Outcomes and Utilization of Therapeutic Hypothermia in Post-Cardiac Arrest Patients in Teaching Versus Non-Teaching Hospitals: Retrospective Study of the Nationwide Inpatient Sample Database (2016)

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Abstract

Background

Using therapeutic hypothermia (TH) reduces the core body temperature of survivors of cardiac arrest to minimize the neurological damage caused by severe hypoxia. The TH protocol is initiated following return of spontaneous circulation (ROSC) in non-responsive patients. Clinical trials examining this technique have shown significant improvement in neurological function among survivors of cardiac arrests. Though there is strong evidence to support TH use to improve the neurologic outcomes in shockable and nonshockable rhythms, predictors of TH utilization are not well-characterized. Our study tried to evaluate TH utilization, as well as the effect of the teaching status of hospitals, on outcomes, including mortality, length of stay, and total hospitalization charges.

Method

We conducted a retrospective analysis of the Healthcare Cost and Utilization Project - Nationwide Inpatient Sample (HCUP-NIS) database. Patients with an admitting diagnosis of cardiac arrest, as identified by the corresponding International Classification of Disease, 10th Revision (ICD-10) code for the year 2016 were analyzed. In addition, we identified TH using the ICD-10 procedure code. A weighted descriptive analysis was performed to generate national estimates. Groups of patients admitted to teaching hospitals were compared to those admitted in non-teaching hospitals. Patients were stratified by age, sex, race, and demographic and clinical data, including the Charlson Comorbidity Index (CCI), for these two groups, and statistical analysis was done for the primary outcome, in-hospital mortality, as well as the secondary outcomes, including length of stay (LOS) and total hospitalization charges. Fisher’s exact test was used to compare proportions and student’s t-test for continuous variables. Statistical analysis was completed by linear regression analysis.

Results

A total of 13,780 patients met the inclusion criteria for cardiac arrest admission. The number of patients with cardiac arrest admitted to a teaching hospital was 9285. A total of 670 patients received TH, with 495 admissions to teaching hospitals. The population of females in the hypothermia group was 270. The mean age of patients received TH was 59.4 years. In patients who received TH, 65% were Caucasians followed by Hispanics (16%), with no significant statistical racial differences in groups (p=0.30). The majority of patients with TH in both groups (teaching vs. non-teaching admissions) had Medicare (58.8% vs 49.5%; p=0.75). Hospitals in the southern region had the most admissions in both groups (45.7% and 31.3%), with the northeast region having the least non-teaching hospital admissions (8.5%) and approximately similar teaching hospital admissions in other regions (~22%) (p=0.27). The total number of deaths in this group was 510, out of which 370 were in a teaching hospital. After adjusting for age, sex, race, income, the CCI, hospital location, and bed size, mortality was not significantly different between these two groups (p=0.797). We found increased LOS in patients admitted to teaching hospitals (p=0.021). With a p-value of 0.097, there were no differences in total hospitalization charges in both groups.

Conclusion

There were no significant differences in mortality or total hospitalization charge between patients admitted with cardiac arrest to a teaching hospital and received TH as compared to a non-teaching hospital although patients admitted to teaching hospitals stayed longer.
Introduction

This study aimed to understand the utilization of TH in post-cardiac arrest patients admitted to teaching vs. non-teaching hospitals, as well as the outcomes, including mortality, length of stay, and total hospitalization charges.

The annual incidence of out-of-hospital cardiac arrests (OHCA) in the United States is reported to be more than 340,000. Mortality is estimated to be nearly 90% and approximately 9% of the survivors were noted to have good neurological function [1].

Therapeutic hypothermia (TH) has been shown to mitigate global cerebral ischemia and improve recovery from the neurological problems caused by severe hypoxia in cardiac arrest and neonatal asphyxia [2-4]. Since its initial description by Hippocrates in 400 BC (of its ability to reduce hemorrhage in the wounded), it was extended to be studied mainly as a neuroprotective measure in multiple settings such as after cardiac arrests, prolonged open-heart surgeries, traumatic brain injuries, and ischemic stroke [5].

After various animal models showed improved functional recovery and reduced cerebral histological defects with TH, this was also extended into human studies, with promising results [2-3,6-9]. The pathophysiologic basis for this benefit is believed to be multifactorial but mostly thought to be related to metabolic suppression and reduced cerebral oxygen demand with induced hypothermia [10-12].

