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Short paper

Incorporating baseline functional status to improve validity of neurological outcome assessments following cardiac arrest

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Abstract

Background: Neurological status at hospital discharge is routinely used to assess patient outcome after cardiac arrest. However, attribution of impairment to the arrest is valid only if baseline neurological status is known. This study evaluated whether incorporating baseline neurological status improves performance of a widely employed neurological outcome scale for quantifying arrest-attributable morbidity.

Methods: Retrospective cohort study of two U.S. hospitals. Neurological function was assessed via Cerebral performance category (CPC), an ordinal five-point scale with 1 indicating sufficient cognition to lead an independent life and 5 representing brain death. Hospitalized adult patients who suffered in-hospital cardiac arrest for which cardiopulmonary resuscitation was attempted between 2011–2015 were included. Patients were identified through a quality improvement registry that captures all inpatient arrests in the two hospitals.

Results: Of 486 patients who suffered in-hospital cardiac arrest, 124 (25.5%) had baseline abnormal neurological function (pre-hospitalization CPC>1). Although 54 patients had a normal discharge CPC of 1, 80 patients had no change in CPC from their prior baseline (11.1% vs. 16.5% met criterion for "normal" outcome defined as CPC of 1 vs. change-in-CPC of 0; McNemar $p < .01$; kappa for agreement: .78, 95% CI .69–.86). Across several formulations of criteria for "good" neurological outcome, similar discordance existed between conventional definitions considering only discharge CPC and modified definitions that included change-in-CPC from baseline.

Conclusions: Incorporating change-in-CPC into criteria for "good" neurological outcome post-arrest yields discordant results from traditional approaches that consider discharge CPC only and increases face validity of reporting arrest-related morbidity.

Keywords: Cardiac arrest, Cerebral ischemia, Cardiopulmonary resuscitation, Clinical trials as topic, Critical care outcomes

Introduction

Long-term neurological impairment occurs commonly among survivors of cardiac arrest.[1] Perhaps the most widely used technique for assessing neurological outcome in cardiac arrest research is the Cerebral Performance Category (CPC).

First proposed for clinical trials by the Brain Resuscitation Clinical Trial Study Group in 1986[2,3] and adapted from Jennett et al.,[4] CPC is

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an ordinal scale that ranges from 1 to 5, with (1) indicating neurological function sufficient to lead a normal life; (2) indicating moderate neurological disability precluding normal life but with preserved independence; (3) indicating severe neurological impairment causing dependence on others for activities of daily living; (4) indicating coma or vegetative state; and (5) indicating death or brain death.

Since its introduction, CPC has been used widely to measure neurological function post-cardiac arrest, as a key endpoint for several prominent clinical trials in the field[5–7] and a core recommended outcome measure for cardiac arrest registries.[8]

While most randomized trials of out-of-hospital cardiac arrest exclude patients with preexisting neurological impairment, observational studies and epidemiologic registries often do not exclude such patients. Defining favorable neurological outcome as CPC of 1 or 2, as is convention for many randomized trials, is inappropriate for research or quality improvement initiatives unless patients without baseline normal neurological function are excluded from evaluation. Exclusion of such patients, which often have the greatest pre-arrest morbidity, risks biasing findings especially for in-hospital arrest studies where baseline impaired neurological function may be common. A truer reflection of the impact of cardiac arrest on neurological status would incorporate pre-arrest neurological function.

In this study, we evaluated the potential role for using change in CPC from pre-arrest baseline to post-arrest follow-up, which we term Change-in-CPC, or ΔCPC, to provide a more accurate characterization of loss of function attributable to a cardiac arrest event.

Methods

Patient population

The patients in this study were identified from a longitudinal in-hospital cardiac arrest (IHCA) quality improvement registry from two affiliated academic hospitals between 2011 and 2015. Included patients were aged 18 years or older and suffered IHCA for which cardiopulmonary resuscitation was attempted. Patients who suffered cardiac arrest in the operating room, emergency department, or pre-hospital setting were excluded. Use of IHCA registry quality improvement data for this research study was approved by the institutional review board with waiver of informed consent.

