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Short paper

Influence of comorbidity on survival after out-of-hospital cardiac arrest in the United States

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Abstract

Aim: Association between survival rate and Elixhauser Comorbidity Index (ECI) among individuals suffering an out-of-hospital cardiac arrest (OHCA) in the United States (US).

Methods: We utilized the US National Emergency Department Sample (NEDS) dataset to retrospectively identify individuals experiencing OHCA between January 1, 2006 to December 31, 2015; using the *International Classification of Diseases, Ninth Revision-Clinical Modification* (ICD-9-CM) and *Tenth Revision-Clinical Modification* (ICD-10-CM) codes. Logistic regression analysis with twenty-nine ECIs as predictor variables were performed to compute for odds ratio (OR), after controlling for age and gender. Linear regression analysis performed to assess survival trend after clustering based on ECI. We also assessed the association of ECI with survival rate after stratifying patients based on cardiac rhythm (shockable versus non-shockable).

Results: We identified 1,282,520 (16.4%, survived-to-discharge) weighted observations presenting primarily after OHCA in the US during the study period. Annual percentage change (APC) in survival rate among OHCA patients with no ECI and those with >3 ECI was −1.53% (95% CI: −1.98% to −1.09%, $P_{trend} < 0.001$) and 1.2% (95% CI: 0.69%−1.7%, $P_{trend} = 0.001$), respectively. Adjusted OR for ECI was 1.31 (95% CI: 1.3−1.31, $P < 0.001$). Percentage change in the survival rate among shockable and non-shockable rhythm was 5.6% (95% CI: −3.9% to 15.13%, $P_{trend} = 0.127$) and 1.04% (95% CI: 0.01%−2.07%, $P_{trend} = 0.05$), respectively, with a unit increase in ECI.

Conclusion: In the US, OHCA patients with higher ECI have greater survival-to-discharge rate, demonstrating "comorbidity paradox".

Keywords: Comorbidity paradox, Out-of-hospital cardiac arrest, Survival-to-discharge, United States

Introduction

Out-of-hospital cardiac arrest (OHCA) is a medical emergency with an estimated management cost of $455 billion annually in the United States (US).[1] Studies from the national patient population in Australia and Europe have demonstrated poor chances of survival after OHCA among patients with higher comorbidities.[2,3] While higher body mass index has shown to improve the survival rate among those experiencing sudden cardiac arrest (OHCA or in-hospital cardiac arrest [IHCA]).[4] Furthermore, there is conflicting evidence with regards to the association between overall comorbidities and survival rate after cardiac arrest.[3,5] Due to significant variation in comorbidities[6] and OHCA survival rate[7] across the globe, we sought to analyze the association between comorbidity burden, as defined by Elixhauser Comorbidity Index (ECI), and survival rate after OHCA in the US population.

We utilized the US National Emergency Department Sample (NEDS) dataset to conduct a retrospective cross-sectional study to analyze the impact of ECI on survival-to-discharge rate among

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patients with OHCA in the US from January 1, 2006 to December 31, 2015. Additionally, we also assessed the impact of ECI after stratifying patients based on the cardiac rhythm (shockable versus non-shockable).

Methods

Data source

The NEDS, sponsored by the Healthcare Cost Utilization Project (HCUP), is the largest all-payer emergency department (ED) visit database in the US, and yields estimates from the hospital ED visits.[2] Thirty-seven states provide ED and inpatient visit data annually to constitute the NEDS. The strength of NEDS relies on is its geographical diversity (68.7% of the total US resident population and 78.2% of all ED visits) and consistency in data reporting. We analyzed the data in compliance with the Health Insurance Portability and Accountability Act of 1996. Therefore, this study was exempted from the Institutional Review Board's approval.

