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# Prognostication via early computed tomography head in patients treated with targeted temperature management after cardiac arrest

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ABSTRACT

*Background:* We evaluated computed tomography head (CTH) imaging obtained prior to targeted temperature management (TTM) in patients after cardiac arrest, and its role in prognostication.
*Methods:* In this retrospective cohort study in a tertiary-care hospital, 341 adults presenting with out-of-hospital cardiac arrest received a CTH prior to TTM. Associations between outcomes and neuroimaging variables were evaluated with Chi-square analysis for significant associations that yielded a composite neuroimaging score—Tennessee Early Neuroimaging Score (TENS). Univariable and multivariable logistic regression analysis including TENS as an independent variable and the four outcome dependent variables were analyzed.
*Results:* Four of the neuroimaging variables—sulcal effacement, partial gray-white matter effacement, total gray-white matter effacement, deep nuclei effacement—had significant associations with each of the four outcome variables and yielded TENS. In multivariable logistic regression models adjusted for potential confounders, TENS was associated with poor discharge CPC (OR 2.15, 95%CI 1.16–3.98, $p = .015$), poor disposition (OR 2.62, 95%CI 1.37–5.02, $p = .004$), in-hospital mortality (OR 1.99, 95%CI 1.09–3.62, $p = .024$), and ICU mortality (OR 1.89, 95%CI 1.12–3.20, $p = .018$).
*Conclusion:* Imaging prior to TTM may help identify post-cardiac arrest patients with severe anoxic brain injury and poor outcomes.

## 1. Introduction

Targeted temperature management (TTM) to goal temperature 32–36 °C is the standard-of-care for minimizing anoxic brain injury after cardiac arrest for ventricular fibrillation and ventricular tachycardia [1–3]. However, neuroprognostication and meaningful selection of patients for TTM after cardiac arrest remain unclear. Prior to adoption of hypothermia, good clinical examination after 72 h, shorter duration of pulselessness, ventricular fibrillation or ventricular tachycardia as initial rhythm, witnessed arrest, younger age, and lower admission lactate levels were associated with good neurological outcome [4–7]. Post-TTM studies have utilized multi-modal approaches of exam and ancillary monitoring such as malignant EEG patterns and somatosensory evoked potentials to try to identify salvageable patients [8,9]. But functional recovery after cardiac arrest remains poor [10], and neuroprognostication post-TTM presents new challenges due to increased duration of sedation and suppression of the neurological exam.

The utility and timing of imaging in neuroprognostication for cardiac arrest patients post- TTM remains unclear. The American Academy

*Abbreviations:* CTH, computed tomography head; TTM, targeted temperature management; TENS, Tennessee Early Neuroimaging Score; OR, odds ratio; CI, confidence interval; MRI, magnetic resonance imaging; ROSC, return to spontaneous circulation; GCS, Glasgow Coma Score; SBP, systolic blood pressure; GWME, gray-white matter effacement; CPC, cerebral performance category; ICU, intensive care unit; ROC, receiver operator characteristic; AUC, area under curve; YI, Youden Index; BMI, body mass index

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of Neurology classified the role of neuroimaging in neuroprognostication as inconclusive [7]. Quantitative imaging in computed tomography of the head (CTH) [11–13], magnetic resonance imaging (MRI) [14,15], and combined clinical and imaging parameters have shown promise and improved prognostic sensitivity and specificity [16]. However all of these studies were retrospective and small, while the utility of imaging prior to the initiation of TTM was never investigated.

At our center, we systematically evaluated all patients with cardiac arrest with CTH before initiating TTM. We sought to evaluate the potential association and predictive ability of neuroimaging findings prior to TTM with clinical outcomes in cardiac arrest patients.

