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Authors

Khan, Muhammad Zia
Sulaiman, Samian
Agrawal, Pratik
et al.

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Targeted temperature management in cardiac arrest patients with a non-shockable rhythm: A national perspective

Muhammad Zia Khan, MD[a], **Samian Sulaiman, MD**[a], **Pratik Agrawal, MD**[a], **Mohammed Osman, MD**[a], **Muhammad U. Khan, MD**[a], **Safi U. Khan, MD**[a], **Sudarshan Balla, MD**[a], **Muhammad Bilal Munir, MD**[a,b]

[a]Division of Cardiovascular Medicine, West Virginia University Heart and Vascular Institute, Morgantown, WV, USA,

[b]Division of Cardiovascular Medicine, University of California San Diego, La Jolla, CA, USA.

Abstract

Introduction—Retrospective studies have shown conflicting benefit of utilizing targeted temperature management (TTM) in cardiac arrest (CA) patients with a non-shockable rhythm and presently there is only one randomized trial in this realm. We sought to determine trends and outcomes of TTM utilization in these patients from a large nationally representative United States population database.

Methods and Results—Data were derived from National Inpatient Sample (NIS) from January 2006 to December 2013. All patients were identified using the *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*) codes. Patients with evidence of shockable rhythm (ventricular tachycardia, ventricular flutter and ventricular fibrillation) were excluded. Trends in TTM utilization and mortality were assessed over our study period. Various outcomes were measured in patients receiving TTM and no TTM in unmatched and propensity matched cohorts. Logistic regression analysis was done to determine predictors of mortality. A total of 1,185,479 CA patients were identified in whom cause of arrest was a non-shockable rhythm. Overall, there was a steady increase in TTM utilization over our study period. In propensity-matched groups, mortality was higher in patients in whom TTM was utilized compared to non-TTM group (72.9% vs 68.7%, $P < .01$). In adjusted analysis, TTM remains an independent predictor of increased mortality in our group. Mortality remained high with TTM utilization regardless of location of CA.

Conclusions—TTM utilization was associated with increased mortality in CA patients with a non-shockable rhythm. These findings merit further confirmation in a large randomized trial before application into clinical practice.

Reprint requests: Muhammad Bilal Munir, MD, West Virginia University Heart & Vascular Institute and University of California San Diego Sulpizio Cardiovascular Center, 1 Medical Drive, Morgantown, West Virginia 26505. muhamad.munir@hsc.wvu.edu.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2020.04.023.

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Targeted temperature management (TTM) or hypothermia protocol is one of the established lifesaving modality utilized in management of comatose cardiac arrest patients in post-resuscitation phase. The landmark randomized trials done in early 2000 showed significant improvement in neurologically intact survival if prompt application of TTM was undertaken after resuscitation.[1,2] These trials enrolled patients with sudden cardiac arrest (SCA) in whom the initial presenting rhythm was either pulseless ventricular tachycardia or ventricular fibrillation (shockable rhythms). The only randomized data in SCA patients due to a non-shockable rhythm came from the recent HYPERION trial.[3] In this study, 584 patients were subjected to either normothermia or hypothermia after SCA due to a non-shockable rhythm. Although benefit was witnessed in hypothermia group in terms of favorable neurological survival at 90-days, overall mortality was not different in each group. The prevalence of pulseless electrical activity (PEA) and asystole (non-shockable rhythm) is high among patients with SCA and ranges anywhere from 60% to 80%.[4–6] Few observational studies assessing outcomes of TTM utilization in patients with initial non-shockable rhythm have shown conflicting results with a trend towards both benefit and potential harm.[7–11] American Heart Association (AHA) guidelines recommend class I (level of evidence C) indication for utilization of TTM in patients with non-shockable rhythm.[12] Since the proportion of SCA patients with initial presentation of non-shockable rhythm is relatively high compared to patients with shockable rhythm, it is imperative that further evidence be sought with respect to TTM utilization from real world settings. We, therefore, studied trends and outcomes of TTM utilization in SCA patients with non-shockable rhythm from a large nationally represented United States (US) population.

Methods

Data were derived from National Inpatient Sample (NIS). NIS is part of Healthcare Cost and Utilization Project (HCUP) databases and is made possible by a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ).[13] The NIS is derived from all States participating in HCUP, representing more than 97 percent of the US population. NIS allows national estimates of healthcare utilization, costs, and outcomes. Institutional review board approval and informed consents were not required for this study given the de-identified nature of the NIS database.

We analyzed NIS data from January 2006 to December 2013 using the International Classification of Diseases, 9th Revision, Clinical Modification (*ICD-9-CM*) codes. Patients ≥18 years of age were included. SCA patients were initially identified by search for *ICD-9* codes of 427.5 in all diagnosis and by *ICD-9* codes of 99.60 (cardiopulmonary resuscitation, not otherwise specified) and 99.63 (closed chest cardiac massage) in all procedure fields. This initial selection gave us all SCA patients with shockable and non-shockable rhythms regardless of in-hospital or out-of-hospital arrest. Patients with codes of 427.1 (ventricular tachycardia), 427.41 (ventricular fibrillation) and 427.42 (ventricular flutter) in any diagnosis field were then excluded. After excluding these *ICD-9* codes, the codes 427.5, 99.60 and 99.63 represented patients in whom SCA was due to a non-shockable rhythm (PEA or asystole). These *ICD-9* codes are well studied in administrative datasets previously.[14–17] The *ICD-9* procedure code of 99.81 was used in all procedures fields to identify patients undergoing TTM. Please see Figure 1 describing patient selection for our study.

Selected AHRQ comorbidities were generated as binary variables for analysis. Baseline characteristics and hospital outcomes for patients undergoing TTM and not undergoing TTM were assessed. We further analyzed the patient characteristics and outcomes based on whether the location of SCA was in-hospital or out-of-hospital. Since AHA guidelines were updated in 2010,[18] we also did another sensitivity analysis to assess baseline characteristics and outcomes of study population from years 2006 to 2010 and 2011 to 2013. Trend weights were utilized till 2011 and discharge weights were applied to data 2012 onwards to generate national estimates. All analyses were done on weighted sample.

