hospital demonstrated generally similar results to the main analysis (Supplemental Table 1).

Two demographic variables had significant interaction effects with invasive cardiac procedures. Among patients who did not undergo cardiac catheterization, progressively lower median income was not associated with survival. However, in the group that underwent cardiac catheterization, patients in the highest income strata saw the most improvement (aHR: 0.21, 0.14 – 0.32, $p<0.01$), with progressively less benefit in the next lowest income group (aHR: 0.46, 0.37 – 0.59, $p<0.01$) and in the lowest income group (aHR: 0.57, 0.27 – 0.87, $p=0.06$). Among the cohort that did not have ICDs inserted, females had increased survival compared to males. In the group that had ICDs inserted, compared to male patients without ICD insertion, both male patients and female patients with an ICD placement had increased survival. However, females demonstrated less benefit than males following ICD placement (aHR: 0.66 versus 0.49, respectively).

Discussion

Multiple studies have identified male sex, black race and lower socioeconomic status as predictors of poor outcomes at hospital discharge for survivors of cardiac arrest.^{4–7, 10} We observed similar outcome disparities based on sex, but not race, in a large clinical cohort of cardiac arrest survivors which persist well beyond hospital discharge. We additionally found progressively attenuated benefits from cardiac catheterization with lower incomes, in a model that controlled for arrest and patient characteristics. Finally, we identified prolonged drive time from home to any hospital, a measure of health care access, as an important risk factor for lower survival.

We looked for interactions between sex, race, income, and invasive procedures, in their associations with outcome. In a model that evaluated the interaction between median ZIP code income and cardiac catheterization, we found a progressively attenuated benefit from cardiac catheterization at lower income levels. This finding could reflect a higher burden of coronary artery disease²⁸ among those in lower income households, underscoring the

challenge of chronic disease management in patients with greater myocardial jeopardy. Alternatively, progressively attenuated benefits could be the result financial barriers that jeopardize aspects of follow-up care such as clinic attendance, prescription refills or insurance status.^{29, 30} Additional work needs to be done to understand the underlying driver of this quality gap.

We additionally identified an interaction between female sex and benefit from ICD placement. Among patients who did not have an ICD placed, females had increased long-term outcomes. Males who had an ICD inserted had increased long-term outcomes compared to males who did not, as did females – but to a lesser extent. We feel these results primarily reflect differences in underlying disease burden and the indications for ICD. It is of interest that women with an ICD insertion had less benefit from the procedure than men, but this cannot be teased with the level of clinical detail available in our dataset.

We evaluated the association between patient home proximity to any acute care hospital and outcome. We intentionally did not use the travel time from home to the reported treating hospital, as we were interested determining the significance of general accessibility – the travel time to the nearest hospital. We postulated that accessibility could have two effects on the long-term outcomes of cardiac arrest survivors: (1) greater travel distances to appointments could impact follow-up adherence, and (2) greater travel distances to the nearest hospital could affect survival for time-sensitive emergencies. We found that travel times of more than twenty minutes were associated with significantly increased mortality, a finding that was robust to other time thresholds in a planned sensitivity analysis and persisted in a multivariable model that explicitly controlled for rural home location, barriers to care or primary care scarcity. This finding is important, as it shows that accessibility represents a distinct risk factor from rurality or HRSA designated MUA/Ps, and an additional potential hazard of safety net hospital closure.³¹ Urban and rural classifications may not be a sufficiently sensitive measure of access, as Jordan et. al showed that large proportions of urban populations in South West England live >25km from a hospital.³²

An unexpected finding was that rural home ZIP code location was associated with increased survival in a model that controlled for drive time and MUA/P designation. This suggests that some health effects of rurality are driven in part by proximity to care, though more work is needed to explore these relationships. On the other hand, urban residence may suggest improved geographic access to care that is not realized in practice due to other barriers (such as insurance coverage) or may be complicated by health modifying aspects of cities.^{33–36} The intersection of our three measures of access was not a prespecified hypothesis, therefore the finding could have been the result of chance (the 95% confidence interval for rural location was close to 1.0 in the fully adjusted model).