With accumulating evidence from two major randomized and several non-randomized trials, the TH protocol was officially incorporated in post-resuscitation guidelines by the International Liaison Committee on Resuscitation (ILCOR) and the American Heart Association (AHA) in 2005 [2-3,13]. A strong level of evidence exists to recommend the use of TH in comatose, out-of-hospital cardiac arrest survivors whose initial rhythm was ventricular fibrillation or pulseless ventricular tachycardia. However, it is also being used regularly in survivors with an initial non-shockable rhythm (asystole/pulseless electrical activity) and in-hospital cardiac arrest situations based on the consensus of expert opinion.

After the initial introduction, the protocol did not receive widespread recognition, as the rate of implementation among physicians was reported to be only at 30%-40% [14]. Many barriers were recognized, and active measures and strategies were implemented to change this clinical practice. Though TH utilization remains variable, predictors of utilization are not well-understood.

Generally, teaching hospitals are big establishments, and they are considered as being well-equipped with resources and leading physicians among the staff. It is usually assumed that patients who are being treated in these centers are getting high-quality health-care [15]. Therapeutic hypothermia utilization and its outcome is one of the surrogates of quality care provided by the hospitals. This review seeks to evaluate retrospectively the utilization rates and outcomes of the use of TH in teaching vs. non-teaching hospitals.

Materials And Methods

Study design and database description

This retrospective cohort study included patients hospitalized in 2016 due to a cardiac arrest. The Nationwide Inpatient Sample (NIS) database 2016 was used to select the patient population. We have chosen the 2016 dataset, as this was the only available current dataset with a fully integrated International Classification of Disease, 10th Revision, Clinical Modification code at the time of this study. The database is created and maintained by the Agency for Healthcare Research and Quality (AHRQ), which is one of the largest publicly available databases. It contains both patient and hospital-level information. There are 30 discharge diagnoses and 15 procedures recorded for each patient based on the International Classification of Disease, 10th Revision, Clinical Modification (ICD-10-CM). All non-federal acute care hospitals participate in this database. Hospitals are stratified according to bed size, teaching status, urban vs. rural location, as well as geographic region. As this is a stratified probability sample, a 20% sample of all hospitals within the stratum is collected. The discharges from the acute care hospitals are recorded and weighted to ensure they are nationally representative. In 2016, 4575 hospitals from 46 states plus the District of Columbia participated in the NIS database, covering more than 97% of the U.S. population [16].

Study patients

Patients admitted with a cardiac arrest were identified using ICD 10-CM codes. The ICD-10 codes were for cardiac arrests in the setting of cardiac conditions, with other specific and nonspecific conditions. As there is no definite code for shockable vs non-shockable rhythm, it was not included in our study. The ICD-10 procedure code was applied to identify the use of TH (Annexure 1). Patients with cardiac arrest who received TH were included in our study population.
Study variables
The NIS database identifies the participating hospitals according to their geographical location, rural vs. urban location, and teaching vs. non-teaching status, as well as per their size in terms of bed numbers. We included in our study the teaching and non-teaching status of hospitals for comparison.

This study also evaluated other confounders such as age, sex, race/ethnicity, the median yearly income for the patient’s zip code, patient’s comorbidities, hospital location (rural or urban), and geographic region (Northeast, Midwest, West, or South). For comorbidity, we used the Charlson Comorbidity Index (CCI) for administrative data and re-categorized it into groups as CCI=0, CCI=1, CCI=2, and CCI≥3. These variables were part of prior studies done on this topic as well.

Statistical analysis
The statistical analysis was performed using STATA version 15.1 (Stata Corp, College Station, Texas) to generate variance estimates and p-values. To calculate unadjusted odds ratios for primary and secondary outcomes, we used univariate linear regression analysis. We adjusted for the above-mentioned confounders using multivariate linear regression analysis. Fisher’s exact test was used to compare proportions and the student’s t-test for continuous variables. The p-value threshold for statistical significance was 0.05.

Outcomes
The primary outcome of this study was in-hospital mortality in patients admitted with out-of-hospital cardiac arrest and who received TH in teaching vs. non-teaching hospitals. We also reviewed the overall utilization of TH in these patients in the same setting. The in-hospital mortality is provided in the NIS database for each discharge. Further analysis was done to see the effect of the teaching status of hospitals on mortality as well as secondary outcomes, including the length of stay (LOS) and total hospitalization charges.