Study design

OHCA was identified using the *International Classification of Diseases, Ninth Revision-Clinical Modification* (ICD-9-CM) and *Tenth Revision-Clinical Modification* (ICD-10-CM) codes. Patients with age >18 years presenting with a primary diagnosis of cardiac arrest (*ICD-9-CM*, 427.5; *ICD-10-CM*, I46, I46.2, I46.8, I46.9), ventricular fibrillation (*ICD-9-CM*, 427.41; *ICD-10-CM*, I49.01) or ventricular flutter (*ICD-9-CM*, 427.42; *ICD-10-CM*, I49.02) were included. A shockable rhythm is defined as those with either ventricular fibrillation (VF) or ventricular flutter (a.k.a ventricular tachycardia, VT), and all other patients were categorized as non-shockable rhythm. Weighted ECI, mortality score and readmission scores were computed from the 29 comorbid conditions; methodology and appropriate codes are provided by the Agency of Healthcare Research and Quality. The sum of ECI was clustered into four subgroups; such modeling has been adopted in previous studies: 0, 1, 2, and >3.[8,9] We excluded patients undergoing cardiopulmonary resuscitation (CPR) in the ED using ICD-9 (99.60 and 99.63) or *ICD*-10 (5A19054, 5A12012 and 5A2204Z) procedure codes to eliminate patients presenting to ED for alternative reasons and suffering cardiac arrest while in the ED.

Outcomes

The primary outcome measure was to assess linear trends and association of survival-to-discharge rate among patients experiencing OHCA with various Elixhauser comorbidity measures. The secondary outcome was to analyze the trends in survival-to-discharge rate with increasing clustered ECI after stratifying based on cardiac rhythm.

Statistical analysis

The analysis was performed after applying for discharge weights provided in the dataset. Normally distributed continuous data are reported as mean and standard deviation (SD) and compared using the unpaired 2-tailed *t*-test. Continuous data not normally distributed are presented as the median and interquartile range (IQR) and compared using the Wilcoxon rank-sum test. Categorical data are presented as a weighted absolute number with percentage and compared using the Pearson χ^2 test. Annual percentage change (APC) with 95% confidence interval (CI) for survival-to-discharge rate (dependent factor) during the study period was computed using linear regression analysis with the year (independent factor) as a continuous variable. Logistic regression analysis with binary outcome was performed to compute for odds ratio (OR) among different ECIs after controlling for age and gender. ECI variables are not mutually exclusive and exhaustive. All the tests were two-sided and the *P*-value less than or equal to 0.05 was considered statistically significant. Analyses were conducted using STATA, version 15.1 (STATA Corp, Texas, USA).

Results

We identified 1,282,520 weighted observations presenting to the ED primarily after OHCA in the US between January 1, 2006 and December 31, 2015; of whom only 209,643 (16.4%) survived-to-discharge after hospitalization. Mean (SD) of age for the study population was 65.8 (17.2) years; 62% were men. Median (IQR) ECI for the entire cohort was zero (0–2). Mean age among the study cohort increased with increasing ECI cluster (62 [17.8] years among ECI zero vs 65 [14.3] years among ECI > 3; $P <$ 0.001), while, the proportion of men decreased (65% among ECI zero vs 59% among ECI > 3; $P <$ 0.001). Hypertension (64.7%) was the most common comorbid condition in the study population, followed by diabetes mellitus (without chronic complications) (17%) and fluid/electrolyte disorder (16.9%). Demographic and ECI variables have been summarized in Table 1.

Linear trend in the survival rate during the study period after classifying them based on the ECI cluster have been summarized in the Fig. 1. Annual percentage change (APC) in survival-to-discharge rate after hospitalization to the presenting hospital among those with zero ECI was −1.53% (95% CI: −1.98% to −1.09%, $P_{trend} < 0.001$), while those with one ECI had APC of 0.04% (95% CI: −0.21% to 0.28%, $P_{trend} = 0.74$), two ECI had 0.3% (95% CI: −0.09% to 0.7%, $P_{trend} = 0.11$) and with > 3 ECI had 1.2% (95% CI: 0.69%−1.7%, $P_{trend} = 0.001$) (represented in Fig. 1A−D, respectively).