We did not observe worse long-term outcomes for black patients following cardiac arrest. This finding is similar to observations from the Veteran's Affairs hospital system, where black patients had lower rates of cardiac catheterization following acute myocardial infarction, yet better long-term outcomes compared to white patients.³⁷ Our result is also consistent with contemporaneous results coming from the CARES registry for long-term outcomes among elderly survivors of cardiac arrest, where black patients did not have worse

survival compared to white patients.³⁸ In contrast, a recent report that showed long-term survival remains poorer for black patients, though the cohort was limited to in-patient non-elderly adults.³⁹ It therefore appears that the quality gap based on race may be narrowing, though perhaps not in all subgroups.

Our study has several limitations. Our analysis included patients treated in a single healthcare system in Southwestern Pennsylvania and may not reflect the racial diversity of other regions. However Allegheny County ranks second in overall population in Pennsylvania and has a racial breakdown of 80.7% white, 13.4% black, 3.6% Asian and 2.3% other or mixed race, compared to the remainder of the country with 77.1% white, 13.3% black, 5.6% Asian and 4.0% other or mixed race.²⁵ Additionally, we captured patients from several hospitals, diversifying post-arrest care somewhat and improving generalizability. A second limitation of our analysis was our inability to evaluate clinic follow-up after discharge or patient proximity to outpatient clinic locations. Although geographic availability of specialists, clinics and rehabilitation facilities likely has an effect on long-term outcome, Pennsylvania does not maintain records of either. However, our use of proximity to the nearest acute care hospital is still relevant, as this represents the closest definitive care in an emergency and prior work has described hospital closures to be associated with mortality rates from myocardial infarction and accidental injury,⁴⁰ as well as fewer referrals to specialist care.⁴¹ Furthermore, recent health care proposals at the national level emphasize the role of states in providing safety net services. Our findings show that proximity matters for survivors of cardiac arrest, and it is associated with improved quality in a way that is distinct from conventional measures of rurality.

Conclusions

We observed persistent long-term outcome disparities based on sex, income, and post-hospital discharge geographic access to acute care after controlling for patient characteristics, arrest characteristics, and invasive procedures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
A–C. Univariate proportional hazard of long-term outcome after cardiac arrest for patients by race (A), sex (B), and median ZIP code income (C).

Figure 2.

A–C. Univariate proportional hazard of long-term outcome after cardiac arrest for patients by residence in a medically underserved area or population (A), residence by drive time to the closest acute care hospital (B), and residence in an urban or rural area (C).

Table 1

Cohort characteristics (n=891)

Age, <i>median (IQR)</i>	61 (51 – 72)
Female, <i>n (%)</i>	362 (41)
Race, <i>n (%)</i>	
White	726 (81)
Black	165 (19)
Residence in a rural ZIP code, <i>n (%)</i>	584 (66)
Estimated drive time from patient home to nearest acute care hospital (minutes), <i>median (IQR)</i>	7.9 (5.0 – 13.4)
Residence greater than 20 minutes from a hospital, <i>n (%)</i>	93 (10)
Estimated drive distance from patient home to nearest acute care hospital (miles), <i>median (IQR)</i>	4.4 (2.6 – 7.6)
Residence in a Medically Underserved Area/Population, <i>n (%)</i>	239 (27)
Patient home ZIP code median annual income, <i>median (IQR)</i>	\$45,100 (38,110 – 52,773)
Patient home ZIP Code annual income less than \$30,000, <i>n (%)</i>	61 (7)
Patient home ZIP Code annual income less than \$60,000, <i>n (%)</i>	702 (79)
Patient home ZIP Code annual income greater than \$60,000, <i>n (%)</i>	128 (14)
Out of hospital cardiac arrest location, <i>n (%)</i>	475 (52)
Rhythm, <i>n (%)</i>	
VT/VF	439 (49)
PEA	208 (23)
Asystole	111 (12)
Unknown	142 (16)
Charlson, <i>median (IQR)</i>	2 (1 – 3)
Cardiac catheterization, <i>n (%)</i>	355 (40)
Implanted cardioverter-defibrillator insertion, <i>n (%)</i>	309 (34)
Prior implanted cardioverter-defibrillator, <i>n (%)</i>	223 (25)
Discharge CPC, <i>n (%)</i>	
1	223 (25)
2	95 (10)
3	539 (60)
4	43 (5)
Died during follow up, <i>n (%)</i>	344 (38)