Results
Patient characteristics and utilization of TH
There were 7,135,090 discharges in 2016 [15]. A total of 13,780 cardiac arrests were admitted in 2016. Six-hundred seventy patients received TH, with 495 admissions to the teaching hospital and a mean age of 59 years. The population of females in the TH group was 270. Of the patients who received TH, 65% were Caucasians followed by Hispanics (16%), with there being no significant statistical racial differences in groups (p=0.30). The majority of patients with TH in both groups (teaching vs non-teaching admissions) had Medicare (58.8% vs 49.5%; p=0.75). Hospitals in the southern regions had the most admissions in both groups (45.7% and 31.3%), with hospitals in the northeast having the least non-teaching hospital admissions (8.5%) and approximately similar teaching hospital admissions in other regions (~22%) (p=0.27). A majority of patients in teaching hospitals (34.3%), as well as non-teaching hospitals (45.7), had Charlson Comorbidity Index ≥3. Table 1 provides the detailed characteristics of our study population.
### TABLE 1: Patient and hospital characteristics

| Patient Characteristic: | Total | Teaching Hospital | Nonteaching Hospital | p-value |
|-------------------------|-------|-------------------|---------------------|---------|
| No. (%) of patients     | 670   | 495 (73.8)        | 175 (28.2)          |         |
| Female, No. (%)         | 235 (47.5) | 35 (20.0)        | 175 (28.2)          | 0.308   |
| Race/Ethnicity, No (%)  |       |                   |                     | 0.483   |
| White                   | 313 (63.3) | 113 (64.5)       | 200 (63.7)          |         |
| African-American        | 82 (16.7) | 17 (9.7)         | 65 (17.1)           |         |
| Hispanic                | 38 (7.8)  | 28 (16.1)        | 10 (3.2)            |         |
| Asian or Pacific Islander| 32 (6.7)  | 6 (3.2)          | 26 (3.2)            |         |
| Native American         | 0 (0)   | 6 (3.2)          | 4 (0.8)             |         |
| Other                   | 27 (5.6) | 6 (3.2)          | 21 (3.5)            |         |
| Median age, Y, (95% CI) | 63.9 (63.2-64.7) | 59.7 (56.8-62.7) | 58.5 (52.8-64.2)   | 0.751   |
| Charlson Comorbidity Index Score |       |                   |                     | 0.188   |
| 0                       | 94 (19.4) | 35 (20.0)        | 59 (17.1)           |         |
| 1                       | 143 (29.2) | 30 (17.1)        | 113 (17.1)          |         |
| 2                       | 84 (17.2)  | 30 (17.1)        | 54 (17.1)           |         |
| ≥3                      | 168 (34.3) | 80 (45.7)        | 88 (28.2)           |         |
| Median annual income for patient's Zip code, US$, No. (%) |       |                   |                     | 0.272   |
| 1-42999                 | 148 (29.9) | 31 (17.0)        | 117 (31.3)          |         |
| 43,000 - 53,999         | 132 (26.8) | 67 (38.2)        | 65 (17.0)           |         |
| 54,000 - 70,999         | 107 (21.6) | 57 (32.3)        | 50 (14.3)           |         |
| >71,000                 | 107 (21.6) | 16 (11.8)        | 91 (26.2)           |         |
| Insurance type, No. (%) |       |                   |                     | 0.751   |
| Medicare                | 245 (49.5) | 103 (58.8)       | 142 (35.7)          |         |
| Medicaid                | 88 (17.8)  | 31 (17.7)        | 57 (32.3)           |         |
| Private                 | 145 (29.4) | 36 (20.6)        | 109 (35.0)          |         |
| Uninsured               | 16 (3.16)  | 5 (2.9)          | 11 (3.2)            |         |
| Hospital characteristics |       |                   |                     |         |
| Hospital region, No. (%)|       |                   |                     | 0.272   |
| Northeast               | 120 (24.2) | 15 (8.6)         | 105 (30.0)          |         |
| Midwest                 | 110 (22.2) | 40 (22.9)        | 70 (20.1)           |         |
| South                   | 155 (31.3) | 80 (45.7)        | 75 (21.9)           |         |
| West                    | 110 (22.2) | 40 (22.9)        | 70 (20.1)           |         |

**In-hospital mortality based on teaching status of hospital**

Patients who were admitted to teaching hospitals with a cardiac arrest and received TH had a mortality rate of 75% (510 patients). Whereas overall mortality in cardiac arrest patients were 10,260 out of 13,780.
admitted (74.5%).

