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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

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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.

Keywords

Stroke; Cerebrovascular disease; Cardiopulmonary Resuscitation; CPR; Survival

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 (IH CPR), 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 IH CPR 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 IH CPR.[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 IH CPR resulted in the Utstein Guidelines.[5] However compliance with the Utstein Guidelines has not been measured, and evidence describing IH CPR 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 IH CPR 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 IH CPR among patients with cerebrovascular disease.

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 IH CPR 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.

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]

Inclusion and Exclusion Criteria

All studies published in English with survival to hospital discharge as a primary outcome in adult patients (age ≥ 18) following IH CPR 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.

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.

Variables from all categories were summarized, and simple proportions of the number of reviewed studies including any given variable over the total number of articles were calculated. Frequency distributions of those proportions were generated using Apple Numbers™ and resulting figures are presented in Supplement 3. An accompanying list of categorized variables with notations of particular articles that include specific variables is available in Supplement 4.

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 IH CPR). 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]

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 Figure 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).

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 IH CPR among the three studies meeting primary inclusion criteria (Figure 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) (Figure 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.[23] Time to measurement of outcome was the most common reason for variation in outcomes between studies. Survival to hospital discharge (a specified search term) was present in 96% of articles reviewed. Return of spontaneous circulation (ROSC) was reported in 9 (39%) studies. Two of three studies measuring neurological status after IH CPR adhered to Utstein guidelines.[6,7]

Discussion

This systematic review and meta-analysis identified three studies of in-hospital CPR measuring survival to hospital discharge among cerebrovascular disease patients. There was a low rate of survival to hospital discharge (8%) among the 561 patients included in this meta-analysis (Figure 2). Relaxed criteria for study inclusion, also including cerebrovascular disease as a comorbid diagnosis, identified 20 additional studies. Among the combined meta-analyzed group of studies (n=23), the overall rate of survival hospital to discharge among patients with primary admitting or comorbid diagnosis of cerebrovascular disease was 16%. This is similar to previous estimates of survival after IH CPR among undifferentiated general inpatient populations.[9,24,25]

A key finding of our analysis is that we identified only three studies that reported survival outcomes specifically among new/acute cerebrovascular disease patients.[7,9] These studies were from neurological or neurosurgical intensive care unit populations, and found low rates of survival to hospital discharge despite successful return of spontaneous circulation (ROSC). Only two studies [6,7] adhered to Utstein guidelines for reporting neurological outcome after IH CPR, which highlights the need for continued efforts to improve data quality and reporting.

Experts agree that advanced care planning requires reliable estimates of survival outcomes after IH CPR.[28,29] Although numerous studies were identified using broader inclusion criteria, few studies specifically reported stratified outcomes by cerebrovascular disease diagnosis. For example, two studies presented admitting diagnoses of cerebrovascular disease, but outcomes were not reported by subgroup.[26,27] The reporting of outcomes without stratifying by primary diagnosis can limit the generalizability of previous studies to bedside decision-making. The likelihood of successful resuscitation, and a patient's goals and preferences are key factors in CPR decision-making given the high potential for harm or suffering associated with CPR.[30] Beyond the high risk for not surviving to ROSC, survival to hospital discharge is uncommon among general inpatient populations.[24,25] Chest compressions incur pain from rib or sternal fractures, and there is potential for pain from direct current cardioversion.[31,32] Older patients have even greater risk for pain and suffering given frequent baseline multiple comorbidities and frailty. Taken together, our analysis identifies an ongoing risk of misaligning patient and family expectations related to variation in the quality of reporting CPR outcomes given current best estimates of poor survival among hospitalized cerebrovascular disease patients.

To our knowledge, this is the first systematic review and meta-analysis of IH CPR and neurological disease. The lack of standardized reporting of survival outcomes after IH CPR may relate to the studies being examined spanning twenty years, (1995 to 2015), during which time there were two versions of the Utstein Template for reporting CPR outcomes. [5,4] In particular we identified three areas of inconsistent reporting: 1) patient characteristics as they pertain to health status during the pre-arrest and arrest phases, 2) characteristics of the cardiac arrest event itself. 3) post-resuscitation and reporting of outcome factors. These areas may be improved with greater editorial and peer-review enforcement of Utstein recommended categories of variables in future studies.

