CLINICAL RESEARCH STUDY

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External Validation of the Simple NULL-PLEASE Clinical Score in Predicting Outcome of Out-of-Hospital Cardiac Arrest

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ABSTRACT

BACKGROUND: Rapid clinical decision-making on further management of patients with out-of-hospital cardiac arrest may be challenging. Recently, a "futility" score (NULL-PLEASE) incorporating multiple adverse resuscitation features (**N**onshockable rhythm, **U**nwitnessed arrest, **L**ong no-flow or **L**ong low-flow period, blood **P**H <7.2, **L**actate >7.0 mmol/L, **E**nd-stage chronic kidney disease on dialysis, **A**ge ≥85 years, **S**till resuscitation, and **E**xtracardiac cause) has been proposed to help identify patients with out-of-hospital cardiac arrest unlikely to survive; however, external independent score validation is lacking.

METHODS: We retrospectively validated the NULL-PLEASE predictive ability for early in-hospital outcome of out-of-hospital cardiac arrest in a single-center cohort of 547 consecutive patients with out-of-hospital cardiac arrest who were admitted from April 2013 to October 2016 (mean age, 66.3 ± 13.2 years); 227 patients (41.5%) died. Because pH and lactate were inconsistently measured, a modified NULL-PLEASE score excluding both variables was calculated as the principal analysis. A sensitivity analysis included the subgroup with pH data available (n = 177).

RESULTS: Long low-flow period and age ≥85 years were independently associated with fatal outcome (both $P < .001$). Patients with a modified NULL-PLEASE score of ≥5 had a 3.3-fold greater risk of fatal outcome compared with a score of 0 to 4 (odds ratio, 3.34; 95% confidence interval [CI], 2.29-4.89; $P < .001$); 77% of nonsurvivors had a score ≥5; NULL-PLEASE showed a modest predictive ability for fatal outcome (c-statistic 0.658; 95% CI, 0.613-0.704; $P < .001$). Sensitivity analysis yielded similar results, with 88% of nonsurvivors having a score ≥5.

CONCLUSIONS: The NULL-PLEASE score was predictive for early in-hospital outcome of out-of-hospital cardiac arrest, with a 3.3-fold greater odds for fatal outcome at the score values of ≥5.

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KEYWORDS: In-hospital mortality; NULL-PLEASE score; Outcome; Out-of-hospital cardiac arrest; Prediction; Resuscitation

Out-of-hospital cardiac arrest annually occurs in 250,000 to 300,000 patients worldwide.[1] Despite some regional variations, all published out-of-hospital cardiac arrest survival rates are disappointingly low. In a large meta-analysis of 79 cohort studies with a total of 142,740 patients with out-of-hospital cardiac arrest, pooled survival rates to hospital admission and subsequent hospital discharge were 23.4% (95% confidence interval [CI], 20.7-26.1) and 7.6% (95% CI, 6.7-8.4), respectively,[2] with no significant improvement over a 30-year period covered in the meta-analysis (from 1980 to 2008).

In well-organized prehospital systems, successful return of spontaneous circulation with cardiopulmonary resuscitation may be achieved in up to 50% of patients with out-of-hospital cardiac arrest, but a far smaller proportion survive

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to hospital discharge.[3] Most recent international guidelines for postresuscitation care consistently emphasize the importance of an early use of invasive and interventional strategies in patients with out-of-hospital cardiac arrest to improve their ultimate survival,[4,5] although clinical decision-making on the termination of resuscitation efforts or use of expensive, sometimes lengthy postresuscitation care resources may be challenging.

The European Resuscitation Council and the European Society of Intensive Care Medicine offer a prognostication algorithm based on clinical examination, biomarkers, imaging, and electrophysiologic testing, which should be initiated 5 days after out-of-hospital cardiac arrest or 72 hours after completing the targeted temperature management treatment.[6] Notwithstanding various ethical issues,[7] there is a clear need for accurate prognostic assessment that would facilitate an earlier identification of patients with out-of-hospital cardiac arrest who would clearly benefit from intensive advanced postresuscitation care.

