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병원 밖 심정지 환자의 소생 후 신경학적 예후 예측

Prediction of neurological outcomes following the return of spontaneous circulation in patients with out-of-hospital cardiac arrest: Retrospective fast-and-frugal tree analysis

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Abstract

Prediction of neurological outcomes following the return of spontaneous circulation in patients with out-of-hospital cardiac arrest: Retrospective fast-and-frugal tree analysis

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Aim: Although various quantitative methods have been developed for predicting neurological prognosis in patients with out-of-hospital cardiac arrest (OHCA), they are too complex for use in clinical practice. We aimed to develop a simple decision rule for predicting neurological outcomes following the return of spontaneous circulation (ROSC) in patients with OHCA using fast-and-frugal tree (FFT) analysis.

Methods: We performed a retrospective analysis of prospectively collected data archived in a multi-centre registry. Good neurological outcomes were defined as cerebral performance category (CPC) values of 1 or 2 at 28-day. Variables used for FFT analysis included age, sex, witnessed cardiac arrest, bystander cardiopulmonary resuscitation, initial shockable rhythm, prehospital defibrillation, prehospital ROSC, no flow time, low flow time, cause of arrest (cardiac or non-cardiac), pupillary light reflex, and Glasgow Coma Scale score after ROSC.

Results: Among the 456 patients enrolled, 86 (18.9%) experienced good neurological outcomes. Prehospital ROSC (true = good), prompt or sluggish light reflex response after ROSC (true = good), and presumed cardiac cause (true = good, false = poor) were selected as nodes for the decision tree. Sensitivity, specificity, positive predictive value, and negative predictive value of the decision tree for predicting good neurological outcomes were 100% (42/42), 64.0% (119/186), 38.5% (42/109), and 100% (119/119) in the training set and 95.5% (42/44), 57.6% (106/184), 35.0% (42/120), and 98.1% (106/108) in the test set, respectively.

Conclusion: A simple decision rule developed via FFT analysis can aid clinicians in predicting neurological outcomes following ROSC in patients with OHCA.

Keywords : **cardiac arrest, neurological outcome, prognosis, OHCA fast-and-frugal tree analysis**

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Contents

I. Introduction

The rate of survival to discharge among patients with out-of-hospital cardiac arrest (OHCA) is approximately 10% worldwide [1, 2]. Among those who have achieved sustained return of spontaneous circulation (ROSC), more than half experience circulatory shock and hypoxic ischaemic injury resulting in death [3, 4].

Accurate prognostic indicators are critical when providing information to patient families and making decisions regarding whether to initiate or withdraw life-support measures [5]. Current guidelines recommend that neurological outcomes in patients with OHCA should be predicted based on the results of careful clinical examinations, electrophysiologic responses (somatosensory evoked potentials and electroencephalography), serum levels of neuron-specific enolase, and brain imaging findings [6]. This multimodal approach minimises the risk of falsely predicting poor outcomes, which may lead to the withdrawal of life-sustaining treatment.

However, neurological outcomes following OHCA are influenced by various parameters, including both patient factors (age, sex, and location of cardiac arrest) and resuscitation factors (initial rhythm, bystander-witnessed cardiac arrest, bystander-performed cardiopulmonary resuscitation [CPR], and the time from cardiac arrest to ROSC). Therefore, various scoring models (e.g., OHCA score, 5-R score, and RACA score) have been developed for patients with OHCA during early the post-resuscitation period [7-9]. Although these scores provide a quantitative method for predicting prognosis, they are too complex for use in clinical practice. Some researchers have instead proposed the use of decision tree models [10-12], which are helpful during classification tasks based on a range of predictor variables (e.g., when classifying survivors of OHCA with good or poor neurological outcomes) [10-12].

A decision tree is a simple representation for classifying and predicting the value of a target variable. A decision tree is a flow-chart-like structure, whereroot node has many branch nodes. Each node represents a test for an attribute, each branch denotes the result of a test, and terminal node holds a class label. There are many specific decision tree algorithms, Iterative Dichotomiser 3, Chi-squared Automatic Interaction Detector, Conditional Inference Trees, MARS, Classification And Regression Trees.