Descriptive statistics were presented as frequencies with percentages for categorical variables and as means with standard deviations for continuous variables. Baseline characteristics were compared using a Pearson χ^2 test and Fisher's exact test for categorical variables and independent samples t-test for continuous variables. To account for potential confounding factors and selection bias, a propensity score-matching model was developed using logistic regression to derive two matched groups for comparative outcomes analysis. A nearest neighbor 1:1 fixed ratio, parallel, balanced propensity-matching model was made using a caliper width of 0.2. To avoid loss of data before propensity matching, missing values were calculated with Markov Chain Monte Carlo (MCMC) multiple imputation. To most extent, data was evenly matched after propensity matching (please see Table I). Logistic regression was performed to estimate odds ratios (ORs) with 95% confidence intervals (CIs) to determine predictors of mortality and TTM utilization in our cohort. Initially, binomial logistic regression model was used to identify variables from demographic data (Table I) that were significantly associated with mortality and TTM utilization ($P < .10$). These variables were then subsequently utilized in a multiple logistic regression model to identify factors predicting mortality and TTM utilization. A type I error rate of <0.05 was considered statistically significant. All statistical analyses were performed using statistical package for social science (SPSS) version 24 (IBM Corp) and R 3.6.

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. No extramural funding was used to support this work.

Results

A total of 1,185,479 (unweighted = 248,640) patients with non-shockable SCA were identified from January 2006 to December 2013. Out of these, 11,657 patients underwent TTM treatment. Patients who underwent TTM were younger when compared to patients not undergoing TTM (60.9 vs 67.4 years, $P < .01$). 559,535 (47.1%) patients were women and they have low proportion of undergoing TTM (44.6% vs 47.2%, $P < .01$). TTM utilization was high among White Americans and low in Black and Hispanic population (Table I). A total of 818,466 (69%) patients died at discharge in crude analysis. Mortality was higher in patients undergoing TTM (73.5%) when compared to patients not undergoing TTM (69%). Propensity matched analysis is shown in Table II. Mortality continues to be higher in TTM group compared to non-TTM group (72.9% vs 68.7%, $P < .01$). Over our study years there has been an increased trend of patients undergoing TTM (Figure 2). Males had slightly higher percentage of undergoing TTM as compared to females. Overall, mortality seemed to

be on the downward trend in SCA patients with a non-shockable rhythm (Figure 3). Baseline characteristics and outcomes stratified based on in-hospital and out-of-hospital non-shockable SCA are shown in supplementary table 1 and 2. TTM utilization was significantly associated with worsened mortality in out-of-hospital non-shockable SCA (72.4% vs 62.6%, $P < .01$) while no difference in mortality was noted with TTM utilization based on in-hospital SCA (75.3% vs 75.3%, $P = .97$). Mortality continued to be higher when TTM was utilized before and after year 2010 (73.4% vs 70.2%, $P < .01$ and 73.6% vs 67.3%, $P < .01$). Please see supplementary table 3 and 4 for detailed results.

Predictors of mortality in our cohort are shown in Figure 4. It should be noted that TTM utilization was found to independently predict mortality in SCA patients in which initial rhythm was non-shockable (OR 1.554, 95% C.I. 1.486–1.625). Black race (OR 1.205, 95% C.I. 1.19–1.22), Hispanics (OR 1.155, 95% C.I. 1.136–1.173) and key co-morbidities such as liver disease (OR 1.712, 95% C.I. 1.672–1.752), peripheral vascular disease (OR 1.017, 95% C.I. 1.002–1.031) and renal failure (OR 1.027, 95% C.I. 1.016–1.038) were independently associated with increased mortality in our cohort. Compared to rural location of the hospital, both urban non-teaching (OR 0.89, 95% C.I. 0.876–0.905) and urban teaching (OR 0.861, 95% C.I. 0.847–0.875) hospitals were associated with improved survival after non-shockable SCA.

Predictors of TTM utilization in patients with non-shockable SCA are shown in supplementary table 5. Female gender (OR 0.95, 95% C.I. 0.942–0.959), Blacks (OR 0.817, 95% C.I. 0.77–0.866), Hispanics (OR 0.689, 95% C.I. 0.638–0.744) and patients with key comorbidities such as congestive heart failure (OR 0.804, 95% C.I. 0.761–0.849), liver disease (OR 0.572, 95% C.I. 0.514–0.637), metastatic cancer (OR 0.449, 95% C.I. 0.388–0.5419) and renal failure (OR 0.82, 95% C.I. 0.816–0.865) have lower odds of TTM utilization.

Discussion

In this large and nationally representative sample of US population, we have shown that patients in whom SCA was due to non-shockable rhythm, the mortality was higher when TTM was utilized in post resuscitation phase in both matched and un-matched cohorts. In adjusted multi-variate regression analysis, TTM is an independent predictor of mortality in these patients.