## 2. Material and methods

### 2.1. Patient selection and study protocol (standard protocol approvals, registrations, patient consents)

Institutional review board approval was obtained for the retrospective evaluation of a prospectively-collected cohort evaluating clinical outcomes in adult patients with out-of-hospital cardiac arrest who were treated with TTM in a tertiary-level center during the period January 2011 to December 2016. As per hospital policy, all patients undergoing hypothermia after cardiac arrest were prospectively enrolled in a hospital registry. All data was retrospectively reviewed for accuracy by blinded intensivists through review of the medical record (CS, RS, AY, LM, DK, and AS).

We used the following inclusion criteria: initiation of TTM within 6 h of arrest, witnessed or unwitnessed ventricular tachycardia and ventricular fibrillation rhythms (pulseless electrical activity and asystole was included if etiology was presumed to be hypoxic or cardiac and arrest was witnessed), return to spontaneous circulation (ROSC) ≤ 60 min, respiratory failure, Glasgow Coma Score (GCS) ≤ 8 after ROSC, and systolic blood pressure (SBP) ≥ 90 mmHg. Exclusion criteria are listed below: confirmed hemorrhagic stroke, recurrent cardiac arrests prior to initiation of TTM, etiologies for cardiac arrest thought to be secondary (i.e. metabolic pathologies) and not due to cardiac causes, pre-existing do not resuscitate code status, active bleeding, baseline poor functional status (i.e. bedbound, severe dementia, severe deficits at baseline), history of metastatic cancer with presumed very poor prognosis, baseline temperature < 30 °C prior to initiation of TTM, pregnancy, and no imaging present prior to TTM.

Baseline demographics, past medical history, and clinical outcomes—functional outcome, disposition, mortality, vasopressor use, kidney injury, status epilepticus, and infection—were recorded as previously described [17].

TTM was carried out in accordance with established guidelines [18–20]. Surface cooling with goal temperature 32–33 °C was the standard of care followed by strict fever prevention during the post-rewarming phase.

### 2.2. Radiological evaluation

Radiological characterization of CTH findings was rated by three neurologists (JC, NG, KA), who were placed together in a reading room, simultaneously looked at images, and marked down dichotomous results (“yes” vs. “no”) for presence of radiological findings. In cases of disagreement between the three raters, scoring of different neuroimaging variables was based on majority consensus.

Six qualitative radiological findings indicating degree of anoxic brain injury were evaluated: presence of watershed infarcts, sulcal effacement, partial gray-white matter effacement (GWME), total GWME, global cerebral edema, and effacement of deep nuclei. Watershed infarct was defined as the presence of hypodense lesions in watershed territory areas between the anterior cerebral artery-middle cerebral artery and the middle cerebral artery-posterior cerebral artery regions [21]. Sulcal effacement was defined as a > 25% loss of cortical margins either unilaterally or bilaterally at the level of the centrum semiovale [22].

GWME, modified by a protocol delineated by Torbey et al. [11], was defined as a lack of differentiation between gray and white matter at the axial image level of the basal ganglia and centrum semiovale. GWME was further divided into partial GWME (≤75% effacement) and total GWME (> 75% effacement).

Global cerebral edema included sulcal effacement, partial or total GWME, and mass effect into the lateral ventricles or basal cisternal effacement [23]. Effacement of deep nuclei included partial or total GWME and lack of differentiation of either the caudate, putamen, globus pallidus, or thalamus [24].

### 2.3. Clinical outcomes

The following clinical outcomes were evaluated: cerebral performance category (CPC) score at discharge, disposition, in-hospital mortality, and mortality within the intensive care unit (ICU). Discharge CPC score was dichotomized to “good” (score 0–2) or “poor” (score 3–5). Disposition was dichotomized into “good” (home or rehab) or “poor” (skilled nursing facility, long-term ventilator wean facility, hospice, or death). Palliative withdrawal of care was grouped with death in mortality outcomes.