The classification and regression tree (CART) model is a recursive partitioning algorithm to calculate nodes and branches and is commonly used to evaluate neurological prognosis in patients with cardiac arrest in previous studies [10-12]. Table 1 summarizes previous studies using decision trees for predicting neurological prognosis. Fischer et al. in 2006 demonstrated the utility of using a prognostic tree for the prediction of awakening, nonawakening in severe anoxic coma. In 2013, three papers on prediction models using CART and recursive partitioning methods were published. Goto et al. analyzed data for 390226 adult patients who had undergone OHCA, from Japanese database for 2005 through 2009 [11]. Recursive partitioning analysis of the development cohort for 10 predictors indicated that 4 predictors for survival and CPC 1 to 2 were shockable initial rhythm, young age, witnessed arrest and witnessed by EMS personnel. The AUCs for that model in the cohorts for development and validation were 0.85 and 0.88 [11]. Greer et al. in 2013 also studied to build new algorithms using CART for prognostication of comatose cardiac arrest patients [19]. From 2000 to 2007, 500 consecutive patients in non-traumatic coma were prospectively enrolled. Motor response was often chosen as a root node, and spontaneous eye movements, pupillary reflexes, eye opening and corneal reflexes were often chosen as splitting nodes [19]. However, the CART model is also complex due to the many nodes, which makes it difficult to apply in clinical practices.

Fast-and-frugal tree (FFT) analysis is a supervised learning method uses information in a specific, sequential order to perform binary classification tasks. Every nodes has two branch nodes, one of them is a exit branch. This algorithm prevents the overfitting by using only some of the valuable information among the vast amount of data. So it is faster and more intuitive to make decisions from limited time and information. Relative to CART analysis, FFT analysis is advantageous in terms of its frugality and simplicity. FFT relies only on a few cues, allowing for fast and accurate decision-making based on limited information, without the need for statistical training or a calculation device [13].

Therefore, in the present study, we aimed to develop an FFT model for predicting neurological outcomes during the early post-resuscitation period in patients with OHCA.

Table 1. Previous studies using decision trees for predicting neurological prognosis

Year	Journal	Setting	Institution	Type	Sample size	Outcome	Methods	Model performance
2006	Critical Care Medicine	Prospective	Single center	OHCA, ROSC	62	Awakening date, GCS after 1yr	Recursive partitioning	Cross validation at 19%, sensitivity 5%
2013	Critical Care	Prospective	Japan database	Nontraumatic OHCA	390226 (307896/82330)	Survival with favorable neurologic outcome, survival at 1month	Recursive partitioning	AUC development 0.85 validation 0.88
2013	Resuscitation	Prospective	Single center	Nontraumatic coma	500 (200PCAS)	Neurologic outcome mRS score at 6months	CART	No validation
2013	Critical Care Medicine	Retrospective	366 hospital	IHCA	52527 (38092/14435)	Survival to discharge with good neurologic function	CART	AUC development 0.718 to 0.766 validation 0.683 to 0.746
2014	Critical Care	Prospective	Japan database	OHCA	5379 (3698/1686)	Survival with favorable neurologic outcome, survival at 1month	Recursive partitioning	AUC 0.88 sensitivity 69.7%
2014	American Journal of Cardiology	Retrospective	Single enter	OHCA	184	Survival to discharge with favorable neurologic outcome	Propensity analysis CART	Sensitivity 90.7%, specificity 47.5%, PPV 34.5% NPV 94.4%
2016	Resuscitation	Retrospective	Japan database	bystander-witnessed OHCA	204277	Response time threshold and favorable neurologic outcome	CART	AUC 0.622 to 0.634

CART,classification and regression tree; OHCA,out-of-hospital cardiac arrest; IHCA,in-hospital cardiac arrest; GCS,glasgow coma scale; mRS,modified Rankin Scale; AUC,area under Curve; PPV,positive predictive value; NPV,negative predictive value

II. Methods

2.1. Study Design and Setting

We performed a retrospective analysis of prospectively collected data archived in a multi-centre registry. Survivors of OHCA admitted to three urban tertiary teaching hospitals between December 2013 and August 2017 were prospectively registered under the approval of the Institutional Review Board (IRB No. H-1408-012-599, J-1408-012-599, and B-1401-234-402), who waived the requirement for written informed consent due to the nature of the study. The Institutional Review Board also approved this retrospective analysis (IRB No. 1803-073-929).

The registry contains data regarding age, sex, pre-arrest cerebral performance category (CPC), and characteristics of cardiac arrest, including the location of cardiac arrest, collapse time, witness of the cardiac arrest event, bystander CPR, emergency medical service (EMS) activation time, EMS arrival time, prehospital rhythm, prehospital defibrillation, emergency department (ED) visit time, and acquisition of sustained ROSC. Post-resuscitation variables consisted of first laboratory results (serum pH and serum lactate), whether extracorporeal membrane oxygenator CPR (ECPR) was applied, ST-segment elevation on 12-lead electrocardiography (ECG), Glasgow Coma Scale (GCS) score in the ED, pupillary light reflex in the ED, and coronary angiography during the subsequent admission period. The aetiology of OHCA was defined as cardiac or non-cardiac by the attending physicians in the ED. Non-cardiac causes were categorised into respiratory, neurological, sepsis, haemorrhage, and malignancy. The aetiology of OHCA was presumed to be cardiac unless the evidence suggested a non-cardiac cause. Outcome variables included mortality and CPC at 28 days.