To the best of our knowledge, this is the largest cohort of SCA patients assembled to-date to study outcomes after SCA event when rhythm was non-shockable. Current AHA guidelines confer class I indication for utilization of hypothermia protocol in patients in whom SCA was caused by non-shockable rhythm although the level of evidence is primarily based on observational studies (level of evidence: C).[12] HYPERION is the only recently conducted randomized trial that purely enrolled SCA patients with a non-shockable rhythm.[3] The study showed a significantly improved neurologically intact survival in hypothermia group when compared to normothermia group (HR 4.5, 95% C.I. 0.1–8.9). No significant differences were noted in overall mortality that remained high in both groups (81.3% vs 83.2%). It should be noted that in HYPERION trial, active rewarming was done in normothermia group

if their body temperature at randomization was less than 36.5 C. Our data, however, do not inform on core body temperature of patients after they sustained SCA in contrast to HYPERION trial. The observational studies done in this realm largely confer conflicting results. Perman et al[9] studied approximately 519 SCA patients using data from Penn Alliance for Therapeutic Hypothermia (PATH) registry. All of these patients were documented to have a non-shockable rhythm at initial presentation. After balancing for confounding variables, they found that utilization of TTM was associated with increased survival at discharge (28.9% vs 17.6%, $P < .01$). In a multi-variate model, they also reported TTM to be an independent predictor of survival (OR 2.8, 95% C.I. 1.6–4.7) as well as neurological recovery (OR 3.5, 95% C.I. 1.8–6.6). On the contrary, a pilot study conducted by Kim et al[7] on the effectiveness of in-field cooling showed increased mortality (albeit non-statistically significant) in sub-group of SCA patients in whom the initial rhythm was non-shockable after utilization of cooling protocol. They also found increased survival among SCA patients with a non-shockable rhythm if cooling was not utilized. Similarly, in a study on 1145 consecutive SCA patients, Dumas et al[8] have found that TTM was not associated with improved neurological outcomes if initial rhythm was non-shockable (OR 0.71, 95% C.I. 0.37–1.16). In a cohort study from Get With the Guidelines-Resuscitation Registry, SCA patients with non-shockable rhythm were found to have lower in-hospital survival if TTM was utilized (RR 0.87, 95% C.I. 0.76–0.99).[10] Similarly, another registry data of 6000 patients showed that utilization of TTM was associated with worse neurological outcomes at discharge in patients in whom SCA was attributable to a non-shockable rhythm (OR 1.44, 95% C.I. 1.03–2.00).[11] Similarly, a sub study of TTM trial comparing hypothermia strategy of 33 C versus 36 C in patients with non-shockable SCA showed no significant difference in improved neurological outcomes in either arm (OR 0.67, 95% CI 0.08–4.73).[19] Our real-world data from national cohort of more than 1.18 million patients with SCA due to non-shockable rhythm showed that utilization of TTM was in fact associated with increased mortality at discharge and that difference was statistically significant (72.9% vs 68.7%, $P < .01$). These findings need to be studied further in a large randomized trial before clinical applicability to SCA patients with a non-shockable rhythm.

Our study also showed TTM to be an independent predictor of mortality in SCA patients in which cause of arrest was deemed a non-shockable rhythm. The association between SCA cause and first documented rhythm has been studied before with shockable rhythms likely related to cardiac etiology.[8] On the other hand, anoxia largely contributes to PEA and asystole (non-shockable rhythms). It has been speculated that combination of both anoxia and ischemia as witnessed in non-shockable SCA results in far greater cerebral damage when compared to SCA due to shockable rhythm.[20,21] In the setting of this deranged and unique pathophysiology, the risk-benefit ratio of TTM utilization that clearly favors SCA patients with shockable rhythm may not be applicable to SCA patients in whom the cause of arrest was due to non-shockable rhythm. More studies are needed to further explore this potential correlation especially in light of the fact that the incidence of SCA due to non-shockable is on the rise in general population.

Our study also showed that TTM was underutilized in female patients after they sustained SCA due to a non-shockable rhythm (Figure 2 and supplementary table 5). Previous studies have shown prevalence of disparate care in female patients in context of SCA. In a study

utilizing NIS database, Kim et al have shown that from years 2003–2012, increase in TTM utilization was less pronounced in females (0–1.8%) when compared to males (0–2.1%) after they sustained SCA due to a non-shockable rhythm.[22] Even though our study did not show benefit of utilizing therapeutic strategy of TTM in patients with non-shockable SCA, these data do provide an opportunity to identify etiologies behind such disproportionate care which could narrow sex-based disparities in caring for patients post-SCA.

Our analysis also showed nearly similar incidence of in-hospital and out-of-hospital SCA over our study period. Earlier studies evaluating epidemiology of in-hospital SCA showed reduced incidence of this entity when compared to out-of-hospital SCA. It should be noted that these studies reported data from either single institution or from small group of hospitals in a similar geographic location.[23–25] No standard methodology of assessing in-hospital SCA incidence currently exists. For example, one method of evaluating incidence of in-hospital SCA is to count the number of times a hospital's emergency response team is activated, however, this can result in overcounting (erroneous activation of emergency response team) or undercounting (in-hospital SCA occurring in emergency department or operative rooms) of such events.[26] Additionally, hospitals that frequently implement do-not-resuscitate (DNR) order before a SCA event are shown to report lower incidence of in-hospital SCA when compared to hospitals with infrequent implementation of DNR order.[27] In a most recent study evaluating incidence of in-hospital SCA from 2008–2017 using data from Get With the Guidelines-Resuscitation Registry, Holmberg et al have reported that true incidence of in-hospital SCA may be underestimated by 38% in comparison to earlier studies.[28] They predicted annual incidence of in-hospital SCA to be approximately 292,000 which is similar to annual incidence of out-of-hospital SCA. Our study has also reported nearly similar incidence of in-hospital and out-of-hospital SCA which is concomitant with Holmberg et al data. This further reinforces the fact that efforts should be directed equally to prevention and management of both in-hospital and out-of-hospital SCA as they contribute to a similar burden on health care resources.