Data collection

Clinical characteristics including age, sex, comorbidities, etiology of arrest, return of spontaneous circulation, and survival to discharge were obtained from the existing registry.

Manual chart review was performed to ascertain CPC prior to admission (baseline) and at discharge (post-IHCA). Pre-hospitalization CPC was assessed as the patients' neurological status prior to the onset of any acute illness that led to acute-care hospitalization. CPC was assigned by physician review of available documentation from the history & physical, social work and case management notes, nursing notes, physical and occupational therapy notes, and discharge summaries. CPC ascertainment was performed independently by two physicians blinded to each other's evaluation. CPC raters were provided a standardized table with detailed descriptions of criteria for each CPC level (Table E1 in online supplement). Inter-rater differences in CPC assessment were resolved by consensus to determine the rating used in analyses.

Definitions of favorable outcome

Five outcome formulations for CPC were considered. Conventional approaches included CPC of 1 at discharge (normal CPC) and CPC of 1–2 at discharge (often described as a "good" or "favorable" neurological outcome). Modified approaches using ΔCPC included ΔCPC of 0 (no change in CPC from pre-hospitalization, arguably patient-specific "normal"), and ΔCPC of 0–1 (no more than a one-unit change in CPC). Finally, a combined outcome of either discharge CPC of 1–2 or ΔCPC of 0 was evaluated. ΔCPC of 0 was assigned for the one patient who had CPC rated better (lower) at discharge than pre-hospitalization.

Statistical analysis

Descriptive statistics were reported as mean ± SD or percent and compared between patients with baseline normal (CPC 1) versus abnormal (CPC>1) neurological function using t-test and Fisher's exact test, respectively. Agreement between dichotomized definitions for favorable neurological outcome formulated with CPC versus ΔCPC was quantified via Cohen's kappa and also by reporting raw proportions. McNemar's test was used to examine the hypothesis that the proportion of patients classified as having favorable neurological outcome was unequal (discordant) with different formulations using CPC and ΔCPC. For all analyses, a two-sided alpha of .05 was considered statistically significant. Analyses were performed using SAS 9.3.

Results

Patient characteristics

A total of 524 patients who underwent IHCA were identified and retrospectively reviewed. For 38 patients, insufficient data were available to ascertain CPC at baseline, leaving 486 patients (92.7%) for inclusion in the analysis. There were no significant differences in arrest etiology between included patients versus those excluded for insufficient data to ascertain baseline CPC (Table E2).

Baseline pre-hospital cerebral performance category

One in four patients (n = 124; 25.5%) who experienced IHCA had a baseline pre-hospitalization CPC greater than 1, including 7% of patients (n = 34) who had a baseline pre-hospital CPC of 3, often considered a "poor" neurological outcome (Fig. 1). Patients with a baseline normal CPC (CPC of 1) were significantly younger (58 ± 16 vs. 66 ± 16 years; $p < .01$), likelier to have ventricular tachycardia or ventricular fibrillation as the initial arrest rhythm (19.1% vs. 8.9%; $p < .01$), and likelier to have a favorable neurological outcome of CPC 1 or 2 on hospital discharge (29.3% vs. 14.5%; $p < .01$). Additional patient characteristics by baseline CPC are presented in Table 1.

Discharge cerebral performance category

The distribution of CPC at hospital discharge among patients suffering IHCA was as follows: CPC 1 in 11.1% of patients; CPC 2 in 14.4% of

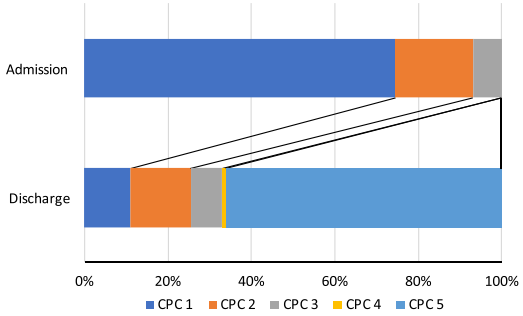

Fig. 1 – Distribution of admission and discharge Cerebral Performance Categories in the study population. CPC (1): neurological function sufficient to lead a normal life; CPC (2): moderate neurological disability precluding normal life but with preserved independence; CPC (3): severe neurological impairment causing dependence on others for activities of daily living; CPC (4): coma or vegetative state; CPC (5): death or brain death.

patients; CPC 3 in 7.4% of patients; CPC 4 in 1.0% of patients; and CPC 5 in 66.0% of patients.

