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Clinical paper

Factors associated with post-arrest withdrawal of life-sustaining therapy☆

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ABSTRACT

Introduction: Most successfully resuscitated cardiac arrest patients do not survive to hospital discharge. Many have withdrawal of life sustaining therapy (WLST) as a result of the perception of poor neurologic prognosis. The characteristics of these patients and differences in their post-arrest care are largely unknown.
Methods: Utilizing the Penn Alliance for Therapeutic Hypothermia Registry, we identified a cohort of 1311 post-arrest patients from 26 hospitals from 2010 to 2014 who remained comatose after return of spontaneous circulation. We stratified patients by whether they had WLST post-arrest and analyzed demographic, arrest, and post-arrest variables.
Results: In our cohort, 565 (43%) patients had WLST. In multivariate regression, patients who had WLST were less likely to go to the cardiac catheterization lab (OR 0.40; 95% CI: 0.26–0.62) and had shorter hospital stays (OR 0.93; 95% CI: 0.91–0.95). When multivariate regression was limited to patient demographics and arrest characteristics, patients with WLST were older (OR 1.18; 95% CI: 1.07–1.31 by decade), had a longer arrest duration (OR 1.14; 95% CI: 1.05–1.25 per 10 min), more likely to be female (OR: 1.41; 95% CI: 1.01–1.96), and less likely to have a witnessed arrest (OR 0.65; 95% CI: 0.42–0.98).
Conclusion: Patients with WLST differ in terms of demographic, arrest, and post-arrest characteristics and treatments from those who did not have WLST. Failure to account for this variability could affect both clinical practice and the interpretation of research.

Introduction

Individuals who suffer cardiac arrest experience high rates of morbidity and mortality. Even when patients survive the initial arrest event, prognosis can be poor.[1,2] Until the last few decades, it was assumed that the chances of regaining meaningful functional neurologic recovery in survivors who remained comatose post-arrest were low. However, with the use of more aggressive bundles of care focusing on targeted temperature management (TTM) and hemodynamic optimization, outcomes are improving, and more patients are discharged from the hospital with meaningful neurologic recovery.[3–5]

Despite these advances, most post-cardiac arrest patients suffer some degree of anoxic brain injury.[6] This brain injury, or at least the expectation of it, is a common cause of death for post-arrest patients.[7,8] The majority of successfully resuscitated post-arrest patients who remain comatose die after withdrawal of life-sustaining therapies (WLST) based on a presumed poor neurologic outcome.[7,9–11] This is appropriate for patients with non-recoverable neurologic injuries, but post-arrest prognosis is difficult and it often takes many days post-arrest to determine outcomes.[6,8] Indeed, remaining comatose post-arrest may lead

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patients to have WLST earlier than recommended for an "adequate" neuroprognostic decision to be made.[9,10]

Although guidelines address the need for neuroprognostication in WLST decision-making, the specific factors potentially influencing the decision to pursue WLST remain incompletely explored. To address this gap in knowledge, we sought to characterize the demographic, arrest, and post-arrest factors associated with WLST in post-arrest patients.

Methods

This is a retrospective cohort study utilizing data from the Penn Alliance for Therapeutic Hypothermia (PATH) Registry. The PATH registry is a national, online repository for patient data from multiple centers utilizing TTM in the management of post-cardiac arrest patients. This was a multi-center study evaluating patient data from 27 institutions and was approved by the University of Pennsylvania Institutional Review Board with a waiver of informed consent.

We identified adult comatose post-arrest patients between 2010–2014 from the PATH registry with information on do not resuscitate (DNR) orders and WLST. Patients were excluded if they were not successfully resuscitated post-cardiac arrest, if they were younger than 18 years of age, and if they had missing information on DNR status or outcome at hospital discharge. Patient demographic data including age, race and sex were compiled. The following patient comorbidities were abstracted: acute stroke or transient ischemic attack, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), dementia, diabetes mellitus (DM), end stage renal disease (ESRD), hypertension, metastatic or hematologic cancer, peripheral vascular disease (PVD), HIV/AIDS, and congestive heart failure (CHF). Finally, arrest variables (location of arrest, suspected etiology, initial pulseless rhythm, and duration of arrest), and post-arrest variables (whether the patient received TTM, had documented neurology or cardiology consultations, went to the cardiac catheterization laboratory, went to the electrophysiology laboratory, had electroencephalography (EEG) performed, had a computerized tomography (CT) scan of the head or brain Magnetic Resonance Imaging (MRI), had echocardiography performed, and the length of hospital stay) were collected for each patient. The primary outcome, WLST, was documented in the chart by the attending critical care physician and was defined not simply as change in code status, but as the decision to actively withdraw supportive therapies and provide comfort measures only.

