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Intubation is not a marker for coma after in-hospital cardiac arrest: a retrospective study

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Abstract

Introduction—In-hospital cardiac arrest (IHCA) strikes over 200,000 people in the United States annually. Targeted temperature management (TTM) is considered beneficial in other settings, but there is no prospective data for IHCA. Recent work on TTM and IHCA found an association between TTM and worse outcome. However, the authors used intubation as a marker for coma to determine eligibility for TTM. The validity of this approach is unexplored.

Methods—Retrospective, single center study of adult patients with IHCA occurring in an intensive care unit, intubated prior to or during the event, or immediately after ROSC. We evaluated the percentage of patients documented as comatose after arrest, defined as Glasgow Coma Score (GCS) < 8 for the primary analysis. We also evaluated the difference in hospital survival in patients with GCS < 8 versus ≥ 8. Two sensitivity analyses using different methods for defining coma using post-ROSC GCS were conducted.

Results—29/102 (28%) intubated patients had a post-ROSC GCS ≥ 8, and 22 (22%) were documented as following commands. Survival in patients with GCS ≥ 8 vs. <8 was 62% (18/29) vs. 37% (27/73) in unadjusted analysis (p=0.02). The adjusted odds ratio for survival to hospital discharge was 3.81 (95%CI: 1.37–10.61, p=0.01). Results were similar in both sensitivity analyses.

Conclusions—Intubation prior to or during IHCA was not a valid marker of coma after ROSC. Post-ROSC mental status was associated with hospital survival, and thus could be an important confounder when conducting observational studies on the association of TTM with outcomes in this patient population.

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Introduction

In-hospital cardiac arrest (IHCA) strikes over 200,000 people yearly in the United States, with 75% mortality.¹ Little research exists on treatments², including targeted temperature management (TTM), which has only been studied prospectively in out of hospital cardiac arrest (OHCA).^{3–5} Based on randomized controlled trials in the OHCA population, TTM is currently recommended for patients with OHCA who remain comatose after return of spontaneous circulation (ROSC). TTM is also suggested for patients who achieve ROSC but remain comatose after IHCA, but this suggestion is based entirely on observational studies and extrapolation from studies in OHCA.^{6,7}

A recent study utilizing a large national IHCA database evaluated the association of TTM with hospital mortality and found an association with worse outcome.⁸ However, the analysis was limited by a lack of data on coma immediately after arrest. Accurate assessment of coma after arrest is important, as being comatose after ROSC has long been thought to be associated with a worse prognosis.⁹ TTM is also only indicated in patients who are comatose after arrest. Therefore, in a retrospective study, a group not treated with TTM is more likely to include patients who were not comatose after ROSC unless they are specifically excluded. This could lead to lower survival in the group receiving TTM being incorrectly attributed to the treatment, when in fact this association was caused by a higher prevalence of coma. To compensate for the lack of information on coma, the authors of the aforementioned study used intubation, either at the time of or after the arrest, as a marker for coma. The authors reasoned that all but a very small number of patients who were intubated would be comatose.

In this brief report, we evaluated that assumption. We hypothesized that a substantial number of patients who were intubated at the time of or immediately after arrest would not be comatose after ROSC. We also hypothesized that post-arrest coma would be associated with hospital mortality, serving as a potential confounder in an analysis of the association of TTM with outcome in this population.

Methods

This single center, retrospective analysis was approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations. All patients who obtained ROSC for at least 20 minutes after IHCA occurring in an intensive care unit (ICU) from 2010–2016 were screened. Only patients intubated before or during the arrest or immediately after ROSC were included. Descriptive statistics were used to compare baseline characteristics including age, initial rhythm, and downtime (defined as time from recognition of arrest to time of ROSC). Categorical variables were reported as numeric values and percentages, and continuous variables as means or medians, depending on the normality of the data. The primary outcome was the proportion of patients not comatose immediately after arrest, as determined by a Glasgow Coma Score (GCS) ≥ 8 . GCS is routinely entered by nursing every 4 hours in our ICU's. The secondary outcome was the unadjusted difference in survival to hospital discharge in patients with GCS ≥ 8 compared to <8 after ROSC, determined by a Chi-square test. We then used multivariate logistic regression to assess the association of

survival with post-arrest GCS, adjusting for age, initial rhythm, downtime, and whether TTM was used. The GCS cutoff of 8 was chosen a priori based on clinical experience. As there is no defined GCS cutoff between coma and non-coma, we also ran logistic regressions (1) using a Glasgow Motor Score of 6 or documentation of following commands to indicate that a patient was not comatose and (2) using post-ROSC GCS as a continuous variable as sensitivity analyses.