The following limitations of this analysis should also be considered. Selection bias is possible by failing to identify all relevant publications. Results from the primary inclusion criteria can be biased by selection of the admitting diagnoses of cerebrovascular disease or another neurological impairment. Given effect of this selection may overestimate the effect of a cerebrovascular diagnosis on CPR survival, previous reviews were used identify a comparison rate of overall survival after IH CPR in a mixed patient population instead of using an internal control rate. Studies included in the primary inclusion category lacked details on pre-existing conditions, limiting conclusions that can be drawn on an individual patient level. Initial search terms were broad to identify all relevant articles, and search terms were then narrowed in a stepwise fashion to allow for sequential screening and careful review of the search strategy. Discharge destination to hospice care was not commonly listed among studies identified and not included in the analysis. If this variable were included as a poor outcome, the estimated rate of survival after IH CPR would have been lower than our reported estimates. With the exception of one randomized trial, all studies identified were cross-sectional, non-randomized and retrospective.[35] As a result, meta-analysis with adjustment for study quality, statistical models used, and patient case-mix was not possible. All studies meeting primary inclusion criteria were from tertiary care centers and findings may not be generalizable to all hospitals.

Conclusions

There are few studies that report survival to hospital discharge after CPR among cerebrovascular disease patients. Survival is lower among cerebrovascular disease patients relative to general inpatient populations undergoing CPR. These findings synthesize the limited empirical basis for discussions about resuscitation, and highlight the need for more disease stratified reporting of outcomes after inpatient CPR.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Flow diagram of published studies included in the analysis.

CPR Cardiopulmonary Resuscitation, ECMO Extracorporeal membranous oxygenation, ECPR Extracorporeal cardiopulmonary resuscitation.

Figure 2.

Meta analysis of studies measuring survival to hospital discharge after CPR among cerebrovascular disease patients.

ES effect size, 95% CI 95% confidence interval.

Horizontal axis and effect size represents the proportion of cerebrovascular disease patients undergoing CPR who survived to hospital discharge. Weighting is based on the simple proportion of subjects contributed by each study to the pooled (overall) survival estimate.

Figure 3.

Proportion Surviving to Hospital Discharge by Publication Year

ES effect size, 95% CI 95% confidence interval.

* Merchant *et al.*[33] (2014) not included due to inability to extract raw data.

Horizontal axis and effect size represents the proportion of cerebrovascular disease patients undergoing CPR who survived to hospital discharge. Weighting is based on the simple proportion of subjects contributed by each study to the pooled (overall) survival estimate.

Table 1

Survival to hospital discharge among studies of in-hospital CPR specifying patients with primary diagnosis of cerebrovascular disease. (N=3)

Author, year Country	Study Design (years)	Age, mean ($\pm$ SD)	No. subjects (N) No. subjects with cerebrovascular disease n (%)	Cardiac Arrest Characteristics Collected	Survival to hospital discharge N (%)
Ružman <i>et al</i> [8] (2013) Croatia	Single-center, retro-spective cross sectional (2007–2011)	69 (12.6) 76% > age 60.	N=309 Ischemic stroke: 79 (26) Intracerebral hemorrhage: 56 (18)	Pre-arrest: Age, presumed cause, length-of-stay, pre-arrest disease state Arrest: Location, shift, time of day, hospital ward, time to CPR, CPR duration, ventilation, defibrillation, drugs, chest compression	8 (2.6%) Overall ROSC rate: 10 (3.2%)
Rabinstein <i>et al</i> [7] (2004) United States	Single-center, retro-spective cross sectional, (1994–2001)	Median age 65 (range 16–81)	N= 38	Pre-arrest: Age*, sex, primary admitting diagnosis*, comorbidities, cardiac arrest causes** Arrest: location, initial rhythm, CPR duration, time to cardiac arrest after hospital admission. Post-arrest: modified Rankin scale, discharge location, cause of death	7 (18%) Stroke-only, Survival to hospital discharge: 3 (21%)§
Yi <i>et al</i> [9] (2006) South Korea	Single-center, retro-spective cross sectional, (1992–2002)	54 (9.4) (range 19–88)	N= 214	Pre-arrest: Age, sex, primary admitting diagnosis*, comorbidities. Arrest: CPR duration. Post-arrest-Recovery of spontaneous respiration, collapse to ROSC, pupillary light reflex, caloric vestibular reflex, level of consciousness.	19 (8.9%). Age > 60 not a significant predictor of outcome.

SD Standard Deviation, ROSC Return of Spontaneous Circulation.