### 2.4. Statistical analysis

Cohen's kappa and percent agreement was used to evaluate inter-rater reliability between three neurologists (JC, NG, KA) for each of the six neuroimaging variables. Associations between the six neuroimaging variables and four clinical outcome variables were evaluated via Chi-square analysis. Neuroimaging variables that yielded significant associations were combined to create a composite neuroimaging score, The Tennessee Early Neuroimaging Score (TENS). Receiver operator characteristic (ROC) curves were then calculated to evaluate the predictive value of TENS via area under curve (AUC). Afterwards, the Youden Index (YI) [25,26] was used to determine the optimal cut-off points for each of the four outcome measures. The Youden Index is a method that summarizes the performance of a diagnostic test for a dichotomous result, which is based on the equal weighting of sensitivity and specificity and allows selecting the maximum value as the criterion for optimum cut-off points.

Univariable and multivariable logistic regression analyses were used to determine independent predictors for the four clinical outcome variables. A $p$ value < .1 was selected as a cut-off in univariable logistic regression analysis for inclusion of candidate variables in multivariable logistic regression models. Predictor variables were significant if $p < .05$ was retained in the multivariable model. Associations were presented as OR with corresponding 95% CIs. All multivariable logistic regression analyses were conducted using the Wald backward selection procedure. The Statistical Package for Social Science (version 23.0 for Windows; SPSS Inc., Chicago, IL) was used for statistical analyses.

### 2.5. Data availability statement

De-identified participant data, study protocol, and statistical analysis plan can be shared by request from any qualified investigator by contacting the corresponding author.

## 3. Results

We identified a total of 646 patients with out-of-hospital cardiac arrest who were referred to our center during January 2011–December 2016. Of these, 155 patients died prior to our evaluation. Of the 491 patients evaluated, we identified a total of 389 patients treated with TTM following cardiac arrest during the study period. Of these, 341 patients received CTHs prior to TTM and were analyzed. Baseline

**Table 1**
Baseline characteristics of patients treated with therapeutic hypothermia after cardiac arrest.

| Variable | *n* = 341 |
|---|---|
| Mean age (years, SD) | 60 (14) |
| Female gender, *n* (%) | 192 (56) |
| Race | |
| White, *n* (%) | 92 (27) |
| Black, *n* (%) | 233 (68) |
| Hispanic, *n* (%) | 3 (1) |
| Asian, *n* (%) | 1 (0) |
| Other, *n* (%) | 5 (2) |
| Missing, *n* (%) | 7 (2) |
| Witnessed arrest, *n* (%) | 303 (89) |
| Initial rhythm | |
| Ventricular fibrillation, *n* (%) | 172 (50) |
| Ventricular tachycardia, *n* (%) | 22 (7) |
| Pulseless electrical activity, *n* (%) | 90 (26) |
| Asystole, *n* (%) | 57 (17) |
| Mean cardiopulmonary resuscitation time (min, SD) | 19 (11) |
| Additional in-hospital cardiac arrest, *n* (%) | 83 (24) |
| Median Body Mass Index (IQR) | 28 (24–34) |
| Diabetes mellitus, *n* (%) | 131 (38) |
| Coronary artery disease, *n* (%) | 183 (54) |
| End-stage renal disease, *n* (%) | 34 (10) |
| Hyperlipidemia, *n* (%) | 170 (50) |
| Current smoker, *n* (%) | 75 (22) |
| Median glasgow coma scale on admission (IQR) | 3 (3–3) |

**Table 2**
Outcomes in patients treated with therapeutic hypothermia after cardiac arrest.

| Variable | *n* = 341 |
|---|---|
| Organ injury | |
| Acute kidney injury, *n* (%) | 182 (53) |
| Pneumonia, *n* (%) | 44 (13) |
| Status epilepticus, *n* (%) | 55 (16) |
| Lactic acidosis, *n* (%) | 239 (70) |
| Vasopressor use, *n* (%) | 159 (47) |
| Norepinephrine, *n* (%) | 140 (41) |
| Dopamine, *n* (%) | 29 (9) |
| Dobutamine, *n* (%) | 38 (11) |
| Phenylephrine, *n* (%) | 7 (2) |
| Clinical outcomes | |
| Median CPC[a] score (IQR) | 5 (1–5) |
| Poor CPC[a] score, *n* (%) | 231 (68) |
| Hospital mortality, *n* (%) | 219 (64) |
| Mortality in intensive care unit, *n* (%) | 175 (51) |
| Palliative withdrawal of care, *n* (%) | 176 (52) |
| Poor disposition [b], *n* (%) | 239 (70) |