Using a multivariate linear regression analysis that adjusted for patient and hospital-level confounders, we found the adjusted coefficient of mortality was -0.028, 95% CI -0.24-0.19, and p-value of 0.797. Patients without insurance (self pay) had decreased mortality (coefficient 0.43, p= 0.014, 95%CI 0.086-0.77). Patients admitted to a medium bed size hospital showed decreased mortality (coefficient -0.30, p=0.006, 95%CI -0.51 – 0.87). There was no effect of racial difference and hospital location or region on mortality. Detailed results are summarized in Table 2.

| Mortality | Coefficient | Linearized Std. Err. | P     | [95% Conf. Interval] |
|-----------|-------------|----------------------|-------|----------------------|
| Teaching hospital | -0.0282254 | 0.1097373 | 0.797 | -0.2434768 0.1870261 |
| Age      | 0.0003119 | 0.0031306 | 0.921 | -0.0058288 0.0064525 |
| Female   | -0.0030135 | 0.0793216 | 0.97  | -0.1586041 0.1525772 |

Race

| Race                      | Coefficient | Linearized Std. Err. | P     | [95% Conf. Interval] |
|---------------------------|-------------|----------------------|-------|----------------------|
| African American          | 0.0309733 | 0.1187131 | 0.794 | -0.2018844 0.2638309 |
| Hispanic                  | 0.0580718 | 0.128843  | 0.652 | -0.1946557 0.3107993 |
| Asian or Pacific Islander | -0.1578534 | 0.1941726 | 0.416 | -0.538726 0.2230192 |
| Native American           | 0.1481538 | 0.1542157 | 0.337 | -0.1543426 0.4506503 |
| Other                     | 0.0521277 | 0.147022  | 0.723 | -0.2362582 0.3405135 |

Median annual income in patient’s zip code, US$ (reference 1 - 42,999)

| Median annual income | Coefficient | Linearized Std. Err. | P     | [95% Conf. Interval] |
|----------------------|-------------|----------------------|-------|----------------------|
| 43,000 - 53,999      | -0.0575723 | 0.1228186 | 0.639 | -0.2980907 0.1829461 |
| 54,000 - 70,999      | 0.0584806 | 0.1168395 | 0.617 | -0.1707019 0.287663  |
| >71,000              | 0.1329478 | 0.1269793 | 0.295 | -0.1161242 0.3820197 |

Primary Payer (reference medicare)

| Primary Payer          | Coefficient | Linearized Std. Err. | P     | [95% Conf. Interval] |
|------------------------|-------------|----------------------|-------|----------------------|
| Medicaid               | -0.0341967 | 0.1259209 | 0.786 | -0.2811924 0.2127991 |
| Private                | 0.0810423  | 0.0855511 | 0.344 | -0.0867675 0.248852  |
| Self-pay               | 0.4293107  | 0.1749926 | 0.014 | 0.0860598 0.7725615  |

Charlson comorbidity score

| Charlson comorbidity | Coefficient | Linearized Std. Err. | P     | [95% Conf. Interval] |
|----------------------|-------------|----------------------|-------|----------------------|
| 1                    | -0.0514546  | 0.1135377 | 0.65  | -0.2741606 0.1712514 |
| 2                    | -0.026537   | 0.1335714 | 0.843 | -0.2885394 0.2354653 |
| ≥3                   | 0.0788199   | 0.0982482 | 0.423 | -0.1138954 0.2715352 |

Urban hospitals (reference-rural)

| Urban hospitals        | Coefficient | Linearized Std. Err. | P     | [95% Conf. Interval] |
|------------------------|-------------|----------------------|-------|----------------------|
| -0.2374598             | 0.1429704   | 0.097                | -0.5178985 0.0429789 |

Hospital region (reference Northeast)

| Hospital region        | Coefficient | Linearized Std. Err. | P     | [95% Conf. Interval] |
|------------------------|-------------|----------------------|-------|----------------------|
| Midwest                | 0.1657511   | 0.0918772 | 0.071 | -0.0144674 0.3459697 |
| South                  | -0.0914026  | 0.1214781 | 0.452 | -0.3296839 0.1468786 |
The results related to secondary outcomes are as follows.

