Review article

Survival after in-hospital cardiac arrest among cerebrovascular disease patients

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ABSTRACT

Stroke is a leading cause of death and disability, and while preferences for cardiopulmonary resuscitation (CPR) are frequently discussed, there is limited evidence detailing outcomes after CPR among acute cerebrovascular neurology (inclusive of stroke, subarachnoid hemorrhage (SAH)) patients. Systematic review and meta-analysis of PubMed and Cochrane libraries from January 1990 to December 2016 was conducted among stroke patients undergoing in-hospital CPR. Primary data from studies meeting inclusion criteria at two levels were extracted: 1) studies reporting survival to hospital discharge after CPR with cerebrovascular primary admitting diagnosis, and 2) studies reporting survival to hospital discharge after CPR with cerebrovascular comorbidity. Meta-analysis generated weighted, pooled survival estimates for each population. Of 818 articles screened, there were 176 articles (22%) that underwent full review. Three articles met primary inclusion criteria, with an estimated 8% (95% Confidence Interval (CI) 0.01, 0.14) rate of survival to hospital discharge from a pooled sample of 561 cerebrovascular patients after in-hospital CPR. Twenty articles met secondary inclusion criteria, listing a cerebrovascular comorbidity, with an estimated rate of survival to hospital discharge of 16% (95% CI 0.14, 0.19). All studies demonstrated wide variability in adherence to Utstein guidelines, and neurological outcomes were detailed in only 6 (26%) studies. Among the few studies reporting survival to hospital discharge after CPR among acute cerebrovascular patients, survival is lower than general inpatient populations. These findings synthesize the limited empirical basis for discussions about resuscitation among stroke patients, and highlight the need for more disease stratified reporting of outcomes after inpatient CPR.

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Stroke is the fifth most common cause of death in the United States and results in over 6-million deaths worldwide each year [1]. When considered among other etiologies for cerebrovascular disease, and despite a recent trend toward overall reduction in mortality, the rising prevalence of stroke among older persons makes aligning goals of care with interventions expected to improve survival and prevent disability a mainstay of stroke care [2].

The use of cardiopulmonary resuscitation among cerebrovascular patients varies widely. Among patients receiving in-hospital cardiopulmonary resuscitation (IHCPR), the likelihood of survival to hospital discharge relates to the severity of the patient's condition, comorbidities and characteristics of the cardiac arrest event itself [3–5]. Among mixed populations of inpatients, estimates of survival to discharge after IHCPR are variable, ranging from 7% to 32% [6]. Therefore it is critical to measure disease-specific arrest and outcome characteristics, in order to allow for identification of the patients most likely to have favorable outcomes after IHCPR [7–9].

In the setting of an acute admission for cerebrovascular disease, a high risk of mortality or severe disability increases the importance of discussing preferences for cardiopulmonary resuscitation (CPR). Previous efforts by the American Heart Association to standardize gathering and reporting of outcomes after IHCPR resulted in the Utstein Guidelines [5]. However compliance with the Utstein Guidelines has not been measured, and evidence describing IHCPR outcomes for patients admitted with a cerebrovascular disease remains limited. Individual patient factors, such as admitting

diagnosis, are key determinants of outcome, but previous systematic reviews and meta-analyses have pooled diverse patient populations, but rarely stratified outcomes by disease subgroup [10,11]. No previous systematic review or meta-analysis has examined IHCPR outcomes among cerebrovascular disease patients [7–9]. In order to better inform decision-making and direct future study, we performed a systematic review and meta-analysis of outcomes after IHCPR among patients with cerebrovascular disease.

1. Methods

Study design and search strategy were created in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA), Meta-analysis of Observational Studies in Epidemiology (MOOSE), and the Utstein Templates for Resuscitation Registries guidelines [12,13,5]. The pre-defined study population of interest was patients with cardiac arrest undergoing IHCPR with primary diagnosis of a cerebrovascular disease. Given limited disease-specific data from preliminary search results, a "cerebrovascular disease diagnosis" was defined as patients with any of the following subtypes: i) ischemic stroke, ii) intracerebral hemorrhage, or iii) subarachnoid hemorrhage. The primary outcome of interest was survival to hospital discharge.

1.1. Data sources and search strategy

The Pubmed/MEDLINE and Cochrane databases were searched for published studies between January 1990 and December 2016, using the following Medical Subject Headings (MeSH): In-hospital, cardiopulmonary resuscitation, cardiac arrest, and patient outcomes; neurosurgical, ICU, and CPR; subarachnoid hemorrhage, intracerebral hemorrhage, and acute cerebrovascular accident (Supplement 1). Reference lists of select articles were hand-searched for studies potentially missed by search terms. Dual-screening was conducted on all abstracts by two researchers [A.T., C.F.] using Abstrackr software to identify articles for potential inclusion [14]. Abstrackr is an open-source screening program, which uses an algorithm to predict which citations could be most relevant for a defined search strategy [15].

