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Clinical paper

Conversion to shockable rhythms is associated with better outcomes in out-of-hospital cardiac arrest patients with initial asystole but not in those with pulseless electrical activity☆

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ABSTRACT

Background: The prognostic implication of conversion from initially non-shockable to shockable rhythms in patients with out-of-hospital cardiac arrest (OHCA) remains unclear. Our objective is to determine whether the conversion to shockable rhythms is a reliable predictor of short- and long-term outcomes both in patients who initially presented with pulseless electrical activity (PEA) and in those with asystole.
Methods: A secondary analysis was performed on non-traumatic OHCA cases ≥18 years old with PEA or asystole as initial rhythms, who were treated in the field and enrolled in the Resuscitation Outcomes Consortium (ROC) PRIMED study (clinicaltrials.gov/ct2/show/NCT00394706). We reported the characteristics and outcomes for those patients with or without shocks delivered in the field. Logistic regression analysis assessed the association of shock delivery with pre-hospital return of spontaneous circulation (ROSC), survival to hospital discharge and favorable neurological outcome as well.
Results: Of the 9902 included cases, 3415 (34.5%) were initially in PEA and 6487 (65.5%) were in asystole. 744 (21.8%) PEA and 1134 (17.5%) asystolic patients underwent rhythm conversions and received subsequent shocks. For asystolic patients, the adjusted odds ratios (ORs) of shock delivery for pre-hospital ROSC, survival to discharge and favorable neurological outcome were 1.862 (95%CI 1.590–2.180), 3.778 (95%CI 2.374–6.014) and 4.154 (95%CI 2.192–7.871) respectively, while for PEA patients they were 0.951 (95%CI 0.796–1.137), 1.115 (95%CI 0.720–1.726) and 1.373 (95%CI 0.790–2.385) respectively.
Conclusions: Conversion to shockable rhythms was associated with better outcomes in initially asystolic OHCA patients, whereas such associations were not observed in patients initially in PEA.

Introduction

Out-of-hospital cardiac arrest (OHCA) is a major public health problem involving large numbers of individuals worldwide.[1–4] Recent studies have observed a decline in the proportion of OHCA patients who presented initially with shockable arrest rhythms, e.g., ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT), with relatively more with first-recorded rhythms that were non-shockable, e.g., pulseless electrical activity (PEA) or asystole.[1,2,5] Because patients in shockable rhythms have been shown to have significantly better survival outcomes,[6,7] it is reasonable to assume that OHCA patients who underwent conversions from non-shockable to shockable rhythms also have better odds for survival than those who remained in non-shockable rhythms. Nevertheless, the validity of such a hypothesis remains an active topic of discussion, as the results from relevant studies have been thus far inconsistent.[8–10] Such an inconsistency might have been caused by having taken all non-shockable patients as a whole (regardless of specific rhythms) for analysis, as it is apparent in the data from those previous studies that differences existed between the outcomes of OHCA patients who first manifested with PEA and those with asystole. We thereby conducted this study to determine whether the conversion to shockable rhythms and the subsequent reception of shocks is indeed a reliable prognosticator towards better survival outcomes in both OHCA patients presenting with PEA

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and those presenting with asystole, and whether any differences actually existed between those two populations.

Materials and methods

Study population and data source

This study is a secondary analysis on the Resuscitation Outcomes Consortium (ROC) Pre-hospital Resuscitation using an Impedance valve and an Early versus Delayed analysis (PRIMED) dataset (Clinical Trial Registration URL: clinicaltrials.gov/ct2/show/NCT00394706). ROC is a clinical research network consisting of 10 regional research sites (Ottawa, Toronto, Vancouver, Birmingham, Dallas, Pittsburgh, Milwaukee, Portland, Seattle/King County and San Diego) across the United States and Canada,[11–14] and the ROC PRIMED study is a large-scale multi-center randomized controlled clinical trial conducted from June 2007 to November 2009 under the coordination of all ROC research centers.[11–14] A detailed description of the trial's methods and results has been reported elsewhere previously,[15] and access to the anonymized ROC PRIMED dataset can be requested at the website of the National Institutes of Health (NIH): https://biolincc.nhlbi.nih.gov/studies/rocprimed/?q=primed. The present study is a retrospective, observational analysis of this dataset approved by the Institutional Review Boards (IRBs) of ROC and NIH and then downloaded from the NIH website.