Odds of survival among those with no ECI was (OR: 0.5, 95% CI 0.49−5.1; $P < 0.001$), one ECI (OR: 1.13, 95% CI 1.12−1.14; $P < 0.001$), two ECI (OR: 1.41, 95% CI 1.4−1.43; $P < 0.001$), while those with three or more ECI (OR: 2.25, 95% CI 2.22−2.27; $P < 0.001$). Among Elixhauser comorbidity indices, weight loss (OR: 5.03, 95% CI 4.78−5.3; $P < 0.001$) fluid and electrolyte disorder (OR: 3.59, 95% CI 3.54−3.65; $P < 0.001$), blood loss anemia (OR: 3.06, 95% CI 2.7−3.47; $P < 0.001$) and coagulation deficiency (OR: 2.82, 95% CI 2.72−2.92; $P < 0.001$) are among the few ECIs that have highest adjusted (age, gender) odds of surviving when compared to those who do not have this individual comorbidity.

The survival-to-discharge rate among OHCA patients after stratifying based on the cardiac rhythm has been displayed in Fig. 2. Percentage change (PC) in the survival rate among OCHA patients with shockable rhythm was 5.6% (95% CI: −3.9% to 15.13%, $P_{trend} = 0.127$) (Fig. 2A) which among those with non-shockable rhythm was 1.04% (95% CI: 0.01%−2.07%, $P_{trend} = 0.05$) (Fig. 2B).

Discussion

In our study from 1,282,520 OHCA patients in the US between January 1, 2006 to December 31, 2015, we report a significant

Table 1 – Demographic factors associated with survival-to-discharge after hospitalization among OHCA.

	Total (n = 209,643)		OR	95% CI		P value
Age[a]	–		0.99	0.99	0.99	<0.001
Male[b]	132,367	(63.1%)	1.04	1.03	1.05	<0.001
Elixhauser Comorbidity Indices[c]	1	(1−2)	1.31	1.30	1.31	<0.001
Weight loss	2924	(1.4%)	5.03	4.78	5.30	<0.001
Fluid and electrolyte disorders	35,392	(16.9%)	3.59	3.54	3.65	<0.001
Blood loss anemia	388	(0.2%)	3.06	2.70	3.47	<0.001
Coagulation deficiency	5187	(2.5%)	2.82	2.72	2.92	<0.001
Deficiency Anemias	13,055	(6.2%)	2.76	2.70	2.82	<0.001
Diabetes with chronic complications	4713	(2.2%)	2.36	2.27	2.44	<0.001
Valvular disease	2183	(1.0%)	2.22	2.11	2.34	<0.001
Hypothyroidism	8285	(4.0%)	2.17	2.11	2.23	<0.001
Obesity	10,779	(5.1%)	2.13	2.09	2.18	<0.001
Alcohol abuse	5794	(2.8%)	2.09	2.02	2.15	<0.001
Peripheral vascular disease	6316	(3.0%)	2.05	1.99	2.11	<0.001
Renal failure	21,484	(10.2%)	1.81	1.78	1.84	<0.001
Depression	5954	(2.8%)	1.81	1.76	1.87	<0.001
Hypertension	135,630	(64.7%)	1.73	1.71	1.75	<0.001
Drug abuse	4690	(2.2%)	1.69	1.64	1.75	<0.001
Rheumatoid arthritis/collagen vascular diseases	1560	(0.7%)	1.53	1.45	1.62	<0.001
Other neurological disorders	12,993	(6.2%)	1.47	1.44	1.50	<0.001
Chronic pulmonary disease	7730	(3.7%)	1.45	1.42	1.49	<0.001
Psychoses	2308	(1.1%)	1.40	1.33	1.46	<0.001
Congestive heart failure	17,041	(8.1%)	1.36	1.33	1.38	<0.001
Paralysis	1111	(0.5%)	1.30	1.22	1.39	<0.001
Diabetes without chronic complications	35,696	(17.0%)	1.23	1.21	1.24	<0.001
Liver disease	2076	(1.0%)	1.21	1.15	1.27	<0.001
Lymphoma	722	(0.3%)	1.12	1.04	1.22	0.005
Pulmonary circulation disorders	1197	(0.6%)	1.09	1.03	1.17	0.01
Chronic peptic ulcer disease	12	(0.0%)	1.03	0.56	1.91	0.917
Solid tumor without metastasis	3000	(1.4%)	0.69	0.66	0.72	<0.001
Metastatic cancer	1572	(0.7%)	0.66	0.63	0.70	<0.001
HIV and AIDS	4	(0.0%)	0.39	0.15	1.05	0.063
ECI clustered[c]						
0	151,308	(53.4%)	0.5	0.49	0.51	<0.001
1	55,841	(19.7%)	1.13	1.12	1.14	<0.001
2	39,072	(13.8%)	1.41	1.40	1.43	<0.001
>3	36,992	(13.1%)	2.25	2.22	2.27	<0.001

