



## Clinical paper

Neurologic consultation and use of therapeutic hypothermia for cardiac arrest<sup>☆</sup>Elan L. Guterman<sup>a,\*</sup>, Anthony S. Kim<sup>a,b</sup>, S. Andrew Josephson<sup>a,c</sup><sup>a</sup> Department of Neurology, University of California, San Francisco, CA, United States<sup>b</sup> 675 Nelson Rising Lane, San Francisco, CA 94158, United States<sup>c</sup> 505 Parnassus Avenue, Box 0114, San Francisco, CA, 94143, United States

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## ABSTRACT

**Objective:** To determine whether neurologic consultation influences the use of therapeutic hypothermia. **Methods:** We identified adult patients treated for cardiac arrest from October 2009 through September 2015 at 149 academic medical centers and their affiliate hospitals using discharge diagnosis codes in Vizient database. Neurology consultation was defined as a neurologist participating in patient care at any point during the hospitalization. Use of therapeutic hypothermia was identified using procedure codes. We used multivariable models to evaluate the association between neurologic consultation and therapeutic hypothermia before and after adjustment for patient baseline characteristics and hospital factors including inpatient volume and relative volume of cardiac arrest cases.

**Results:** We identified 136,830 hospitalizations for cardiac arrest. The 9,336 (6.8%) encounters involving a neurologist had higher severity of illness, longer hospital stay, and longer intensive care unit stay. There were 5,034 (3.7%) encounters where patients underwent therapeutic hypothermia. Hypothermia use was significantly more common when neurologists were involved during hospitalization (7.9% vs. 3.4%; OR 2.44, 95% CI 2.2–2.6;  $p < 0.01$ ). After adjustment, neurologic consultation continued to be associated with the use of therapeutic hypothermia (adjusted OR 2.5, 95% CI 2.3–2.8), particularly among hospitals in the highest quartile of total inpatient volume (OR 4.6, 95% CI 4.0–5.3). Lower in-hospital mortality was also associated with neurological consultation after adjusting for therapeutic hypothermia (59.2% vs. 61.3%,  $p < 0.01$ ).

**Conclusions:** The involvement of a neurologist in cardiac arrest patients is associated with increased use of therapeutic hypothermia, though therapeutic hypothermia for cardiac arrest likely remains underutilized.

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## Introduction

Cardiac arrest remains a major source of death and neurologic disability [1]. Heart disease is the leading cause of mortality and underlies 1 in 4 deaths in the United States [2,3]. An estimated 50% of coronary artery disease-related deaths are caused by sudden cardiac arrest [4,5]. Although cardiac arrest outcomes have improved, survival is still under 10% [6–9]. Of those who survive, the major-

ity are left neurologically debilitated, so optimizing the neurologic care of patients with cardiac arrest remains a priority [10].

Resuscitation guidelines for post-cardiac arrest care state that patients with coma after cardiac arrest should be transported to a hospital with advanced neurological care and undergo mild hypothermia to maintain a temperature between 32 and 36° Celsius for at least 24 hours [11]. Therapeutic hypothermia is the only intervention shown to improve neurologic outcomes among patients with cardiac arrest [12–15]. Additional neurological management of anoxic brain injury can include seizure management and clarifying prognosis [11].

Therapeutic hypothermia is underutilized despite proven benefits on overall mortality and neurologic outcomes as well as multiple efforts to increase rates using hospital-based protocols, provider education, and regional initiatives [16–20]. The use of other guideline-concordant neurological care is largely unknown including the frequency and availability of EEG monitoring [11].

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Whether involving neurological specialists influences the rate of guideline-based therapeutic hypothermia initiation is also unexplored. We identified a large nationally-representative cohort of patients to study neurologic consultation in the management of cardiac arrest patients and its impact on the use of therapeutic hypothermia.

## Methods

### Design and study cohort

We used Vizient's (formerly University HealthSystem Consortium [UHC]) Clinical Data Base/Resource Manager™ to identify all patients hospitalized for cardiac arrest from October 2009 through September 2015 at the 149 hospitals in the United States that continuously participated in Vizient's Clinical Data Base/Resource Manager™ during the study period. Vizient is a national administrative claims database that provides extracted patient data from nearly 300 academic medical centers and affiliated hospitals.