**Hospital length of stay based on teaching status of the hospital**

The median length of stay for patients who were admitted with a cardiac arrest and received TH in teaching hospitals was 4.33, whereas in non-teaching hospitals, it was 3.45. The multivariate linear analysis showed increased odds of length of stay in teaching hospitals as compared to non-teaching hospitals (coefficient=5.58, p=0.033, 95%CI 0.45-10.71). Patients with income group in the $43,000 - $53,999 range also showed increased length of stay (LOS) (coefficient=6.23, p=0.021, 95%CI 0.93-11.54). Detailed results are summarized in Table 3.

### Table 3: Result of multivariate linear regression for primary outcome mortality

Std err: Standard Error, Conf: Confidence

| Effect                        | Coefficient | Linearized Std. Err. | P       | [95% Conf. Interval] |
|-------------------------------|-------------|----------------------|---------|---------------------|
| West                          | 0.0708363   | 0.1075713            | 0.51    | -0.1401664          | 0.281839 |
| Hospital bed-size (reference small) |            |                      |         |                     |          |
| Medium                        | -0.2974968  | 0.1075469            | 0.006   | -0.5084518          | -0.0865419 |
| Large                         | -0.0990006  | 0.0932798            | 0.289   | -0.2819704          | 0.0839693 |

**LOS**

| Effect                        | Coefficient | Linearized Std. Err. | P       | [95% Conf. Interval] |
|-------------------------------|-------------|----------------------|---------|---------------------|
| Teaching hospital             | 5.582218    | 2.614698             | 0.033   | 0.4534474           | 10.71099 |
| Age                           | -0.0634208  | 0.0726223            | 0.383   | -0.2058706          | 0.0790291 |
| Female                        | 2.766286    | 2.07937              | 0.184   | -1.312431           | 6.845003 |
| Race                          |             |                      |         |                     |          |
| African American              | 0.0031588   | 1.631666             | 0.998   | -3.197379           | 3.203697 |
| Hispanic                      | 8.418846    | 6.932309             | 0.225   | -5.178987           | 22.01668 |
| Asian or Pacific Islander     | -2.016921   | 2.891396             | 0.454   | -7.296138           | 3.262295 |
| Native American               | 1.900837    | 3.823703             | 0.619   | -5.599417           | 9.40109 |
| Other                         | -1.705178   | 2.901342             | 0.557   | -7.396207           | 3.985851 |
| Median annual income in patient’s Zip code, US$ (reference 1 - 42,999) | | | | |
| 43,000 - 53,999               | 6.231577    | 2.704804             | 0.021   | 0.9260613           | 11.53709 |
| 54,000 - 70,999               | 1.931953    | 1.933166             | 0.318   | -1.859982           | 5.723888 |
| >71,000                       | 1.742499    | 1.966798             | 0.376   | -2.115406           | 5.600404 |
| Primary Payer( reference Medicare) |             |                      |         |                     |          |
| Medicaid                      | 4.371632    | 3.769085             | 0.246   | -3.021488           | 11.76475 |
| Private                       | -0.7287483  | 2.159272             | 0.736   | -4.964194           | 3.506698 |
| Self-pay                      | -6.573342   | 3.493908             | 0.06    | -13.4267           | 0.280014 |
#### TABLE 3: Result of multivariate linear regression for length of stay

|                | Coef.   | Linearized Std. Err. | P     | [95% Conf. Interval] |
|----------------|---------|----------------------|-------|----------------------|
| **Teaching hospital** |         |                      |       |                      |
| Age            | -1170.897 | 1069.137             | 0.274 | -3268.078 926.2844   |
| Female         | 31963.85  | 31345.08             | 0.306 | -29521.55 93449.26   |
| **Race**       |         |                      |       |                      |
| African American | 8567.286 | 26231.08             | 0.744 | -42886.68 60021.25   |
| Hispanic       | 170854.1  | 111429.1             | 0.125 | -47721.25 389429.4   |
| Asian or Pacific Islander | -51049.28 | 40473.35             | 0.207 | -130440.4 28341.82   |
| Native American | 75253.86  | 63030.33             | 0.233 | -48384.23 198892     |
| Other          | -33001.68 | 37694.12             | 0.381 | -106941.1 40937.78   |