[a] CPC = cerebral performance category scale. Poor CPC = scores 3–5.
[b] poor disposition = placement in skilled nursing facility, hospice, or death.

characteristics of our study population are displayed in Table 1. Outcomes including end-organ injury, patients requiring vasopressors, and final clinical outcomes (as designated by CPC scores, disposition, and mortality) are included in Table 2. Using our exclusion criteria, we excluded 150 patients from analysis (Fig. 1).

Inter-rater agreement for the six imaging parameters is shown in Table 3. Moderate agreement between the three neurologists was noted with Cohen's kappa values ranging between 0.42 and 0.64 and percent agreement ranging between 0.77 and 0.97. Associations between the six imaging parameters, TENS as a categorical variable, dichotomized TENS (dichotomized to 0 vs. 1–4 and 0–1 vs. 2–4), and the four outcome variables are shown in Tables s1–2. Table 4 summarizes these associations. Watershed infarct and global cerebral edema were not associated with any of the four outcome variables. The other four neuroimaging variables were related to poor clinical outcome, bad disposition, in-hospital mortality, and ICU mortality ($p < .05$).

These four neuroimaging variables (sulcal effacement, partial GWME, total GWME, and deep nuclei effacement) comprised TENS and ranged between 0 and 4 (1 point for each positive variable). Two types of TENS dichotomizations were evaluated: TENS > 0 (score 0 vs. 1–4) and TENS > 1 (score 0–1 vs. 2–4). TENS > 0 and TENS > 1 were compared to the four outcome variables. TENS > 0 had the strongest association with clinical outcomes as noted by Youden Indexes (poor clinical outcome: YI = 0.17, poor disposition: YI = 0.19, in-hospital mortality: YI = 0.18, ICU mortality: YI = 0.16) and lower *p*-values for in-hospital mortality and ICU-mortality (Table 4). TENS > 0 was used as the optimal cut-off for TENS dichotomization in subsequent analyses. When evaluated against the four types of clinical outcome, increasing TENS was associated with lower sensitivity, but higher specificity and positive predictive value for poor clinical outcome, poor disposition, in-hospital mortality, and ICU mortality, respectively (Table s3).

ROC curves evaluating the predictive ability of TENS appeared adequate for poor clinical outcome (AUC 0.60, 95%CI 0.54–0.66; Fig. s1), bad disposition (AUC 0.61, 95%CI 0.54–0.67, Fig. s2), in-hospital mortality (AUC 0.59, 95%CI 0.53–0.65, Fig. s3), and ICU mortality (AUC 0.59, 95%CI 0.53–0.65, Fig. s4).

Table 5 depicts associations between baseline characteristics, including TENS > 0, and poor clinical outcome in univariable and multivariable logistic regression models. The following variables were associated ($p < .1$) with poor clinical outcome in univariable analyses: TENS > 0, age, body mass index (BMI), lactic acidosis, diabetes, hyperlipidemia, and admission Glasgow coma scale (GCS). TENS > 0 (OR 2.15, 95%CI 1.16–3.98, $p = .015$), lactic acidosis present at admission (OR 4.20, 95%CI 2.25–7.84, $p < .001$), and lower admission GCS (OR 0.43, 95%CI 0.27–0.69, $p < .001$) were independently associated with higher odds of poor clinical outcome in multivariable logistic regression analyses.