Legend: Twenty-nine Elixhauser comorbidity index variables arranged in the descending order of the odds ratio.
Abbreviations: OHCA — out-of-hospital cardiac arrest, OR — odds ratio, CI — confidence interval, HIV — human immunodeficiency virus, AIDS — acquired immune deficiency syndrome, ECI − Elixhauser comorbidity index.
[a] Adjusted for gender.
[b] Adjusted for age.
[c] Adjusted for age and gender; data presented as median (interquartile range).

decreasing trend in the survival-to-discharge rate among patients with no ECI, while the survival-to-discharge rate increased among those with >3 ECI. Additionally, higher ECI was associated with an increased survival-to-discharge rate after adjusting for age and gender, demonstrating "comorbidity paradox."

Studies in the past have demonstrated findings contradictory to our study.[3,5] However, in comparison to these studies, our study is more robust due to its large sample size, diverse geographical sampling within the US, consistency in capturing hospital events, and analyzing changing dynamics in the patient population over a decade. Additionally, we have used ECI as opposed to the Charlson Comorbidity Index (CCI), which is the recommended measure for assessing comorbidity burden from the administrative database.[10]

Reiterating findings from our previous study,[4] we not only provide evidence of "Obesity Paradox" (OR: 2.13, 95% CI 2.09−2.18; $P < 0.001$), but also extrapolate these findings to other individual comorbidities, in particular, weight loss, fluid/electrolyte abnormalities, blood loss anemia and coagulation deficiencies among other comorbidity indices. Additionally, in comparison to those with no ECI, a higher proportion of patients with >3 ECI survived-to-discharge irrespective of shockable (VT/VF) or non-shockable rhythm. The most common comorbidities among the study population were hypertension (64.7%), diabetes without chronic complications (17.0%) and