Total hospitalization charges based on the teaching status of the hospital

The median total hospitalization charges were $79,711 and $69,228 for patients admitted to teaching vs. non-teaching hospitals, respectively. With the adjustment of other confounding variables, the total charge in both settings had no significant statistical difference (p=0.097). Patients with the income group in the $43,000 - $53,999 range also showed increased total hospitalization cost in teaching hospitals when compared to non-teaching hospitals (coefficient=117298, p=0.012, 95%CI 26266.84 - 208328.80). Detailed results are summarized in Table 4.
TABLE 4: Result of multivariate linear regression for total hospitalization charges

| Median annual income in patient’s Zip code, US$ (reference 1 - 42,999) | | | | |
|---|---|---|---|---|
| 43,000 - 53,999 | 117297.8 | 46407.32 | 0.012 | 26266.84 | 208328.8 |
| 54,000 - 70,999 | 37797.24 | 32631.09 | 0.247 | -26210.76 | 101805.2 |
| ≥71,000 | 50941.5 | 34978.21 | 0.145 | -17670.53 | 119553.5 |

| Primary Payer (reference Medicare) | | | | |
|---|---|---|---|---|
| Medicaid | 68855.48 | 67385.52 | 0.307 | -63325.58 | 201036.5 |
| Private | -18418.36 | 33716.39 | 0.585 | -84555.25 | 47718.53 |
| Self-pay | -74584.70 | 50477.49 | 0.14 | -173999.6 | 24430.16 |

| Charlson comorbidity score | | | | |
|---|---|---|---|---|
| 1 | 28242.63 | 41859.66 | 0.5 | -53867.8 | 110353.1 |
| 2 | 39060.21 | 38223.52 | 0.307 | -35917.72 | 114038.1 |
| ≥3 | 69719.45 | 50398.13 | 0.167 | -29139.75 | 168578.7 |

| Urban hospitals (reference-rural) | | | | |
|---|---|---|---|---|
| -17705.55 | 57616 | 0.759 | -130723.1 | 95311.98 |

| Hospital region (reference Northeast) | | | | |
|---|---|---|---|---|
| Midwest | -30406.24 | 29218.45 | 0.296 | -87720.12 | 26907.64 |
| South | 28274.62 | 30272.88 | 0.35 | -3107.61 | 87658.84 |
| West | 70030.03 | 60423.75 | 0.247 | -48495.08 | 188555.1 |

| Hospital bed-size (reference small) | | | | |
|---|---|---|---|---|
| Medium | 61012.17 | 44979.45 | 0.175 | -27217.93 | 149242.3 |
| Large | 61100.67 | 35160.51 | 0.082 | -7868.96 | 130070.3 |

**Discussion**

There is limited evidence for the predictors of TH use in out-of-hospital cardiac arrest. The most recent study that was done with this database (2007-2010) and published in 2015 showed an increasing utilization of TH in general from 0.34% in 2007 to 2.49% in 2010 [17].

To the best of our knowledge, our study is the first to compare the outcomes of TH patients based on the teaching status of the hospitals. Several studies in the past have shown low utilization of TH [18-20].

Our study has found a significant increase in the overall utilization of TH to 4.86% (compared to the reported utilization in recent studies), out of which 3.60% were in teaching hospitals. Patients admitted to teaching hospitals were younger (mean age 59 years).

There is no study done to see the effect of the teaching status of hospitals on mortality. Although studies have shown better outcomes in general with the utilization of therapeutic hypothermia [21-23].
Our study has shown that teaching hospital status was not an independent predictor of in-hospital mortality.

There was no effect of race, median income, location, or regional variance on mortality in patients with cardiac arrest who received TH. This signifies that even with limited resources, non-teaching hospitals are doing well regarding the care of one of the sickest categories of patients.

The adjusted length of stay was marginally higher in the teaching status of the hospitals in patient groups that received TH (p=0.021). The literature search has not shown any study commenting on length of stay in patients who received therapeutic hypothermia. Although patients with cardiac arrest seem to stay longer given their level of sickness. This might require further study to identify the underlying causes.