Several clinical scores have been reported to predict the outcome of out-of-hospital cardiac arrest at early stages,[8-10] but no single prognostication tool has been recommended to guide decision-making regarding individual patients with out-of-hospital cardiac arrest. Recently, a new simple "futility" score (the NULL-PLEASE score) has been proposed to help identify patients unlikely to survive out-of-hospital cardiac arrest after admission to the intensive care unit.[11] The score includes several unfavorable arrest- or patient-related characteristics (ie, nonshockable rhythm, unwitnessed arrest, long no-flow or low-flow period, blood pH <7.2, lactate >7.0 mmol/L, end-stage chronic kidney disease on dialysis, age ≥85 years, still ongoing cardiopulmonary resuscitation, and extracardiac cause of arrest). This simple score was originally validated in a small retrospective historical cohort of 56 consecutive patients admitted to the intensive care unit after out-of-hospital cardiac arrest, but external independent validation was lacking for this score.

In the present study, we provide the first external independent validation of the predictive ability of the NULL-PLEASE score for early in-hospital fatal outcome of out-of-hospital cardiac arrest in a single-center, contemporary cohort of 547 consecutive patients with out-of-hospital cardiac arrest.

CLINICAL SIGNIFICANCE

- A "futility" score (NULL-PLEASE) incorporating adverse resuscitation features (**N**onshockable rhythm, **U**nwitnessed arrest, **L**ong no-flow or **L**ong low-flow period, blood **P**H <7.2, **L**actate >7.0 mmol/L, **E**nd-stage chronic kidney disease, **A**ge ≥85 years, **S**till resuscitation, and **E**xtracardiac cause) may help identify patients with out-of-hospital cardiac arrest who are unlikely to survive.
- This validation study shows that the NULL-PLEASE score had a predictive ability for early in-hospital outcome of out-of-hospital cardiac arrest. A high probability of fatality was evident with score of ≥5.

MATERIALS AND METHODS

Patient Selection

We retrospectively retrieved the electronic medical records of consecutive patients who were referred to the Resuscitation Unit of the Emergency Center, Clinical Center of Serbia because of an out-of-hospital cardiac arrest from April 1, 2013, to October 1, 2016. These medical records include demographic data (ie, age and gender), descriptive data on the circumstances of out-of-hospital cardiac arrest (ie, witnessed status, bystander cardiopulmonary resuscitation before the emergency medical unit arrival, approximate duration of the basic life support, and advanced life support before arrival to the Resuscitation Unit), data on the advanced life support in the Resuscitation Unit, diagnosis of the underlying condition presumably resulting in out-of-hospital cardiac arrest, and the ultimate vital status—survivor or nonsurvivor of the out-of-hospital cardiac arrest. However, blood biochemistry data (pH, lactate) were inconsistently recorded in the Emergency Center electronic database during the study period. The study was approved by the hospital Ethical Committee and therefore has been performed in accordance with the ethical standards documented in the 1964 Declaration of Helsinki and its later amendments.

Study Setting

In Belgrade and its closest suburb area (overall ≥2 million of citizens), out-of-hospital cardiac arrest is managed by mobile emergency units. Out-of-hospital resuscitation (including the basic life support and advanced life support measures) is delivered by the emergency teams, which include 1 physician trained in emergency medicine, a nurse technician, and a paramedic. After excluding patients who died before or within the first 5 to 10 minutes of the mobile emergency unit arrival, all other patients with out-of-hospital cardiac arrest in whom at least a brief, transient successful return of spontaneous circulation has been established in the field are by default transported to the Resuscitation Unit of the Emergency Center, Clinical Center of Serbia, either under ongoing cardiopulmonary resuscitation or with established sustained return of spontaneous circulation. The Clinical Center of Serbia is the largest hospital in Serbia and a tertiary healthcare center equipped for all measures of advanced cardiac life support. Although most of the out-of-hospital cardiac arrest cases in Belgrade are referred to the Resuscitation Unit of the Emergency Center, Clinical Center of Serbia, a small number of patients with out-of-hospital cardiac arrest are referred to other city hospitals when out-of-hospital cardiac arrest occurs in the close proximity of the hospital.

The Resuscitation Unit of the Emergency Center establishes the vital status on admission, continues cardiopulmonary resuscitation/advanced life support of the referred patient as