Limitations

NIS is an administrative claim-based database that uses *ICD-9-CM* codes, which are subject to error. Our study, however, have used hard clinical points such as SCA and mortality which are less prone to diagnostic errors. SCA due to non-shockable rhythm (PEA and asystole) was identified using *ICD-9* codes of 427.5, 99.60 and 99.63 while excluding all patients who have concomitant codes for ventricular tachycardia, ventricular flutter and ventricular fibrillation. Similar methodology was applied in earlier studies to extract patients with PEA and asystole from NIS.[15,22] We believe this would have resulted in a very specific SCA cohort in which cause of arrest was due to PEA and asystole but residual mixing of some patients with shockable rhythm could not be ruled out entirely with certainty. NIS collects data on in-patient discharges and each admission is registered as an independent event and patients are not followed longitudinally. Therefore, long-term outcomes could not be ascertained from the present dataset. Also patients' neurological status which is an important marker of morbidity after SCA could not be assessed from the current database. Several important factors that affect patient's prognosis after SCA and may inform need for TTM utilization such as by stander cardiopulmonary resuscitation, time to return of spontaneous

circulation, severity status of the patient and witnessed arrest could not be examined from present data set. Although we have employed propensity score matching to mitigate risk of selection bias in our study, residual confounding due to unmeasured variables cannot be excluded. Additionally, NIS does not inform on technical details of TTM protocol such as target temperature used and methods used to rewarm the patient once duration of hypothermia is achieved.

Conclusion

In this large nationally representative sample of US population, we found that utilization of TTM was associated with increased mortality in SCA patients with non-shockable rhythm. Additionally, TTM was found to be an independent predictor of mortality in this specific patient population group. These findings if confirmed in a large randomized trial could have important clinical implications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrestN Engl J Med 2002;346:549–56. [PubMed: 11856793]
2. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557–63. [PubMed: 11856794]
3. Lascarrou JB, Merdji H, Gouge AL, et al. Targeted temperature management for cardiac arrest with nonshockable rhythm. N Engl J Med 2019 10 2;381:2327–37. [PubMed: 31577396]
4. Cobb LA, Fahrenbruch CE, Olsufka M, et al. Changing incidence of out-of-hospital ventricular fibrillation, 1980–2000. JAMA 2002;288:3008–13. [PubMed: 12479765]
5. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital cardiac arrest of non-cardiac origin. Resuscitation 2007;72:200–6. [PubMed: 17118509]
6. Rea TD, Eisenberg MS, Sinibaldi G, et al. Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. Resuscitation 2004;63:17–24. [PubMed: 15451582]
7. Kim F, Olsufka M, Longstreth WT Jr, et al. Pilot randomized clinical trial of prehospital induction of mild hypothermia in outof-hospital cardiac arrest patients with a rapid infusion of 4 degrees C normal saline. Circulation 2007;115:3064–70. [PubMed: 17548731]
8. Dumas F, Grimaldi D, Zuber B, et al. Is hypothermia after cardiac arrest effective in both shockable and nonshockable patients?: insights from a large registry. Circulation 2011;123: 877–86. [PubMed: 21321156]
9. Perman SM, Grossestreuer AV, Wiebe DJ, et al. The Utility of Therapeutic Hypothermia for Post-Cardiac Arrest Syndrome Patients With an Initial Nonshockable Rhythm. Circulation 2015;132:2146–51. [PubMed: 26572795]
10. Chan PS, Berg RA, Tang Y, et al. Association between therapeutic hypothermia and survival after in-hospital cardiac arrest. JAMA 2016;316:1375–82. [PubMed: 27701659]
11. Mader TJ, Nathanson BH, Soares WE 3rd, et al. Comparative effectiveness of therapeutic hypothermia after out-of-hospital cardiac arrest: insight from a large data registry. Ther Hypothermia Temp Manag 2014;4:21–31. [PubMed: 24660100]
12. Callaway CW, Donnino MW, Fink EL, et al. Post-cardiac arrest care: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2015;132:S465–82. [PubMed: 26472996]

13. Agency for Healthcare Research and Quality. Overview of the national (nationwide) inpatient sample (NIS). Rockville: AHRQ; https://www.hcup-us.ahrq.gov/nisoverview.jsp#about. Accessed on September 29, 2019
14. Johnson NJ, Salhi RA, Abella BS, et al. Emergency department factors associated with survival after sudden cardiac arrest. Resuscitation 2013;84:292–7. [PubMed: 23103887]
15. Kolte D, Khera S, Aronow WS, et al. Regional variation in the incidence and outcomes of in-hospital cardiac arrest in the United States. Circulation 2015;131:1415–25. [PubMed: 25792560]
16. Patel N, Patel NJ, Macon CJ, et al. Trends and outcomes of coronary angiography and percutaneous coronary intervention after out-of-hospital cardiac arrest associated with ventricular fibrillation or pulseless ventricular tachycardia. JAMA Cardiol 2016;1:890–9. [PubMed: 27627616]
17. Shelton SK, Chukwulebe SB, Gaieski DF, et al. Validation of an ICD code for accurately identifying emergency department patients who suffer an out-of-hospital cardiac arrest. Resuscitation 2018;125:8–11. [PubMed: 29341874]
18. Field JM, Hazinski MF, Sayre MR, et al. Part 1: executive summary: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:S640–56. [PubMed: 20956217]
19. Frydland M, Kjaergaard J, Erlinge D, et al. Target temperature management of 33°C and 36°C in patients with out-of-hospital cardiac arrest with initial non-shockable rhythm - a TTM sub-study. Resuscitation 2015;89:142–8. [PubMed: 25629544]
20. Vaagenes P, Safar P, Moossy J, et al. Asphyxiation versus ventricular fibrillation cardiac arrest in dogs. Differences in cerebral resuscitation effects: a preliminary study. Resuscitation 1997;35:41–52. [PubMed: 9259060]
21. Vaagenes P, Ginsberg M, Ebmeyer U, et al. Cerebral resuscitation from cardiac arrest: pathophysiologic mechanisms. Crit Care Med 1996;24:S57–68. [PubMed: 8608707]
22. Kim LK, Looser P, Swaminathan RV, Horowitz J, Friedman O, Shin JH, Minutello RM, Bergman G, Singh H, Wong SC, Feldman DN. Sex-Based Disparities in Incidence, Treatment, and Outcomes of Cardiac Arrest in the United States, 2003–2012. J Am Heart Assoc 2016;5 pii: e003704 [PubMed: 27333880]
23. Hodgetts TJ, Kenward G, Vlackonikolis I, et al. Incidence, location and reasons for avoidable in-hospital cardiac arrest in a district general hospital. Resuscitation 2002;54:115–23. [PubMed: 12161290]
24. Skogvoll E, Isern E, Sangolt GK, et al. In-hospital cardiopulmonary resuscitation. 5 years' incidence and survival according to the Utstein template. Acta Anaesthesiol Scand 1999;43:177–84. [PubMed: 10027025]
25. Sandroni C, Nolan J, Cavallaro F, et al. In-hospital cardiac arrest: incidence, prognosis and possible measures to improve survival. Intensive Care Med 2007;33:237–45. [PubMed: 17019558]
26. Morrison LJ, Neumar RW, Zimmerman JL, et al. Strategies for improving survival after in-hospital cardiac arrest in the United States: 2013 consensus recommendations: a consensus statement from the American Heart Association. Circulation 2013;127: 1538–63. [PubMed: 23479672]
27. Shepardson LB, Youngner SJ, Speroff T, et al. Variation in the use of do-not-resuscitate orders in patients with stroke. Arch Intern Med 1997;157:1841–7. [PubMed: 9290543]
28. Holmberg MJ, Ross CE, Fitzmaurice GM, et al. Annual incidence of adult and pediatric in-hospital cardiac arrest in the United States. Circ Cardiovasc Qual Outcomes 2019;12, e005580. [PubMed: 31545574]