Table s4 depicts associations between baseline characteristics and TENS > 0 and poor disposition in univariable and multivariable logistic regression models. The following variables were associated ($p < .1$) with poor disposition in univariable analyses: TENS > 0, age, body mass index (BMI), lactic acidosis, diabetes, hyperlipidemia, and admission GCS. TENS > 0 (OR 2.62, 95%CI 1.37–5.02, $p = .004$), lactic acidosis (OR 4.71, 95%CI 2.48–8.94, $p < .001$), diabetes (OR 2.14, 95%CI 1.09–4.22, $p = .028$), and lower admission GCS (OR 0.40, 95%CI 0.25–0.66, $p < .001$) were independently associated with higher odds of bad disposition in multivariable logistic regression analyses.

TENS > 0 remained independently associated with both in-hospital mortality (OR 1.99, 95%CI 1.09–3.62, $p = .024$) and ICU mortality (OR 1.89, 95%CI 1.12–3.20, $p = .018$) in multivariable logistic regression analysis (Tables s5, s6). All multivariable logistic regression analyses were performed with both forward and backward selection procedures that obtained identical results.

## 4. Discussion

This is the largest study to systematically evaluate early neuroimaging findings from CTH (prior to TTM initiation) for neuroprognostication in a cohort of patients with out-of-hospital cardiac arrest who also all received TTM. Other studies have included analysis of early head imaging (under 24 h) in patients after cardiac arrest, but evaluated clinical outcomes in patient populations that did not uniformly receive TTM [13,22,27,28]. One study evaluated gray-white matter ratios in out-of-hospital cardiac arrest patients who received TTM, however, only evaluated 51 patients after various exclusion criteria [29].

We evaluated six neuroimaging parameters for detection of anoxic brain damage in CTH but found that only sulcal effacement, partial GWME, total GWME, and deep nuclei effacement were associated with clinical outcomes. By combining these neuroimaging markers into a composite imaging score TENS, we identified independent associations

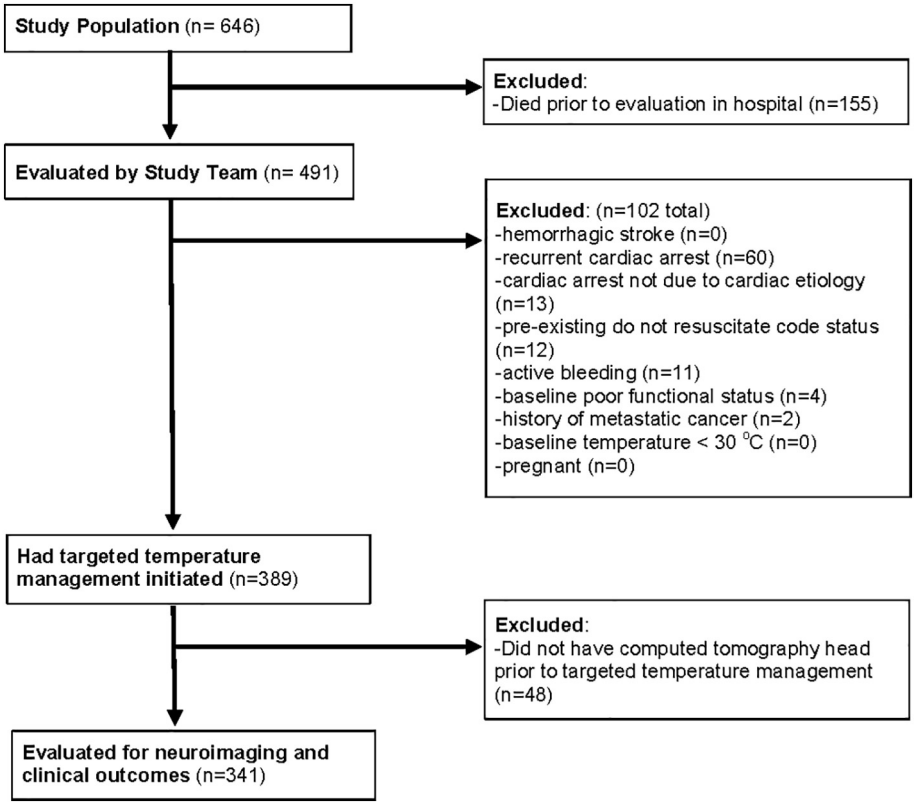


**Fig. 1.** Initial study population and number excluded from analysis.

**Table 3**
Inter-rater agreement between neurologists for interpretation of computed tomography head using Cohen's kappa and percent agreement.

