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Clinical paper

Out-of-hospital cardiac arrest with Do-Not-Resuscitate orders signed in hospital: Who are the survivors?^{\star}



EUROPEAN RESUSCITATION

COUNCIL

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ABSTRACT

Background: Signing Do-Not-Resuscitate orders is an important element contributing to a worse prognosis for out-of-hospital cardiac arrest (OHCA). However, our data showed that some of those OHCA patients with Do-Not-Resuscitate orders signed in hospital survived to hospital discharge, and even recovered with favorable neurological function. In this study, we described their clinical features and identified those factors that were associated with better outcomes.

Methods: A retrospective, observational analysis was performed on all adult non-traumatic OHCA who were enrolled in the Resuscitation Outcomes Consortium (ROC) PRIMED study but signed Do-Not-Resuscitate orders in hospital after admission. We reported their demographics, characteristics, interventions and outcomes of all enrolled cases. Patients surviving and not surviving to hospital discharge, as well as those who did and did not obtain favorable neurological recovery, were compared. Logistic regression models assessed those factors which might be prognostic to survival and favorable neurological outcomes at discharge.

Results: Of 2289 admitted patients with Do-Not-Resuscitate order signed in hospital, 132(5.8%) survived to hospital discharge and 28(1.2%) achieved favorable neurological recovery. Those factors, including witnessed arrest, prehospital shock delivered, Return of Spontaneous Circulation (ROSC) obtained in the field, cardio-vascular interventions or procedures applied, and no prehospital adrenaline administered, were independently associated with better outcomes.

Conclusions: We suggest that some factors should be taken into considerations before Do-Not-Resuscitate decisions are made in hospital for those admitted OHCA patients.

Introduction

Although great progress has been made in technology and strategy for management of out-of-hospital cardiac arrest (OHCA) over the past decades [1,2], the current situation remains frustrating that the overall survival rate of OHCA is still very low, for example, less than 1% in China and about 12% in the United States [3]. More frustrating is that 11%-44% of those survivors have neurological impairment at hospital discharge and 26% have severe restrictions in daily living [4–6].

The "Do-Not-Resuscitate" orders (DNR) are originally designed for patients whose prognosis is poor, especially for those subjects who are bearing irreversible diseases and their lives are coming to the end. Aggressive therapeutic effort will be limited when death is foreseeable and therapeutic tenacity must be avoided after DNR decisions were made by patients or their surrogates. Signing DNR orders in hospital is also very common among those OHCA patients who are successfully resuscitated and subsequently admitted to hospital for further treatment, when they or their family believe that the chances for survival or a meaningful recovery after cardiac arrest are low. One recent study indicated that 32.5% of those patients admitted to hospitals after resuscitation from OHCA had a DNR order signed in the first 24 h and early DNR placement was associated with a decrease in potentially critical hospital interventions, procedures and survival rate [7]. DNR decision has been considered as an important element contributing to a worse prognosis for OHCA patients. However, our data showed that some "lucky" patients of them survived and even recovered with

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favorable neurological outcomes. In this study, we described the characteristics, interventions and outcomes of those admitted OHCA with DNR orders signed in hospital and our aim was to identify those factors associated with a higher chance of survival and lower likelihood of neurological impairment at hospital discharge.

Materials and methods

Study population and data source

This is a secondary study on the Resuscitation Outcomes Consortium (ROC) Prehospital 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 of out-of-hospital cardiac arrest 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, and the ROC PRIMED study is a large-scale randomized controlled clinical trial conducted from June 2007 to November 2009 under the coordination of all ROC research sites. A detailed description of this trial's methods and results has been previously reported elsewhere [8] and access to the anonymous 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 of ROC and NIH and then downloaded from the NIH website.

Selection of study population

A total of 17140 OHCA cases were assessed by EMS providers during the ROC PRIMED study period. Those patients who were admitted to hospital but Do-Not-Resuscitate orders were signed in hospital, were considered eligible for the present study. Patients with age < 18 years or > 89 years, with missing data regarding final outcomes or in-hospital Do-Not-resuscitate order decision statuses, were all excluded. Thus, a total of 2289 admitted OHCA patients with Do-Not-Resuscitate orders signed in hospital were screened as target population. Details in selection process were demonstrated in Fig. 1.

Outcomes and variables

The primary and secondary outcome estimates of this analysis were survival to hospital discharge and favorable neurological outcomes (Modified Rankin Score, MRS \leq 3) at hospital discharge, respectively. We reported the demographics, event characteristics, key interventions in the field, in ED (emergency department) and in hospital, as well as their outcomes for all enrolled cases. The following factors were included in multivariable regression analysis based on evidence from previous studies: age, gender, EMS or bystander witness of the arrest event, bystander CPR (yes or no), location of cardiac arrest (private or public), EMS response time, adrenaline administered (yes or no), application of prehospital advanced airway (yes or no), any shock applied in the field (yes or no), prehospital CPR duration, any obvious cause that caused cardiac arrest (yes or no), Return of Spontaneous Circulation (ROSC) gained in the field (yes or no), thrombolytic therapy in ED or in hospital (yes or no), application of hypothermia in ED or in hospital (yes or no), application of cardiovascular interventions or procedures [including coronary angiography (CAG), percutaneous coronary intervention (PCI), Implantable Cardioverter Defibrillator (ICD) or pacemaker implantation] and assigned group in PRIMED Study (early or late analyzed).



Fig. 1. Target cohort and exclusions. EMS indicates Emergency Medical Service; OHCA, Out-of-Hospital Cardiac Arrest; ROC, Resuscitation Outcomes Consortium; PRIMED, Pre-hospital Resuscitation Using an Impedance Valve and Early Versus Delayed Analysis; DNR, Do Not Resuscitate; N, Number.

Statistical analysis

Demographics, event characteristics, key interventions and outcomes of the entire study population were summarized using descriptive statistics. Continuous data were expressed as medians and interquartile ranges (IQR) and non-parametric tests were used for comparison of continuous data, while categorical data were described using absolute numbers and percentages, and were compared via chisquare analysis or Fisher exact test. Both the primary outcome (survival to hospital discharge) and the secondary outcome (favorable neurological outcomes at discharge) were analyzed using univariate and multivariate logistic regression, which adjusted outcome estimates for those previously defined covariates as listed above. All statistical calculations were performed using the statistical program SPSS 20.0 (IBM Inc., Armonk, NY, USA).

Results

Of all those admitted 2289 OHCA patients with DNR orders in hospital who were enrolled in the ROC PRIMED study, 2156 (94.2%) died in hospital, 132 (5.8%) survived to hospital discharge, and 28 (1.2%) gained favorable neurological outcomes (MRS 0–3) at hospital discharge.

Clinical features of the study population and comparison between subgroups stratified by outcomes at hospital discharge

Table 1 demonstrates the demographics, event characteristics, key

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