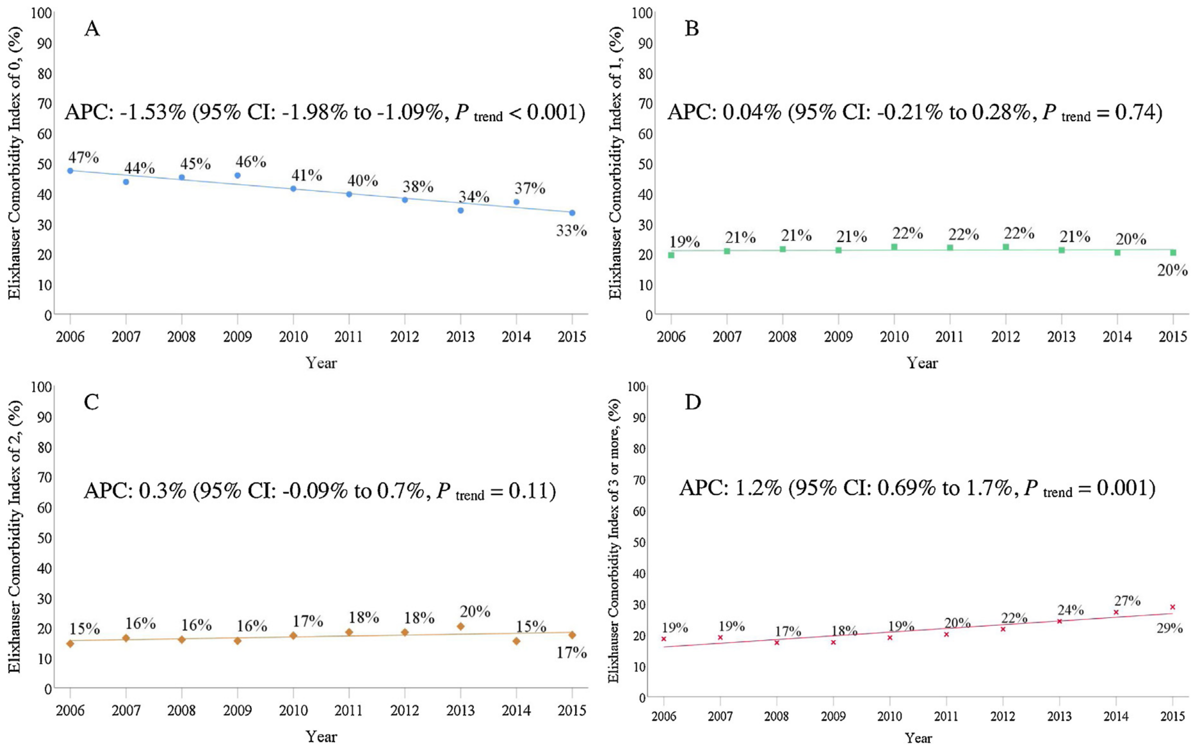

Fig. 1 – Temporal annual trends in survival-to-discharge rate among patients with out-of-hospital cardiac arrest. A–D corresponds to Elixhauser Comorbidity Index 0, 1, 2 and >3, respectively. APC — annual percentage change.

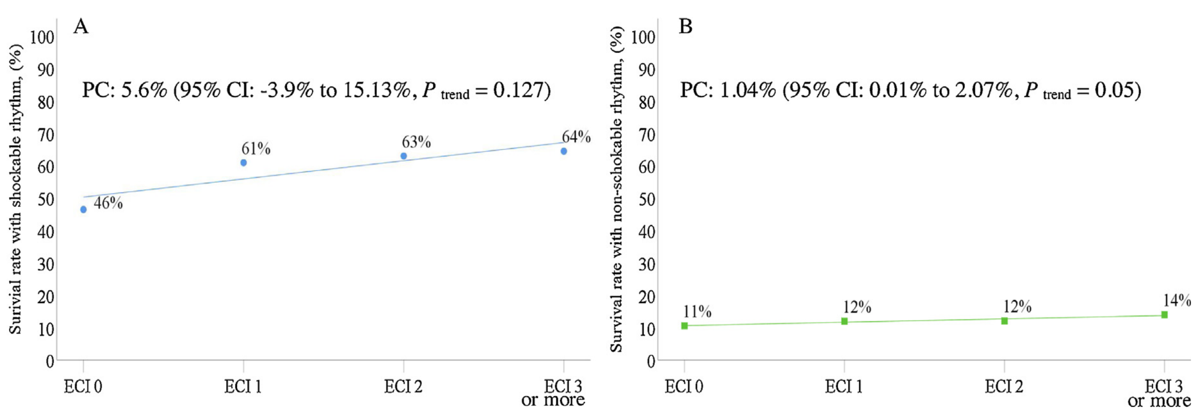

Fig. 2 – Liner trends in survival-to-discharge rate among patients with out-of-hospital cardiac arrest stratified by cardiac rhythm.
The survival rate among patients with shockable rhythm (Fig. 2A) and non-shockable rhythm (Fig. 2B) with increasing Elixhauser Comorbidity Index. PC — percentage change, ECI — Elixhauser Comorbidity Index.

fluid/electrolyte disorders (16.9%). Although pathophysiology behind comorbidity paradox is unclear, it is possible that given higher prevalence of these treatable comorbidities, in light of published literature showing preceding use of cardioprotective therapies such as β-adrenergic blockers, and statins use with improved survival in OHCA[11] with concomitant increased usage of these medications across the US[12,13] could have contributed towards improved survival among patients with higher comorbidities.

This study is limited due to its retrospective nature, inability to accurately determine preceding medication usage and inability to prove causation. This is offset by the large sample size capturing events across the US and the ability to generate a hypothesis of an association.

Conclusion

A higher survival-to-discharge rate is noted among OHCA with greater ECI when compared to no ECI, after adjusting for age and gender.

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Conflict of interest

None.

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