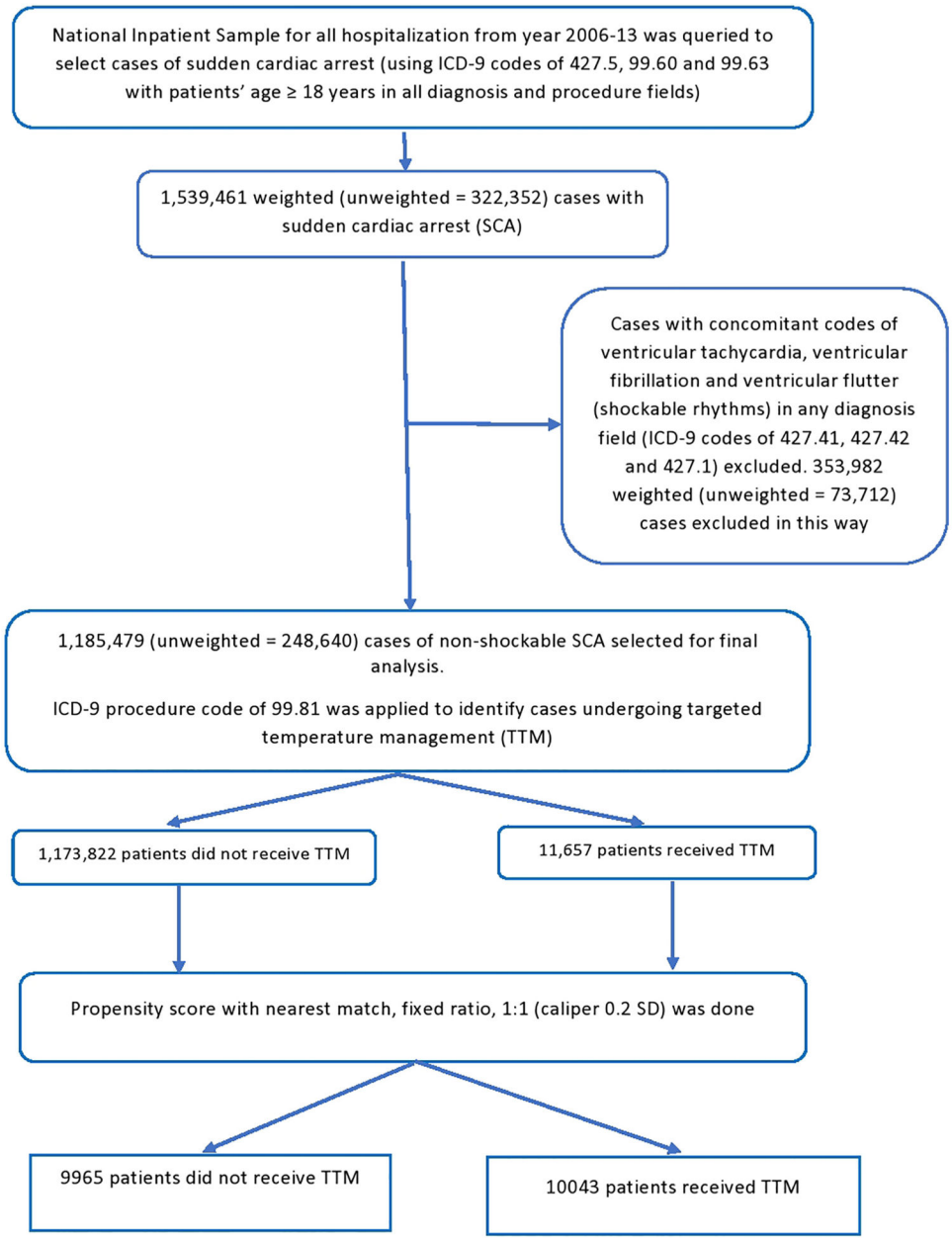

Figure 1.
Flow sheet of patient selection.