Results

We found 108 ICU patients who either had a documented IHCA while intubated or were intubated during or immediately following the IHCA event. Six were excluded because their post-arrest GCS was unable to be determined. Of the remaining 102 patients, 29 (28%) had a post-ROSC GCS ≥ 8 , and 22 (22%) were specifically noted to be following commands. Baseline characteristics of patients with GCS ≥ 8 and <8 are included in Table 1. Survival to hospital discharge in patients with GCS ≥ 8 and <8 was 62% (18/29) and 37% (27/73) in unadjusted analysis ($p=0.02$). (Figure 1) After adjustment for age, downtime, initial rhythm and TTM, the association of GCS with outcome persisted, with an adjusted odds ratio (aOR) for survival to hospital discharge of 3.81 (95% CI: 1.37–10.61), $p=0.01$. In sensitivity analyses, the combined category of a Glasgow Motor Score of 6 or documentation of a patient following commands was associated with an aOR of 2.32 (95% CI: 0.83–6.48), $p=0.108$. As a continuous variable, GCS was associated with an aOR of 1.17 (95% CI: 1.03–1.34), $p=0.020$ per unit increase in GCS.

Discussion

We found intubation before or during an IHCA event was not a valid marker of being comatose after ROSC. This method resulted in a substantial percentage of patients being misclassified as comatose. Patients with higher GCS after ROSC were also more likely to survive to hospital discharge. Patients should only be treated with TTM if they are comatose after ROSC. Therefore, our study suggests that using intubated post-IHCA patients as a proxy for a comatose post-arrest population could lead to an overinflated survival rate in the no-TTM group, driven by the misclassification of non-comatose patients as comatose.

IHCA outcomes have improved over the past decade, but mortality and morbidity remain extremely high.¹ In spite of this, IHCA is relatively under-studied compared to sepsis, stroke, acute myocardial infarction, and even OHCA.^{2,10} Including the recent publication by Chan et al, we are aware of four observational studies and no randomized trials evaluating the association between TTM and outcome after IHCA.^{8,11–13} The largest studies, finding no effect or an association with harm, were not able to include whether post-ROSC coma was present.^{8,12} The remaining two studies excluded patients who were documented as following commands and found an association with improved outcome with TTM, but had other limitations.^{11,13}

In 2015, the International Liaison Committee on Resuscitation (ILCOR) conducted an extensive evidence review on the use of TTM for cardiac arrest, including IHCA. Only one study met the criteria for consideration in that review, and that study was graded as very low

quality evidence. Due to evidence for TTM after cardiac arrest in other settings however, both ILCOR and the American Heart Association continue to suggest the use of TTM for patients who are comatose after IHCA.⁶ Our illustration of the importance of post-ROSC coma when evaluating outcome, and the fact that this information is absent in many large registry databases, emphasizes the importance of not changing practice based on inconclusive observational data. Instead, randomized trials or more granular registry data may be required before we can effectively evaluate whether TTM is beneficial after IHCA.

Our study was limited by its retrospective single-center design and small size. Due to the small number of patients we were unable to adjust for all variables that could also influence GCS and outcome. We included only ICU patients, which is distinct from the prior study by Chan et al. We were also limited by the lack of an established cutoff using GCS that reliably separates comatose and non-comatose patients, a limitation we attempted to mitigate with our sensitivity analyses.

Conclusions

Intubation was not a reliable marker of post-ROSC coma in our population of IHCA occurring in the ICU. Post-ROSC coma may be associated with outcome, and thus is a potential confounder in observational studies of treatments such as TTM. Caution should be used in interpreting results of studies unable to account for post-ROSC coma.

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Survival to Hospital Discharge by Glasgow Coma Score (GCS)

Figure 1.
Hospital survival by Glasgow Coma Score

Table 1

baseline characteristics

	Glasgow Coma Scale <8 n=73	Glasgow Coma Scale 8 n=29	p-value
Age (median years [IQR])	70 [57, 78]	69 [65, 75]	0.724
Male, n(%)	49 (67)	16 (55)	0.257
Initial Rhythm, n(%) [*]			
Asystole	12 (17)	5 (18)	
Pulseless Electrical Activity	48 (67)	10 (36)	0.006
Ventricular Fibrillation/Ventricular Tachycardia	12 (17)	13 (46)	
Arrest downtime (median minutes [IQR]) ^{**}	9 [4, 17]	8 [4, 18]	0.805
Treatment with TTM, n(%)	16 (22)	4 (14)	0.419

^{*} two patients do not have a documented initial rhythm

^{**} three patients do not have a documented arrest downtime