| | Cohen's kappa | Percent agreement |
|---|---|---|
| Watershed infarct | 0.43 | 0.82 |
| Sulcal effacement | 0.46 | 0.79 |
| Partial gray-white matter effacement | 0.42 | 0.77 |
| Total gray-white matter effacement | 0.64 | 0.97 |
| Global cerebral edema[a] | n/a | 0.95 |
| Deep nuclei damage | 0.43 | 0.81 |

[a] Cohen's kappa value could not be evaluated for global cerebral edema due to low numbers for agreement that resulted in an undefined value.

of TENS in multivariable logistic regression models with four markers of clinical outcome: functional outcome, disposition, in-hospital mortality, and ICU mortality.

Our observation that the presence of watershed infarcts and global cerebral edema (suggesting an advanced state of anoxic brain injury) did not correlate with markers of clinical outcome was initially surprising. This finding is also surprising given that total GWME—another marker of advanced anoxic brain injury—did have significant associations with poor clinical outcomes. We reason that global cerebral edema may represent a somewhat more advanced and late-stage anoxic state than total GWME. In our study, global cerebral edema may have been subject to false negatives because of the early period with which CTHs were obtained. Watershed infarcts may have also had false-negatives because of the lower sensitivity of CTH compared to MRI for detecting subtle ischemia in watershed zones.

Of the neuroimaging variables that we evaluated, GWME has been studied most extensively because it is readily quantifiable with lower ratios being associated with worse outcomes [11,12,29]. Although global cerebral edema, sulcal effacement, and effacement of deep nuclei have not been studied in a quantitative manner, their presence can be inferred by GWME as GWME are completed at the level of the centrum

**Table 4**
Summary of associations of neuroimaging parameters with clinical outcomes in patients treated with therapeutic hypothermia after cardiac arrest.

| Neuroimaging variable | *n* (%) | Poor clinical outcome | Poor disposition | In-hospital mortality | Intensive care unit mortality |
|---|---|---|---|---|---|
| Watershed infarct | 35 (10) | X | X | X | X |
| Sulcal effacement | 117 (34) | √ | √ | √ | √√ |
| Partial gray-white matter effacement | 80 (24) | √√ | √√ | √ | √ |
| Total gray-white matter effacement | 15 (4) | √ | √ | √ | √√ |
| Global cerebral edema | 28 (8) | X | X | X | X |
| Deep nuclei effacement | 41 (12) | √√ | √√ | √ | √ |
| TENS[a] | n/a | √√[b] | √√√[b] | √√[b] | √√[b] |
| TENS[a] > 0 | 131 (38) | √√ | √√ | √√ | √√ |
| TENS[a] > 1 | 67 (20) | √√ | √√ | √ | X |

X: no association; √: $p < .05$; √√: $p < .01$; √√√: $p < .001$.

[a] TENS = Tennessee Early Neuroimaging Score. TENS = sum of 4 neuroimaging variables with significant associations (sulcal effacement, partial gray-white matter effacement, total gray-white matter effacement, deep nuclei effacement). Range 0–4.

[b] linear-by-linear association.