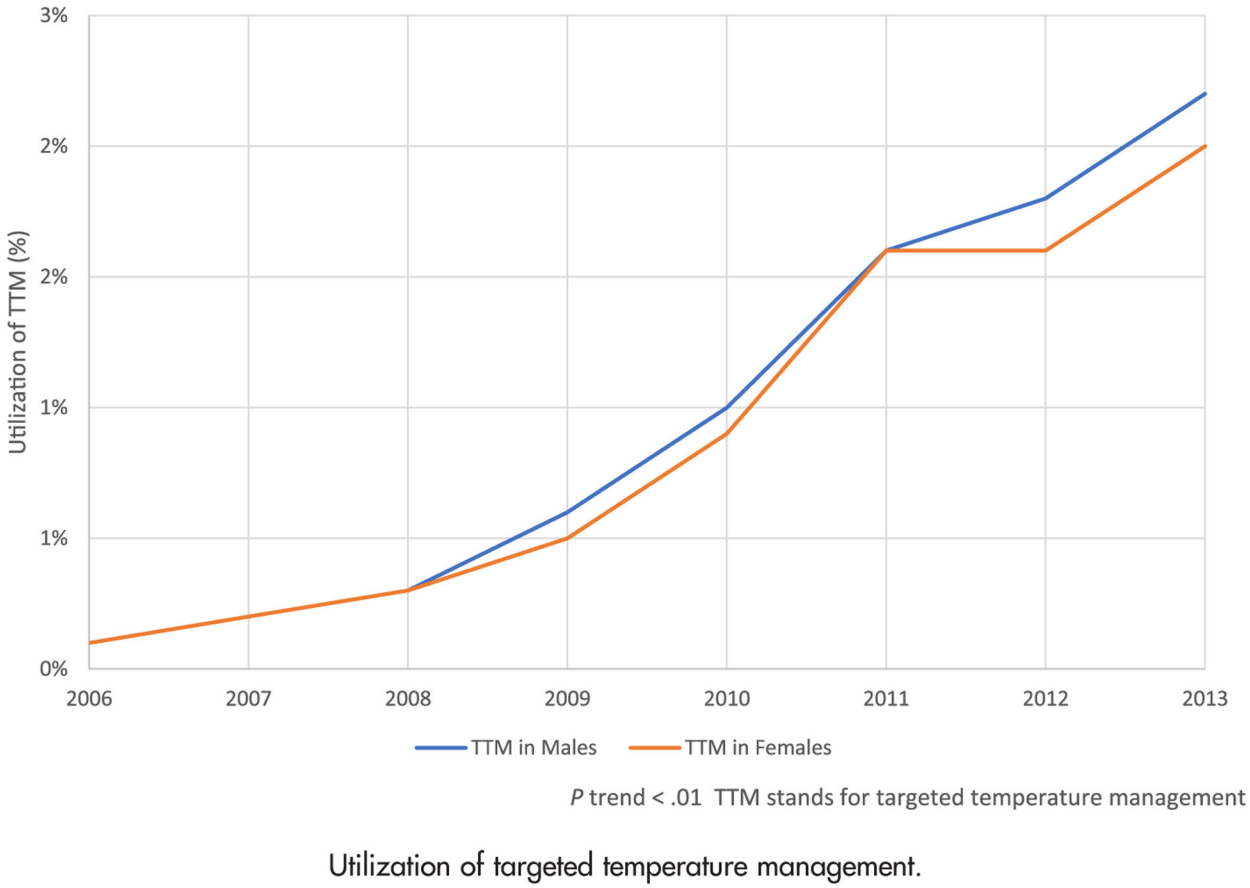

Figure 2.
Utilization of targeted temperature management.