An important factor that we included in our study was the total hospitalization charges as a surrogate to overall resource utilization. We found that there was no statistically significant difference in total hospitalization charges between groups admitted to teaching vs non-teaching facilities who received TH. Although we found higher charges in patients who are in the income group range of $45,000 to $53,999 (p=0.012), even though these groups have no difference in mortality or LOS.

**Limitations**

The limitation of our study is that it is a retrospective cohort study using the NIS dataset, which includes only administrative data. The authors were unable to differentiate between patients with shockable vs. non-shockable rhythms, as proper ICD-10 codes were not available for each type of cardiac arrest. There is no specific ICD 10 for out of hospital cardiac arrests. The AHA statistics showed a total of 550,000 out of hospital cardiac arrests in the year 2016. Our study using these ICD-10 codes showed about 13,000 cases. This discrepancy could be due to the nature of the database we have used in our study. Given it is an administrative database, the difference in coding could be a potential cause of capturing a lower number in this study.

Also, the NIS database has no information regarding details about factors of cardiac arrest variables such as rhythm, bystander cardiopulmonary resuscitation (CPR), location, and witnessed cardiac arrest. We were not able to adjust for these factors.

**Conclusions**

Our study concluded that the teaching status of hospitals does not affect mortality or total hospitalization charges in patients with cardiac arrest who received TH. There was no effect of age, sex, race, insurance provider, or the geographical location of the hospitals on the in-hospital mortality of cardiac arrest patients who received TH. However, the utilization of TH was significantly increased in teaching hospitals. In addition, increased length of stay was found in patients admitted to teaching hospitals. Hospitalization charges were higher in the lower-income group. Further investigations are needed to explore this area of research.

**Appendices**

**Annexure 1**

ICD codes used to identify the study population and procedure

| ICD10-CM codes used to identify cardiac arrest patients | I46.2, I46.8, I46.9 |
| ICD10-CM procedure codes used for therapeutic hypothermia | 6A4Z1ZZ, 6A4Z0ZZ |

**TABLE 5: ICD codes used to identify the study population and procedure**

ICD-10-CM: International Classification of Disease, 10th Revision, Clinical Modification

**Additional Information**

**Disclosures**

**Human subjects:** All authors have confirmed that this study did not involve human participants or tissue.

**Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue.

**Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have
no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**

1. Benjamin E, Muntner P, Alonso A, et al.: Heart disease and stroke statistics—2019 update: a report from the American Heart Association. Circulation. 2019, 5:56-528. [10.1161/CIR.0000000000006569](https://doi.org/10.1161/CIR.0000000000006569)

2. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K: Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med. 2002, 21:557-563. [10.1056/NEJMoa025289](https://doi.org/10.1056/NEJMoa025289)

3. Holzer M, Martens P, Ronie R, et al.: Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. Hypothermia after Cardiac Arrest Study Group. N Engl J Med. 2002, 21:549-556. [10.1056/NEJMoa0212689](https://doi.org/10.1056/NEJMoa0212689)

4. Shankaran S, Laptook AR, Ehrenkranz RA, et al.: Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. N Engl J Med. 2005, 13:1574-1584. [10.1056/NEJMcp050929](https://doi.org/10.1056/NEJMcp050929)

5. Hippocrates: De Vetere Medicina. 460-375 BC. Harvard University Press, Cambridge, Massachusetts; 1925.

6. Nozari A, Safar P, Stezoski SW, et al.: Mild hypothermic cardiopulmonary resuscitation improves outcome after prolonged cardiac arrest in dogs. Crit Care Med. 2004, 32:2110-2116.

7. Hicks SD, DeFranco DB, Callaway CW: Hypothermia during reperfusion after asphyxial cardiac arrest improves functional recovery and selectively alters stress-induced protein expression. J Cereb Blood Flow Metab. 2000, 20:520-530. [10.1079/0143-135X(2000)10-00598](https://doi.org/10.1079/0143-135X(2000)10-00598)

8. de Cruz BJ, Fertig KC, Filiano AJ, Hicks SD, DeFranco DB, Callaway CW: Hypothermic reperfusion after cardiac arrest augments brain-derived neurotrophic factor activation. J Cereb Blood Flow Metab. 2002, 22:843-851. [10.1097/00004647-200207000-00009](https://doi.org/10.1097/00004647-200207000-00009)

9. Benson DW, Williams GR Jr, Spencer FC, Yates AJ: The use of hypothermia after cardiac arrest. Anesth Analg. 1959, 58:423-428.