The distribution of ΔCPC at hospital discharge among patients suffering IHCA was as follows: ΔCPC 0 in 16.5% of patients; ΔCPC 1 in 12.8% of patients; ΔCPC of 2 in 9.5% of patients; ΔCPC of 3 in 13.6% of patients; ΔCPC of 4 in 47.7% of patients.

Agreement between conventional outcome measures and Change-in-CPC

Agreement on what constitutes a "good" outcome differed between conventional CPC criteria and ΔCPC. Only 54 patients would be considered to have a "good" outcome using discharge CPC of 1 as the criterion, compared to 80 patients who had a "good" outcome using ΔCPC of 0 as the criterion (11.1% vs. 16.5%; McNemar $p < .01$; kappa for agreement between "good" outcome definitions: .78, 95% CI .69–.86). The criterion ΔCPC of 0 included all 54 patients with discharge CPC of 1 and an additional 26 patients whose discharge CPC was impaired but did not change from pre-hospitalization CPC. Additional comparisons of formulations for discharge CPC and ΔCPC are presented in Table 2. Summary data for all discharge CPC and ΔCPC values are presented in Table E3 in the online supplement.

Discussion

To facilitate attribution of subsequent morbidity to the cardiac arrest, use of post-arrest CPC to assess neurological outcome requires assuming that baseline CPC is normal (CPC 1). However, in our multi-year cohort, 25% of patients who suffered in-hospital cardiac arrest had grossly impaired neurological function at baseline (CPC greater than 1) prior to hospitalization. Other studies have shown similarly that baseline impaired neurological function is common (>10% of patients) among patients who subsequently experience in-hospital cardiac arrest.[9] Although patients with preexisting cognitive impairment are

Table 1 – Patient characteristics and outcomes.

Characteristic	All included patients (n = 486)	Pre-admission CPC 1 (n = 362)	Pre-admission CPC > 1 (n = 124)	p-Value
Age in years (mean ± SD)	60 ± 17	58 ± 16	66 ± 16	<.01
Female (%)	38.0	34.4	48.4	.01
Known past medical history (%)				
Coronary artery disease	28.6	28.5	29.0	.91
Heart failure with reduced ejection fraction	19.1	20.7	14.5	.15
Heart failure with preserved ejection fraction	6.6	6.1	8.1	.41
Atrial arrhythmia	20.6	17.4	29.8	<.01
Ventricular arrhythmia	1.9	1.7	2.4	.70
Diabetes mellitus	35.4	33.1	41.9	.08
Chronic obstructive pulmonary disease	12.6	11.6	15.3	.28
Cirrhosis	9.5	8.3	12.9	.15
Chronic kidney disease requiring dialysis	10.3	9.4	12.9	.30
Initial rhythm ventricular tachycardia or ventricular fibrillation (%)	16.5	19.1	8.9	<.01
Category of arrest etiology (%)				
Ventricular arrhythmia	16.5	19.1	8.9	.08
Heart block or vagal event	8.8	8.0	11.3	
Circulatory shock	41.6	40.3	45.2	
Respiratory	27.0	26.2	29.0	
Neurologic	2.9	2.5	4.0	
Unknown	3.3	3.9	1.6	
Survival to hospital discharge (%)	34.0	35.6	29.0	.19
Normal CPC of 1 on discharge (%)	11.1	14.6	.8	<.01
Good CPC (1 or 2) on discharge (%)	25.5	29.3	14.5	<.01

CPC denotes Cerebral Performance Category. CPC is an ordinal scale that ranges from 1 to 5, with (1) indicating neurological function sufficient to lead a normal life; (2) indicating moderate neurological disability precluding normal life but with preserved independence; (3) indicating severe neurological impairment causing dependence on others for activities of daily living; (4) indicating coma or vegetative state; and (5) indicating death or brain death.

Table 2 – Agreement between definitions of "good" neurocognitive outcome with formulations of CPC versus Change-in-CPC.