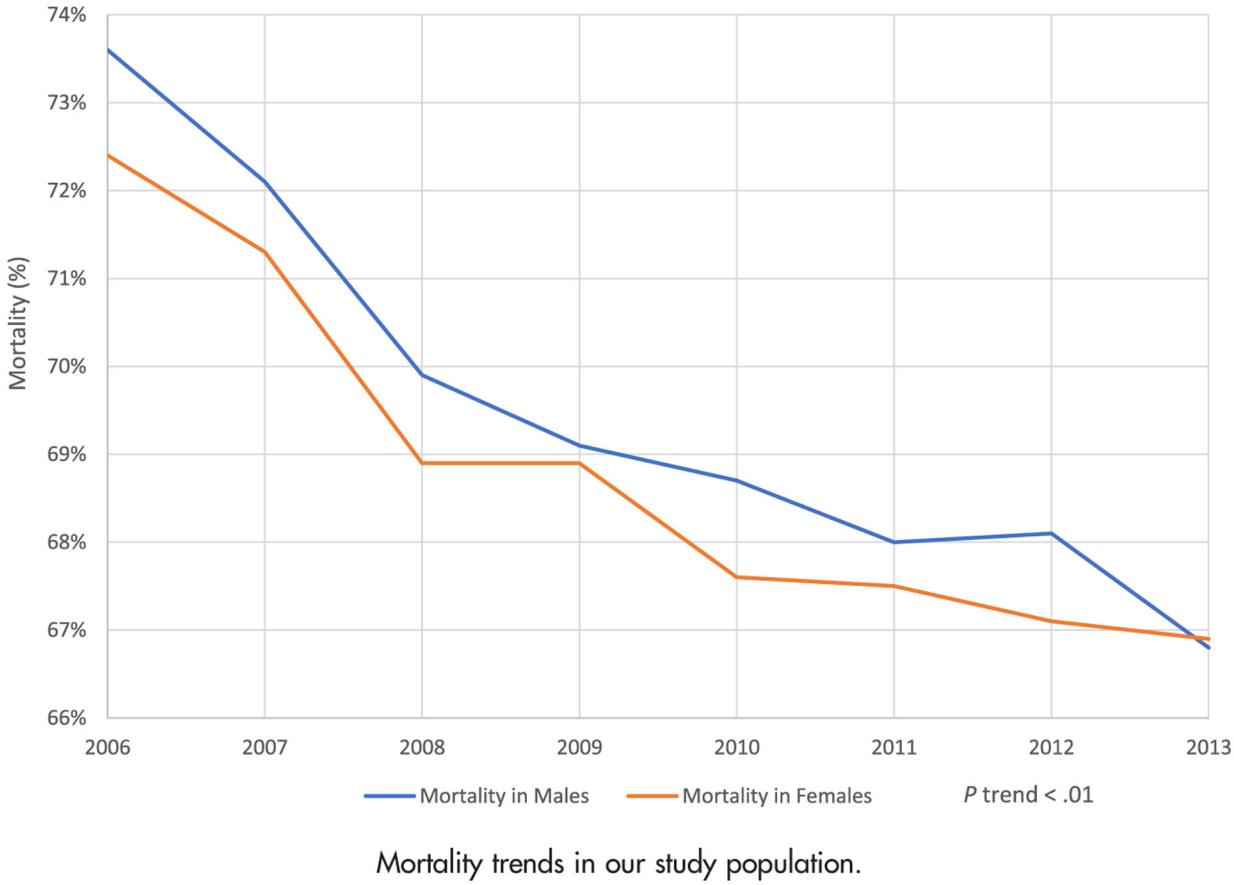

Figure 3.
Mortality trends in our study population.

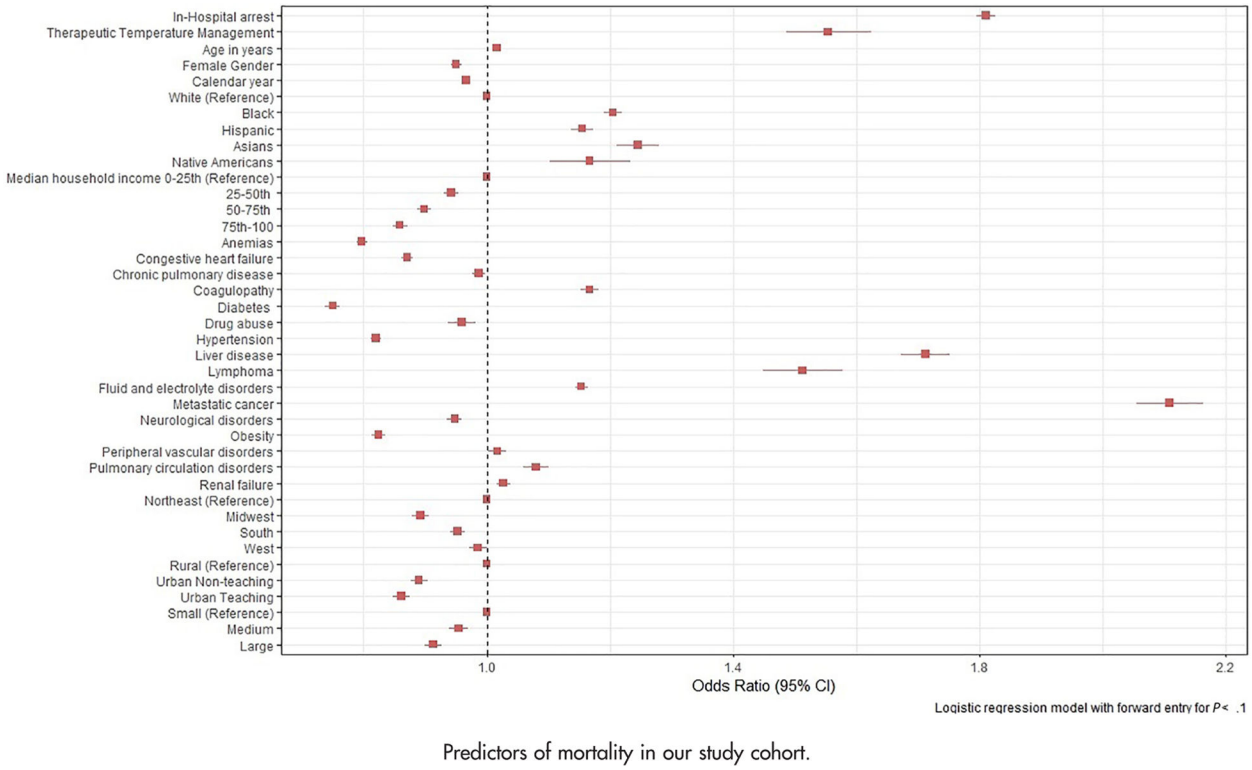

Figure 4.
Predictors of mortality in our study cohort.

Table I.

Baseline characteristics of the study population stratified on the basis of targeted temperature management utilization.