The EMS system for the study location is a single-tier, basic life support ambulance service operated by the national fire department. Ambulance crews provide CPR on-site and while in transit, utilising an autonomic external defibrillator when necessary. They cannot declare death. Therefore, all patients with OHCA should be transferred to the nearest hospitals [14]. Advanced life support is provided after arriving at the ED, and the active withdrawal of life-sustaining therapy is applied only in patients with brain death for the purposes of organ donation.

2.2 Patient Selection

Patients who fulfilled the following criteria were eligible for registration: age ≥ 18 years; non-traumatic cardiac arrest; successful resuscitation during the prehospital period and transfer to a study hospital/successful resuscitation in the ED of a study hospital. Patients who were transferred from another hospital following ROSC and those with pre-arrest CPC values of 3 or 4 were excluded.

2.3 Derivation and Validation of Prediction Model

The primary outcome was defined as good neurologic outcome at 28 days (CPC 1 or 2), which was determined by telephone follow-up of research nurses. Enrolled patients were randomly divided into training and test cohorts at a ratio of 1:1 for the subsequent analysis. The derivation model was constructed using the FFTrees package provided by R software (R Foundation for Statistical Computing, Vienna, Austria [http://www.R-project.org]). The following candidate predictors were considered for inclusion in the FFT model: age, sex, location of cardiac arrest, bystander-witnessed cardiac arrest, bystander CPR, shockable prehospital rhythm (or lack thereof), any shockable rhythm during CPR, time from cardiac arrest to the start of basic life support, time from cardiac arrest to the start of advanced life support, time from cardiac arrest to ROSC, prehospital ROSC, ECPR, ST-segment elevation on 12-lead ECG, GCS (as a full score and GCS-Eye, GCS-Verbal, and GCS-Motor, respectively), light reflex (as prompt, sluggish, or fixed), and cardiac cause.

We have set a sensitivity weight of 0.7 because missing good outcome carries more risk than the opposite in patients with cardiac arrest. Weighted accuracy (WACC) value was calculated by adding the sensitivity multiplied by 0.7 and the specificity multiplied by 0.3. Variables with high WACC values have priority when selected as a node. The maximum number of allowable nodes is limited to three for the simplicity of the model.

FFTs had two branches under each node, where one or both branches were exit branches that triggered an immediate decision [15]. The plot to visualize the top five cues with highest WACC among all cues in the training cohort was constructed. Among those cues, top three cues with highest WACC were used for the three nodes in the final FFTs model. The plots which displayed the number and accuracy of cases classified at each node were constructed in the training and test cohorts, respectively. Statistical measures used for performance analysis included sensitivity, specificity, area under the receiver operating characteristics curve (AUC), positive predictive value, and negative predictive value. Two-by-two tables displaying accuracy statistics were also used to visualise the performance of the FFT model.

2.4 General Statistics

Continuous variables were presented as medians with interquartile ranges (IQRs), while categorical variables were presented as frequencies of occurrence (%). The Wilcoxon rank-sum test was used to compare continuous variables, while the chi-square test or Fisher's exact test was used to compare categorical variables, as appropriate. Two-tailed p-values less than 0.05 were considered to indicate statistical significance. All analyses were performed using either Stata version 13.1 (Stata Corp, College Station, TX) or the FFTrees package in R (http://CRAN.R-project.org).

III. Results

3.1 Patient Selection

During the study period, 1,345 patients with OHCA directly visited study hospitals (Fig 1). Among them, 589 (43.8%) patients experienced sustained ROSC. Among these 589 patients, 456 were enrolled in this study following the exclusion of 133 patients with pre-arrest CPC values of 3 or 4.

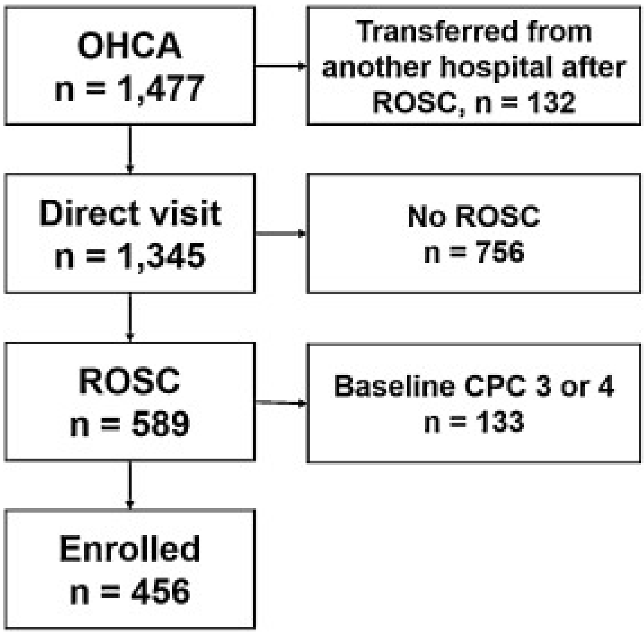

Fig1. Flow chart of patient enrollment.