**Table 5**
Univariable and multivariable logistic regression analyses depicting associations between baseline characteristics[a] and poor clinical outcome[b].

| Variable | Poor clinical outcome[b] | | | |
|---|---|---|---|---|
| | Univariable logistic regression analysis | | Multivariable logistic regression analysis | |
| | Odds ratio (95%CI) | $p$[c] | Odds ratio (95%CI) | $p$ |
| TENS[a] > 0 | 2.08 (1.26–3.41) | 0.004 | 2.15 (1.16–3.98) | 0.015 |
| Age | 1.02 (1.00–1.03) | 0.036 | 1.02 (0.99–1.04) | 0.16 |
| Gender | 0.68 (0.43–1.08) | 0.100 | | |
| Race | 1.09 (0.80–1.50) | 0.580 | | |
| Body mass index | 1.04 (1.01–1.07) | 0.015 | 1.03 (0.99–1.07) | 0.11 |
| Lactic acidosis | 5.42 (3.18–9.25) | < 0.001 | 4.20 (2.25–7.84) | < 0.001 |
| Diabetes mellitus | 2.47 (1.50–4.09) | < 0.001 | 1.80 (0.95–3.44) | 0.073 |
| Coronary artery disease | 1.33 (0.84–2.11) | 0.220 | | |
| End-stage renal disease | 1.95 (0.82–4.62) | 0.130 | | |
| Hyperlipidemia | 1.84 (1.16–2.93) | 0.010 | 1.67 (0.91–3.06) | 0.10 |
| Current smoker | 1.13 (0.65–1.98) | 0.670 | | |
| Glasgow coma scale admission | 0.39 (0.26–0.59) | < 0.001 | 0.43 (0.27–0.69) | < 0.001 |

[a] Neuroimaging based on TENS (Tennessee Early Neuroimaging Score).
[b] Poor clinical outcome based on dichotomized CPC score (scores 3–5).
[c] Cutoff of $p < .1$ in univariate logistic regression analysis was used for selection of candidate variables in multivariable logistic regression models.

semiovale, vertex, and basal ganglia, respectively [11]. However, our findings support that these neuroimaging variables warrant their own standardization and should not simply be regarded as sequela of GWME. For instance, in our definition of global cerebral edema, mass-effect involving the lateral ventricles and/or basal cisterns was essential. Similarly, our definition for sulcal effacement and deep nuclei effacement was potentially more sensitive but less specific than a definition that simply reflected GWME as both of these neuroimaging variables did not necessarily need to be homogeneously and diffusely spread over the entire brain. The presence of anoxic brain injury with watershed zone ischemia after cardiac arrest has been explored using MRI, however, the presence of anoxic injury was defined using quantitative diffusion weighted imaging over the gross brain [14] rather than targeting specific watershed territories as we did.

While quantitative analysis of GWME and obtaining an MRI before initiation of hypothermia may offer better sensitivity for detecting anoxic brain injury, the post-processing time and longer duration of the scan, respectively, may hinder the practicality of using these imaging modalities to prognosticate before initiating TTM. TENS as described in this paper has potential utility because of the time efficiency in obtaining a CTH and applying this score. While a TENS > 0 alludes to potential poor outcome, the positive predictive value is not sufficient to abort TTM. However, as demonstrated in our sensitivity/specificity analyses for the outcome variables (supplemental Table S3), patients who accumulate radiographic abnormalities (TENS > 3) although having low sensitivities, have extremely high likelihoods of having poor outcomes. Combining early imaging with other real-time ancillary monitoring [30–33], may offer clinicians insight into earlier neuroprognostication.

### 4.1. Limitations

This study has several limitations. First, we ignored certain markers associated with poor outcome in TTM after cardiac arrest in our logistic regression analyses. These variables included the presence of shockable versus non-shockable rhythms as the etiology of the cardiac arrest and duration of the cardiac arrest before return of spontaneous circulation. However, we chose this route because as we were primarily targeting imaging evaluation in this study, we believed that the severity of anoxic brain injury due to the duration of pulselessness and associated rhythm would have ultimately been reflected in the CTH obtained before TTM. In addition due to limitations in sample collection as well as lack of wide-spread use, our center did not consistently obtain neuron specific enolase (NSE) samples for assistance in neuroprognostication. However, it should be noted that although several recent studies have shown promising results for NSE and neuroprognostication [34,35], utility of NSE only reaches class IIb evidence in recent guidelines [18].