1.2. Inclusion and exclusion criteria

All studies published in English with survival to hospital discharge as a primary outcome in adult patients (age ≥ 18) following IHCPR were included. Studies of exclusively pediatric patients, out-of-hospital cardiac arrest or CPR, or those that did not include survival to hospital discharge as an outcome were excluded. In a second round of full-text screening, the population of included studies was refined for summary and review, and case-control studies were excluded due to high risk for heterogeneity. Articles that could not be clearly excluded were discussed between reviewers and a consensus determined inclusion was reached. Studies included were then stratified by primary and secondary criteria. Primary inclusion criteria required patients in the study to have admitting diagnoses of cerebrovascular disease: (inclusive of ischemic stroke, intracerebral hemorrhage (ICH), or subarachnoid hemorrhage (SAH)). Secondary inclusion criteria were broader, and therefore analyzed separately, and allowed stroke (inclusive of ischemic stroke, intracerebral hemorrhage, subarachnoid hemorrhage) to be listed as a comorbid or pre-existing condition and not necessarily the primary admitting diagnosis.

1.3. Data extraction and analysis

Data from remaining full text articles was reviewed and double-extracted by two reviewers (A.T., C.F.) to a standardized form

(Supplement 2) for the following measurement categories, and closely followed the Utstein Templates for Resuscitation Registries: study characteristics, patient demographics, cardiac arrest factors, patient assessments, outcomes, setting and timing [4,5].

Study characteristics assessed were publication year, country, and data source, type and year(s). Population characteristics captured were overall number of study subjects, number of patients that had in-hospital cardiac arrest, mean age and percent female. Cardiac arrest factors grouped together any mention of measured pre-arrest, arrest or post-arrest characteristics of the CPR event. Primary outcomes described were survival to hospital discharge and neurological status at discharge, as defined by Cerebral Performance Category (CPC) [16] patient assessment scales. The CPC is a scaled 1 to 5, with scores of one or two indicating "good performance" and "moderate disability" categories of neurological outcome. Additional outcomes mentioned in the studies, such as short-term, long-term outcomes, or use of non-CPC scale to measure patient status, were also summarized. The percentages of the overall study population that survived to hospital discharge, as well as any separate percentage that summarized populations with cerebrovascular disease (if applicable), were calculated. Finally, the location and timing of in-hospital arrest were extracted.

Statistical analyses were conducted using the "Metaprop" command in STATA, version 14.1 [17]. Metaprop is a multifunctional command that first generates study-specific proportions of survival to hospital discharge with Wald 95% Confidence Intervals (CIs) from binomial data (using the number surviving to hospital discharge out of total undergoing IHCPR). Given limitations of the test of heterogeneity (I^2) applied to meta-analyses using smaller number of studies, it was not performed [18–20]. A weighted, pooled estimate for rate of survival to hospital discharge among studies included in the meta-analysis using inverse variance weights from a random effects model was calculated [21].

2. Results

A total 818 abstracts were identified for initial review. A majority of the abstracts (642, 78%) were omitted by the following exclusion criteria: out-of-hospital cardiac arrest or CPR (408, 50%), pediatric CPR (68, 8%), lack of survival to hospital discharge outcome (18, 2%), or other (148, 18%). A detailed screening algorithm with reasons for included and excluded studies is provided in Fig. 1. There were 176 articles (22%) obtained for full review. Three articles met primary inclusion criteria and specifically identified patients with cerebrovascular disease as a primary admitting diagnosis (Table 1). Twenty additional articles met secondary inclusion criteria, with cerebrovascular disease listed as a comorbidity (Supplement 3) [32,35–48].

2.1. Survival after in-hospital CPR

Meta-analysis revealed an estimated 8% (95% CI 0.01, 0.14) pooled rate of survival to hospital discharge from a combined sample of 561 cerebrovascular disease patients that received IHCPR among the three studies meeting primary inclusion criteria (Fig. 2). A separate analysis of studies meeting less strict inclusion criteria of cerebrovascular disease as primary admitting diagnosis or comorbidity resulted in a pooled rate of survival to hospital discharge of 16% (95% CI 0.14, 0.19) (Fig. 3).

Neurological outcomes were measured in 6 (26%) studies, with CPC of 1 or 2 as the most common definition of good outcome [22]. One study used the Glasgow Outcome Score as a measure of poor neurological function [16]. Time to measurement of outcome was the most common reason for variation in outcomes between