Differences in categorical variables by primary outcome (WLST versus no WLST) were analyzed using Chi-square tests. Continuous variables were checked for normality using the skewedness and kurtosis test for normality and then analyzed using a Mann–Whitney *U* test to compare the differences in medians by group. To analyze the relationship between patient- and arrest-level variables and WLST, a multivariate logistic regression model was fit using demographic and arrest factors in order to assess how these variables contribute to WLST. Covariates were included in this model if they had a p-value ≤ 0.25[12,13] and removed from the model using backward elimination using Stata 12.1 (College Station, TX). Potential effect modifiers were examined and model fit was examined both with and without the interaction term(s). In order to evaluate the relationship between post-arrest care modalities and WLST while controlling for patient-level variability, a series of logistic regressions were fit controlling for the relevant demographic and arrest characteristics, as determined by the previous analysis. Tests for trend across ordered groups was performed to assess changes in rates of WLST by year and changes in percentage of WLST performed prior to 72 h post-arrest by year. As this was a multi-center study, post-estimation likelihood ratio tests were performed to evaluate the extent of clustering by site.

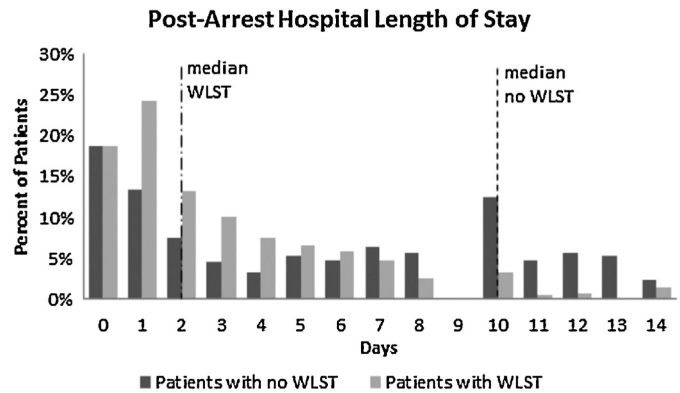

Fig. 1. Post-arrest hospital length of stay by withdrawal of life-sustaining therapies (WLST).

Results

Of 1311 patients meeting inclusion criteria, 565 (43%) patients had WLST. These patients differed in demographic, arrest, and post-arrest characteristics and treatments (Table 1). Patients with WLST were more likely to be older, female, have an unwitnessed arrest, have an initial non-shockable rhythm, and have longer duration of arrest. They were more likely to have an EEG performed and to have a shorter hospital length of stay. They were less likely to have TTM performed, a consultation from the cardiology service, go to the cardiac catheterization lab, have an MRI of the brain, or have echocardiography performed. In terms of comorbidities, patients with WLST were statistically more likely to have COPD, CAD, DM, hypertension, PVD, metastatic cancer, and CHF, but statistically less likely to have a history of acute stroke or transient ischemia attack. The median length of stay was significantly longer in the patients without WLST (WLST: 2 [IQR: 1, 5] days; no-WLST: 10 [IQR: 2, 17]; Fig. 1).

When multivariate regression was limited to patient demographics and arrest characteristics (age, race, sex, whether the arrest was witnessed, duration of arrest, an interaction between etiology of arrest and initial rhythm), patients with WLST were older (OR 1.18; 95% CI: 1.07–1.31 by decade), had a longer duration of arrest (OR 1.14; 95% CI: 1.05–1.25 for each additional 10 min of pulselessness), were more likely to be female (OR: 1.41; 95% CI: 1.01–1.96), and were less likely to have a witnessed arrest (OR 0.65; 95% CI: 0.42–0.98). In multivariate regression analysis controlling for the same demographic and arrest characteristics as well as the year of arrest, patients who had WLST were less likely to go to the cardiac catheterization lab (OR 0.40; 95% CI: 0.26–0.62), and had shorter hospital stays (OR 0.93; 95% CI: 0.91–0.95 by day).

Information on timing of WLST was available in 553/565 (97.9%) patients with WLST. 294/553 (53.2%) of patients who had WLST had it occur in the first 48 h post-arrest ("early WLST"; Table 2). Patients with early WLST were more likely to be older, white, female, and have an initial non-shockable rhythm, a non-cardiac etiology of arrest, an in-hospital cardiac arrest, and a longer duration of arrest. They were less likely to have an electroencephalogram (EEG) performed, receive targeted temperature management (TTM) or a consultation from the cardiology or neurology service, go to the cardiac catheterization lab, have a head CT, or have echocardiography performed. In terms of comorbidities, patients with early WLST only differed from those without in that they were statistically less likely to have a history of acute stroke or transient ischemia attack (TIA). The median length of stay was significantly shorter in the patients with early WLST (1 [IQR: 0, 1] day vs. 8 [IQR: 3, 16] days).

When multivariate regression was limited to patient demographics and arrest characteristics (age, race, sex, whether the