Table 2

Univariate Cox proportional hazard model for mortality and patient characteristics

Variable	Hazard Ratio	95% CI	p-value
Age			
Less than or equal to 45 years	ref	–	–
46 to 80 years	2.75	(2.07 – 3.64)	<0.01
More than 80 years	4.99	(2.80 – 8.89)	<0.01
Female	1.03	(0.92 – 1.16)	0.58
Black	1.16	(1.02 – 1.31)	0.02
Median ZIP code income			
More than \$60,000	ref	–	–
\$30,000 to \$60,000	1.15	(0.80 – 1.63)	0.45
Less than \$30,000	1.35	(0.79 – 2.28)	0.27
Out of hospital cardiac arrest	0.43	(0.32 – 0.57)	<0.01
Shockable rhythm	0.50	(0.44 – 0.58)	<0.01
Good discharge CPC	0.44	(0.35 – 0.56)	<0.01
Charlson comorbidity index			
0	ref	–	–
1–4	2.24	(1.56 – 3.21)	<0.01
5	3.99	(2.73 – 5.85)	<0.01
Cardiac catheterization	0.34	(0.30 – 0.41)	<0.01
Implanted cardioverter-defibrillator	0.66	(0.64 – 0.69)	<0.01
Prior implanted cardioverter-defibrillator	0.83	(0.77 – 0.89)	<0.01
Residence greater than 20 minutes from nearest hospital	1.10	(1.00 – 1.23)	0.049
Residence in a rural ZIP code	0.86	(0.75 – 0.99)	0.04
Residence in a Medically Underserved Area/Population	1.21	(1.09 – 1.34)	<0.01

Table 3

Multivariable Cox proportional hazard model for association between mortality and income, cardiac catheterization, implanted cardioverter-defibrillator insertion, race and measures of health care access (n=891)

<u>Variable</u>	<u>Hazard Ratio</u>	<u>95% CI</u>	<u>p-value</u>	<u>Interaction p-value</u>
Cardiac catheterization, no				
Income more than \$60,000	ref			<0.01
Income \$30,000 to \$60,000	1.14	(0.98 – 1.32)	0.09	
Income less than \$30,000	1.25	(0.78 – 2.00)	0.34	
Cardiac catheterization, yes				
Income more than \$60,000	0.21	(0.14 – 0.32)	< 0.01	
Income \$30,000 to \$60,000	0.46	(0.37 – 0.57)	<0.01	
Income less than \$30,000	0.56	(0.32 – 1.00)	0.05	
Implanted cardioverter-defibrillator, no				
Male	ref			<0.01
Female	0.85	(0.78 – 0.92)	<0.01	
Implanted cardioverter-defibrillator, yes				
Male	0.49	(0.40 – 0.59)	<0.01	
Female	0.66	(0.50 – 0.87)	<0.01	
Residence greater than 20 minutes from nearest hospital	1.48	(1.35 – 1.62)	<0.01	
Residence in a rural ZIP code	0.86	(0.75 – 0.98)	0.02	
Residence in a Medically Underserved Area/Population	0.99	0.91 – 1.08	0.88	
Race				
White	ref			
Black	1.06	(0.85 – 1.33)	0.59	

(Model controls for age, Charlson comorbidity index, prior ICD placement, out-of-hospital arrest location, shockable rhythm and favorable discharge CPC.)