We identified hospitalizations for adult patients aged 18 years or older with a discharge diagnosis code for cardiac arrest (*International Classification of Disease*, 9th revision [ICD-9] 427.5) as previously described, which includes both out-of-hospital and in-hospital cardiac arrests [9,21]. The sensitivity of ICD-9 coding for identifying cardiac arrest is debated but the largest validation cohort of Medicare beneficiaries suggests a positive predictive value of approximately 80% for inpatient claims [22]. While Vizient data is not validated for cardiac arrest specifically, prior studies have validated subsets of Vizient data with an institutional medical record, showing concordance in patient age, gender, length of stay, and 30-day readmission rates [23]. By identifying hospital encounters rather than unique patients, individuals with multiple cardiac arrests during the study period are included in our analysis multiple times; however, it is unlikely that many patients were hospitalized more than once for cardiac arrest and prior therapeutic hypothermia should not impact hypothermia eligibility going forward. We excluded cases where age, sex, and severity of illness were unknown. We excluded hospitalizations longer than one year because these cases more likely reflect long-term care rather than acute inpatient stays. We also excluded cases that Vizient flagged for bad data (Fig. 1).

### Study approval

The study was approved by the University of California, San Francisco Committee on Human Research.

### Variables

Patient age, sex, race, severity of illness, discharge disposition, and discharge year were incorporated into all multivariable models. Severity of illness is a measure of physiologic decompensation and degree of organ dysfunction. The four levels of severity (minor, moderate, major, and extreme) are correlated with resource use [24]. The use of therapeutic hypothermia was identified by ICD-9 procedure code 99.81 [16–18]. Use of EEG was identified by ICD-9 procedure code 89.19 for continuous EEG and ICD-9 procedure code 89.14 for routine EEG [25].

Hospital variables included the total inpatient and neurology cases per quarter. To identify the neurology cases per hospital, we collected physician specialties involved in each inpatient encounter and counted each encounter with a neurologist listed. We defined neurologic consultation as an encounter listing a neurology provider at any point during the hospitalization, whether as a consultant or primary inpatient provider. We refer to this group as neurologic consultants because neurologists are most likely in

a consulting role for patients admitted with cardiac arrest. From these data, we calculated the proportion of cases coded as cardiac arrest for every hospital as well as the proportion of inpatient cases involving a neurologist.

Since many patients with cardiac arrest are not eligible for therapeutic hypothermia, we identified subgroups of patients that are more likely to meet criteria for therapeutic hypothermia use for sensitivity analyses. We collected data on the discharge diagnosis code for ventricular fibrillation (ICD-9 427.41), length of stay in the intensive care unit (ICU), and admission source. Then, we developed more narrowly-defined subcohorts. Subgroup one was restricted to patients who were diagnosed with ventricular fibrillation to exclude patients with a less compelling neurologic and mortality benefit from therapeutic hypothermia (primary cardiac rhythm neither ventricular fibrillation nor nonperfusing ventricular tachycardia) [12–15]. Subgroup two excluded patients whose length of stay was less than one day to eliminate patients who died on arrival. Subgroup three was restricted to patients who were admitted to the ICU. Subgroup four was restricted to patients with a primary diagnosis of cardiac arrest to identify patients who were more likely to have undergone out-of-hospital, as opposed to in-hospital, cardiac arrest. Subgroup five was restricted to patients who were admitted from the community and thus excluded transfer patients who may have undergone therapeutic hypothermia at a different institution.

### Outcomes

The primary outcome was use of therapeutic hypothermia. Secondary outcomes included in-hospital mortality and use of EEG to address additional aspects of post-arrest neurologic care. We also examined the proportion of patients with cardiac arrest who underwent therapeutic hypothermia per hospital to evaluate the primary outcome on an institutional level.

### Statistical analysis

For the univariable analysis, we used Fisher's exact test to compare dichotomous categorical variables and  $\chi^2$  test to compare categorical variables with more than two levels. Continuous variables were compared using Wilcoxon rank sum test because length of hospital stay and length of ICU stay are skewed distributions.

For our primary analysis, we used generalized estimating equations to examine the association between neurologic consultation and the dichotomous outcomes of therapeutic hypothermia use, continuous or routine EEG, and in-hospital death. This model allowed us to address clustering on an institutional level. Multivariable linear regression was used to evaluate the association between neurologic consultation and the proportion of patients with cardiac arrest undergoing therapeutic hypothermia on an institutional level. Regression models included patient-level and institutional variables. The patient-level variables included in every regression were age, sex, race, severity of illness, discharge disposition, and year. The institutional variables included in every regression were the quarterly inpatient volume and the quarterly proportion of inpatient cases with cardiac arrest.

We performed a series of sensitivity analyses to study the consistency of our findings for specific hospital settings and patient populations. First, we divided hospitals into quartiles according to inpatient volume and rates of cardiac arrest, repeating the logistic regression for each hospital quartile to examine how the relationships differed across hospital settings. Second, we performed a grouped-treatment analysis evaluating the association between rates of neurologic consultation and rates of therapeutic hypothermia per hospital quarter to mitigate confounding by indication. Third, we repeated the generalized estimating equations

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