Definition of "good" outcome	Kappa (95% CI)	% Meeting definition of "good" outcome	McNemar p-Value*
CPC 1-2 vs. ΔCPC 0	.62 (.54–.70)	25.5% vs. 16.5%	<.01
CPC 1-2 vs. ΔCPC 0-1	.91 (.87–.95)	25.5% vs. 29.2%	<.01
CPC 1 vs. ΔCPC 0	.78 (.69–.86)	11.1% vs. 16.5%	<.01
CPC 1 vs. ΔCPC 0–1	.46 (.38–.55)	11.1% vs. 29.2%	<.01
CPC 1-2 vs. CPC 1–2 or ΔCPC 0	.95 (.92–.98)	25.5% vs. 27.4%	<.01
CPC 1 vs. CPC 1–2 or ΔCPC 0	.50 (.41–.59)	11.1% vs. 27.4%	<.01

Abbreviations: CPC denotes Cerebral Performance Category; ΔCPC denotes Change-in-CPC from pre-hospitalization baseline to discharge.
* A significant *p*-value from the McNemar test for paired data indicates the marginal proportions of the binary outcomes are significantly different from each other.

explicitly excluded from most out-of-hospital cardiac arrest clinical trials, such patients are widely represented in in-hospital arrest studies and quality improvement registries. When patients with baseline impaired neurological function are included, conventional CPC scoring for patient outcomes lacks face-validity and risks over-estimating the arrest-attributable morbidity.

The present study evaluated the role for considering Change-in-CPC (ΔCPC) between pre-hospitalization baseline and post-arrest hospital discharge, an approach employed rarely in existing literature.[10] The main finding of our study is that "good" neurological outcome assessed with ΔCPC yields discordant results from conventional measures that consider discharge CPC only. Incorporating ΔCPC into criteria significantly increased the number of patients considered to have a "good" neurological outcome post-arrest under several formulations of "good" outcome. Incorporating ΔCPC also improved face-validity by classifying as having a "good" arrest outcome those patients with baseline abnormal neurological function who experienced no post-arrest change in CPC.

Some limitations of this study are of note. First, pre-hospitalization and discharge CPC were ascertained retrospectively via chart review and subject to data available in and interpretation of the clinical medical record. Attribution of disability to cognitive versus physical impairment may be limited. This limitation is common to many IHCA studies, including registry and quality improvement studies, where ΔCPC would be most relevant. Registries with high levels of missing data for pre-hospitalization CPC might not be able to employ ΔCPC as an outcome. Adopting hybrid definitions of "good" outcome that incorporate discharge CPC with ΔCPC when available (as in Table 2) would overcome this issue.

Second, inter-rater variation in CPC rating may be considerable.[11] To overcome this limitation, CPC rating by multiple experts with consensus resolution of discordance is commonly employed, a strategy used in the present study as well.

Third, we did not pre-define a single threshold for "good" ΔCPC. This lack of proposing a single standard was intentional because different criteria may be appropriate for different research questions or study goals. In future studies that incorporate ΔCPC as an outcome, a priori selection of criteria for "favorable neurological outcome" will be essential for study integrity.

Fourth, CPC assessment at time of discharge is recommended for practical reasons by arrest registry consensus guidelines,[8] but lack of re-assessment later in follow-up may miss clinically important subacute recovery with rehabilitation.

Finally, CPC and other similar scales have important limitations as an outcome measure, discussed in detail elsewhere,[11] including limited discrimination of mild from moderate brain injury. The 2018 international guidelines newly recommend modified Rankin score instead of CPC as a core outcome measure for cardiac arrest studies.[12] The present study did not evaluate modified Rankin score or other scales that appear often in the cardiac arrest literature. Still, an analogous change-score approach would be relevant irrespective of particular scoring system used.

Conclusion

Incorporating ΔCPC into criteria for "good" neurological outcome post-arrest (1) yields discordant results from traditional approaches that consider discharge CPC only and (2) increases face validity of the outcome by avoiding incorrect attribution of pre-hospitalization impairment to arrest-related morbidity.

Potential conflicts of interest

All authors report no potential conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.07.006.

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