	Unadjusted baseline characteristics			Adjusted baseline characteristics after propensity score matching		
Variable no. (%)	No TTM[†] (n = 1,173,822)	TTM (n = 11,657)	P value	No TTM[†] (n = 9965)	TTM (n = 10,043)	P value
Age (mean [SD]) years	67.4 (16.4)	60.9 (16.5)	<0.01	60.7 (17.9)	61.0 (16.4)	0.24
Female	554,336 (47.2)	5199 (44.6)	<0.01	4391 (44.1)	4521 (45.0)	0.18
Race						
White	671,262 (65.6)	7105 (67.6)	<0.01	6646 (66.7)	6848 (68.2)	0.02
Black	190,520 (18.6)	1649 (15.7)		1518 (15.2)	1518 (15.2)	
Hispanic	95,740 (9.4)	829 (7.9)		867 (8.7)	784 (7.8)	
Other	36,198 (3)	514 (4.4)		456 (4.5)	483 (4.8)	
Comorbidities						
Anemia	272,289 (23.2)	2721 (23.3)	0.71	2406 (24.1)	2371 (23.6)	0.37
Collagen vascular disease	29,833 (2.5)	271 (2.3)	0.14	274 (2.8)	246 (2.5)	0.18
Congestive heart failure	251,596 (21.4)	1975 (16.9)	<0.01	1737 (17.4)	1716 (17.1)	0.52
Chronic pulmonary disease	302,279 (25.8)	3331 (28.6)	<0.01	2707 (27.2)	2940 (29.3)	<0.01
Pulmonary circulation disorders	72,216 (6.2)	717 (6.1)	0.99	683 (6.8)	652 (6.5)	0.31
Coagulopathy	167,574 (14.3)	1887 (16.2)	<0.01	1544 (15.5)	1604 (16.0)	0.35
Diabetes uncomplicated	280,573 (23.9)	3063 (26.3)	<0.01	2610 (26.2)	2715 (27.0)	0.18
Diabetes with complications	86,881 (7.4)	865 (7.4)	0.94	846 (8.5)	727 (7.2)	0.01
Drug abuse	39,820 (3.4)	950 (8.2)	<0.01	784 (7.9)	818 (8.1)	0.47
Hypertension	636,002 (54.2)	6412 (55.0)	0.08	5447 (54.7)	5625 (56.0)	0.06
Hypothyroidism	119,361 (10.2)	1064 (9.1)	<0.01	1039 (10.4)	967 (9.6)	0.06
Fluid and electrolyte disorders	599,617 (51.1)	7760 (66.6)	<0.01	6809 (68.3)	6769 (67.4)	0.16
Liver disease	53,589 (4.6)	409 (3.5)	<0.01	441 (4.4)	379 (3.8)	0.02
Lymphoma	15,115 (1.3)	72 (0.6)	<0.01	48 (0.5)	63 (0.6)	0.17
Neurological disorders	154,621 (13.2)	2719 (23.3)	<0.01	2339 (23.5)	2370 (23.6)	0.83
Metastatic cancer	48,869 (4.2)	223 (1.9)	<0.01	201 (2.0)	179 (1.8)	0.22
Peripheral vascular disorders	121,089 (10.3)	1072 (9.2)	<0.01	917 (9.2)	958 (9.5)	0.41
Renal failure	297,766 (25.4)	2735 (23.5)	<0.01	2401 (24.1)	2373 (23.6)	0.44
Obesity	116,558 (9.9)	1740 (14.9)	<0.01	1438 (14.4)	1526 (15.2)	0.13

	Unadjusted baseline characteristics			Adjusted baseline characteristics after propensity score matching		
Valvular disease	67,897 (5.8)	695 (6.0)	<0.01	619 (6.2)	616 (6.1)	0.82
Hospital Location						
Rural	122,999 (10.5)	481 (4.1)	<0.01	351 (3.5)	371 (3.7)	0.63
Urban non-teaching	497,106 (42.3)	4755 (40.8)		4407 (44.2)	4385 (43.7)	
Urban teaching	553,717 (47.2)	6421 (55.1)		5207 (52.3)	5287 (52.6)	
Bed size of the hospital						
Small	123,189 (10.5)	936 (8.0)	<0.01	834 (8.4)	825 (8.2)	0.63
Medium	293,328 (25.0)	2397 (20.6)		1962 (19.7)	2054 (20.5)	
Large	757,305 (64.5)	8325 (71.4)		7169 (71.9)	7164 (71.3)	
Region						
Northeast	206,296 (17.6)	2475 (21.2)	<0.01	2390 (24.0)	2273 (22.6)	0.12
Midwest	238,388 (20.3)	2511 (21.5)		1707 (17.1)	1710 (17.0)	
South	484,266 (41.3)	3193 (27.4)		2889 (29.0)	2971 (29.6)	
West	244,872 (20.9)	3089 (30.8)		2979 (29.9)	3089 (30.8)	
Median income						
0–25th	375,898 (32.9)	2997 (26.6)	<0.01	2856 (28.7)	2741 (27.3)	0.16
26–50th	297,557 (26.1)	2495 (22.1)		2093 (21.0)	2163 (21.5)	
51–75th	258,981 (22.7)	3157 (28.0)		2653 (26.6)	2751 (27.4)	
76–100th	209,555 (18.3)	2389 (23.8)		2363 (23.7)	2389 (23.8)	

†Targeted temperature management.

Table II.

Unadjusted and propensity-matched outcomes of the study cohort.

	Unadjusted outcomes			Adjusted propensity-matched outcomes		
Variables no. (%)	No TTM† (n = 1,173,822)	TTM (n = 11,657)	P value	No TTM† (n = 9965)	TTM (n = 10,043)	P value
Died at discharge	809,904 (69.0)	8562 (73.5)	<0.01	6842 (68.7)	7318 (72.9)	<0.01
Discharge disposition of surviving patients						
Routine/self-care	109,950 (30.3)	598 (19.4)	<0.01	1062 (34.0)	515 (18.9)	<0.01
Short-term hospital	40,881 (11.2)	475 (15.4)	<0.01	387 (12.4)	400 (14.7)	
Another type of facility	158,891 (43.7)	1637 (53.0)	<0.01	1259 (40.3)	1466 (53.8)	
Home health care	48,945 (13.5)	331 (10.7)	<0.01	382 (12.2)	305 (11.2)	
Resource utilization, Mean (SD)						
Length of stay, mean (SD), days	8.8 (14.2)	7.8 (10.9)	<0.01	10.0 (19.2)	7.9 (11.3)	<0.01
Cost of hospitalization-mean (SD), $	98,775 (153627)	121,565 (133409)	<0.01	125,834 (199023)	125,391 (137135)	0.855
Non-ST elevation myocardial infarction	107,668 (9.2)	1074 (9.2)	0.88	912 (9.2)	958 (9.5)	0.35
ST elevation myocardial infarction	92,224 (7.9)	1356 (11.6)	<0.01	588 (5.9)	1170 (11.7)	<0.01
Percutaneous coronary intervention	34,764 (3.0)	595 (5.1)	<0.01	202 (2.0)	532 (5.3)	<0.01
Feeding tube utilization	46,661 (4.0)	418 (4.2)	0.29	473 (4.7)	486 (4.2)	0.04
Tracheostomy utilization	59,370 (5.1)	680 (5.8)	<0.01	535 (5.4)	608 (6.1)	0.04

†Targeted temperature management.