10. Polderman KH: Mechanisms of action, physiological effects, and complications of hypothermia. Crit Care Med. 2009, 37:186-202.

11. Erecinska M, Thoresen M, Silver IA: Effects of hypothermia on energy metabolism in mammalian central nervous system. J Cereb Blood Flow Metab. 2005, 25:513-530. [10.1079/NBFE.2005.25.7.513](https://doi.org/10.1079/NBFE.2005.25.7.513)

12. Zhao QJ, Zhang XG, Wang LX: Mild hypothermia therapy reduces blood glucose and lactate and improves neurologic outcomes in patients with severe traumatic brain injury. J Crit Care. 2011, 26:511-515. [10.1016/j.jcrc.2010.08.014](https://doi.org/10.1016/j.jcrc.2010.08.014)

13. Nolan JP, Morley PT, Vanden Hoek TL, et al.: Therapeutic hypothermia after cardiac arrest. An advisory statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation. Circulation. 2005, 8:118-121. [10.1161/01.CIR.0000079019.02601.90](https://doi.org/10.1161/01.CIR.0000079019.02601.90)

14. Brooks SC, Morrison LJ: Implementation of therapeutic hypothermia guidelines for post-cardiac arrest syndrome at a glacial pace: seeking guidance from the knowledge translation literature. Resuscitation. 2008, 77:286-292. [10.1016/j.resuscitation.2008.01.017](https://doi.org/10.1016/j.resuscitation.2008.01.017)

15. Papanikolaou PN, Christidi GD, Ioannidis JPA: Patient outcomes with teaching versus non-teaching healthcare: a systematic review. PLoS Med. 2006, 3:541. [10.1371/journal.pmed.0030541](https://doi.org/10.1371/journal.pmed.0030541)

16. Introduction to the HCUP National Inpatient Sample (NIS) 2016. (2018). [https://www.hcup-us.ahrq.gov/db/nation/nis/NIS_Introduction_2016.jsp](https://www.hcup-us.ahrq.gov/db/nation/nis/NIS_Introduction_2016.jsp).

17. Dresden SM, O’Connor LM, Pearce CG, Courtney DM, Powell ES: National trends in the use of postcardiac arrest therapeutic hypothermia and hospital factors influencing its use. Ther Hypothermia Temp Manag. 2015, 5:48-54. [10.1089/ther.2014.0023](https://doi.org/10.1089/ther.2014.0023)

18. Ahella BS, Rhee JW, Huang K-N, Vanden Hoek TL, Becker LB: Induced hypothermia is underused after resuscitation from cardiac arrest: a current practice survey. Resuscitation. 2009, 68:181-186. [10.1016/j.resuscitation.2009.04.014](https://doi.org/10.1016/j.resuscitation.2009.04.014)

19. Merchant RM, Soar J, Skrifvars MB, et al.: Therapeutic hypothermia utilization among physicians after resuscitation from cardiac arrest. Crit Care Med. 2006, 34:1935-1940.

20. Patel PV, John S, Garg RK, Temes RE, Bleck TP, Prabhakaran S: Therapeutic hypothermia after cardiac arrest is underutilized in the United States. Ther Hypothermia Temp Manag. 2011, 1:199-205. [10.1089/ther.2011.0015](https://doi.org/10.1089/ther.2011.0015)

21. Arrich J, Holzer M, Havel C, Müllner M, Herker H: Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation. Cochrane Database Syst Rev. 2016, 15:CD004128. [10.1002/14651858.CD004128.pub2](https://doi.org/10.1002/14651858.CD004128.pub2)

22. Holzer M, Behringer W: Therapeutic hypothermia after cardiac arrest and myocardial infarction. Best Pract Res Clin Anaesthesiol. 2008, 22:711-728. [10.1016/j.bpa.2008.02.001](https://doi.org/10.1016/j.bpa.2008.02.001)

23. Jena AB, Romley JA, Newton-Cheh C, Noseworthy P: Therapeutic hypothermia for cardiac arrest: real-world utilization trends and hospital mortality. J Hosp Med. 2012, 7:684-689. [10.1002/jhm.1974](https://doi.org/10.1002/jhm.1974)