Selection of study population

Patients who met the following inclusion criteria were considered eligible for analysis: PEA or asystole as initial rhythms; age ≥18 years and ≤89 years; no pre-existing do not resuscitate (DNR) orders; field resuscitations attempted; and arrests of presumed cardiac origin. Patients with missing data regarding pre-hospital return to spontaneous circulation (ROSC), survival to hospital discharge, favorable neurological outcome or shock delivery status were excluded. Cardiac arrests due to obvious causes such as trauma, drowning, exsanguinations, strangulation, electrocution, hanging, and lightning were excluded. Particularly, patients with initial AED no shock advised arrest rhythms were also excluded for lack of ECG strip available to specify their rhythms as either PEA or asystole. All included subjects were subsequently divided into two study cohorts—patients with initial PEA and those with initial asystole. A subset of subjects were included in a sensitivity analysis in which outcome estimates were also adjusted for two chest compression quality measures:mean chest compression rate between 100 and 120 per min, and mean chest compression fraction ≥0.60 during the first five minutes of resuscitation.

Outcomes and exposures

The primary outcome of this analysis is survival to hospital discharge. Secondary outcomes are pre-hospital ROSC and favorable neurological outcome at discharge (Modified Rankin Score, MRS ≤ 3). We deemed all patients with initial non-shockable arrest rhythms who received defibrillations prior to Emergency Department (ED) Arrival (by either bystanders or EMS providers) as having undergone conversions to shockable rhythms. Thus the delivery of shocks is used as a surrogate exposure variable of this study, and those who did not receive any shock in the field were presumed to have remained in non-shockable rhythms. The following factors were considered possible confounders based on evidence from previous studies[8,12,16,17] and were included in the multivariable regression analysis: age, gender, EMS or bystander witness, bystander cardiopulmonary resuscitation (yes or no), location of cardiac arrest (private or public), EMS response time, adrenaline (epinephrine) dosage, application of pre-hospital advanced airway (yes or no) and assigned group in PRIMED study (analyzed early or late). Although the quality of chest compressions may affect the outcomes of this study,[18–20] we were unable to include them in the main multivariable analysis because chest compression data were only available in a limited number of patients. Therefore, to assess the effects of chest compression quality on the study results, a separate sensitivity analysis on those patients was conducted.

Statistical analysis

Demographics and characteristics of the entire study population as well as each separate study cohort (PEA and asystole) were summarized using descriptive statistics. Continuous data were described as medians and interquartile ranges, and categorical data were described using absolute numbers and percentages. Non-parametric tests were used for comparison of continuous data, whereas chi-square analysis was used to compare categorical data. Odds ratios (ORs) were calculated using chi-square analysis, univariable and multivariable logistic regression which adjusted outcome estimates for ten co-variables including age, gender, EMS witness, bystander witness, attempt of bystander cardiopulmonary resuscitation, public location of cardiac arrest, EMS response time, adrenaline dosage, application of pre-hospital advanced airway and assigned group in PRIMED study. Sensitivity analyses were also performed using uni- and multivariable logistic regression, which included mean chest compression rates (either within 100–120 per min or not) and fractions (either ≥0.60 or <0.60 during the first five minutes of resuscitation) as additional adjusting variables. All statistical calculations were performed using the statistical program SPSS 20.0 (IBM Inc., Armonk, NY, USA).

Results

Main categories and outcomes of the study population

Of the 17,177 OHCA patients enrolled in the ROC PRIMED study, 9902 were included for analysis according to the pre-specified inclusion/exclusion criteria (Fig. 1). 3415 (34.5%) patients presented with PEA initially, 744 (21.8%) of whom received subsequent shocks; 6487 (65.5%) were first observed to be in asystole, 1134 (17.5%) of whom were subsequently shocked. In total, 2648 (26.7%) patients had pre-hospital ROSC, 327 (3.3%) survived to hospital discharge, and 185 (1.9%) patients developed favorable neurological outcomes at discharge. The shock delivery status and outcomes of the study subjects are summarized in Fig. 2.

Demographics and pre-hospital characteristics of the study population

Characteristics of the study population, stratified by initial arrest rhythms, are described in Table 1, which demonstrates statistically significant differences ($p < 0.05$) in certain variables (e.g., age, EMS witness, bystander witness, bystander cardiopulmonary resuscitation, public location of cardiac arrest, EMS response time, adrenaline dosage, pre-hospital application of advanced airway) between the two study groups. Of the 9902 included patients, OHCA patients with initial PEA had higher rates of pre-hospital ROSC (41.3% versus 19.1%, $p < 0.01$), survival to hospital discharge (6.6% versus 1.6%, $p < 0.01$) and favorable neurological outcome at discharge (3.9% versus 0.8%, $p < 0.01$) than patients with initial asystole arrest. However, in the group of patients whose initial heart rhythm was asystole, those who received shocks had higher rates of pre-hospital ROSC (28.4% versus 17.1%, $p < 0.01$), survival to hospital discharge (2.9% versus 1.3%, $p < 0.01$) and favorable neurological outcomes (1.5% versus 0.6%, $p < 0.01$) than those who did not. The