Second, the in-hospital mortality reflected in our study (64%) was much higher than previously reported gold-standard studies (48% as reported in Nielsen et al. [3]). We surmise that this can be explained by the epidemiology of our studied population—the stroke belt in the United States—where population is skewed towards having more metabolic risk factors [36] and higher age-adjusted death rates compared to other parts of the developed world [37]. A comparison of chronic illnesses noted in our cohort versus those published in Nielsen et al. [3] or Hypothermia after Cardiac Arrest group [1]) would appear to support this, although this may mitigate the generalizability of our study.

Third, this is a retrospective study and therefore, subject to bias. However, management and data was collected in a prospective registry by ICU physicians, while imaging was retrospectively reviewed and graded by neurologists who were blinded to patient outcome. Fourth, although not specific to our study, the radiographic terminology for our six neuroimaging parameters is generally imprecise, which is reflected by the modest inter-rater agreement in scoring individual components of TENS. We attempted to rectify this by precisely defining these terms as outlined in our methodology to avoid any overlap between the terms. Overall limitations due to imprecise terminology may also have resulted in the modest accuracy for TENS predicting clinical outcomes (supplemental Figs. S1–4). Future studies may improve on inter-rater agreement and neuroprognostication by continuing to homogenize a consensus agreement on these radiological terms and further identifying particular regions of the brain [38] when dealing with radiological variables such as global cerebral edema and sulcal effacement.

Fifth, the diagnostic accuracy of TENS was only tested in our derivation cohort and must be prospectively validated. Sixth, as TENS is a qualitative evaluation by trained neurointensivists, the universal application of this scoring system may be more variable than a purely quantitative tool and requires prospective validation.

Seventh, patients who were palliatively withdrawn from supportive measures by their decision-makers were classified as “positive” for death or poor outcome in the dichotomized clinical outcomes. This would have introduced bias as potential patients who may have survived would have now been associated with a mortality. In fact 176 of our 341 patients had palliative withdrawal of supportive measures. However, of the patients who were palliatively withdrawn, mean and median length of stay were 7.4 and 7.0 days, respectively, so one could surmise that the majority of these patients were palliatively withdrawn by their decision-makers because of a lack of improvement in

neurological status.

## 5. Conclusion

Selection of appropriate patients, overall outcomes, and neuroprognostication after cardiac arrest remains poor. TTM to a target temperature of 32–36 °C after cardiac arrest represents a labor and resource-intensive process. Obtaining imaging prior to initiation of TTM may allow for improved neuroprognostication. Imaging criteria as delineated by TENS will require prospective validation.

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None.

## Author contributions

Dr. Chang: study concept and design, acquisition of data, analysis and interpretation, manuscript writing, critical revision of manuscript for important intellectual content, and takes responsibility for the paper as a whole.

Dr. Tsivgoulis: study concept and design, analysis and interpretation, critical revision of manuscript for important intellectual content.

Dr. Goyal: study concept and design, acquisition of data, critical revision of manuscript for important intellectual content.

Dr. Alsherbini: study concept and design, acquisition of data, critical revision of manuscript for important intellectual content.

Dr. Schuring: acquisition of data, critical revision of manuscript for important intellectual content.

Dr. Shrestha: acquisition of data, critical revision of manuscript for important intellectual content.

Dr. Yankovich: acquisition of data, critical revision of manuscript for important intellectual content.

Dr. Metter: analysis and interpretation, critical revision of manuscript for important intellectual content.

Dr. Sareen: acquisition of data, critical revision of manuscript for important intellectual content.

Dr. Elijovich: critical revision of manuscript for important intellectual content.

Dr. Malkoff: critical revision of manuscript for important intellectual content.

Dr. Murillo: critical revision of manuscript for important intellectual content.

Dr. Kadaria: critical revision of manuscript for important intellectual content.

Dr. Alexandrov: critical revision of manuscript for important intellectual content.

Dr. Sodhi: acquisition of data, critical revision of manuscript for important intellectual content.

## Declaration of Competing Interest

None.

## Acknowledgements

None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jns.2019.116437.

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