3.2 Patient Characteristics

Table 2 compares the characteristics of patients with good CPC (CPC 1 or 2) and poor CPC (CPC 3, 4, or 5) values. Prehospital ROSC, prompt pupillary reflex and cardiac cause were more frequent in patients with good CPC values. There were 86 patients in the good CPC group, 68 patients (79.1%) in CPC 1 and 18 patients (20.9%) in CPC 2. And 370 patients were enrolled in the bad CPC group, composed of CPC 3 (N=12, 3.2%), CPC 4 (N=57, 15.4%), and CPC 5 (N=301, 81.4%). Table 3 compares the characteristics of the training and test cohorts. There were no significant differences between the two groups.

Table 2. Clinical characteristics of enrolled patients based on neurological outcome at discharge

Characteristics	Good CPC (N=86)	Poor CPC (N=370)	*P* value
Demographic characteristics			
Age (y), median (IQR)	54 (47–62)	68 (53–76)	<0.001
Male sex – no. (%)	73 (84.9)	237 (64.1)	<0.001
Characteristics of cardiac arrest			
Location of cardiac arrest – no. (%)			0.001
Place of residence	29 (33.7)	191 (51.6)	
Public place	48 (55.8)	127 (34.3)	
Other	9 (10.5)	52 (14.1)	
Bystander-witnessed cardiac arrest – no. (%)	78 (90.7)	253 (68.4)	<0.001
Bystander-performed CPR – no. (%)	54 (62.8)	156 (42.2)	0.001
Prehospital rhythm – no. (%)			
Shockable rhythm	56 (65.1)	60 (16.2)	<0.001
Ventricular fibrillation	53 (61.6)	56 (15.1)	
Non-perfusing ventricular tachycardia	1 (1.2)	2 (0.5)	
Unknown rhythm but responsive to shock	2 (2.3)	2 (0.5)	
Non-shockable rhythm	30 (34.9)	310 (83.8)	<0.001
Pulseless electrical activity	8 (9.3)	96 (25.9)	
Asystole	3 (3.5)	176 (47.6)	
Unknown first rhythm, not responsive to shock or not shocked	19 (22.1)	38 (10.3)	
Time from cardiac arrest to event – min			
Start of basic life support – median (IQR)	1 (0–3)	3 (0–8)	0.001
Start of advanced life support – median (IQR)*	11 (6–20)	24 (13–33)	0.003
Return of spontaneous circulation – median (IQR)	15 (9–22)	34 (22–48)	<0.001
Prehospital ROSC – no. (%)	69 (80.2)	36 (9.7)	<0.001
Characteristics at ED			
Serum pH†	7.3 (7.1–7.3)	7.0 (6.8–7.1)	<0.001
Serum lactate – mmol/litre‡	9.7 (6.9–12.8)	12.4 (9.4–16.0)	<0.001
ECMO CPR – no. (%)	1 (1.2)	12 (3.2)	0.296
Characteristics after ROSC			
ST-segment elevation on 12-lead ECG – no. (%)	20 (23.3)	28 (7.6)	<0.001
Glasgow Coma Scale – median (IQR)	5 (3–14)	3 (3–3)	<0.001
Pupillary light reflex after ROSC at ED – no. (%)			
Prompt	68 (79.1)	62 (16.8)	<0.001
Sluggish	5 (5.8)	17 (4.6)	
Fixed	13 (15.1)	291 (78.7)	
Cardiac cause – no. (%)	71 (82.6)	100 (27.0)	<0.001
Emergent coronary angiography – no. (%)	32 (37.2)	58 (15.7)	<0.001
Emergent coronary intervention – no. (%)	26 (30.2)	32 (8.7)	<0.001
Coronary angiography during admission – no. (%)	56 (65.1)	71 (19.2)	<0.001
Coronary intervention during admission – no. (%)	38 (44.2)	37 (10.0)	<0.001
Mortality at 28 days – no. (%)	0	301 (81.4)	NA

CPC, cerebral performance category; IQR, interquartile range; CPR, cardiopulmonary resuscitation; ED, emergency department; ECMO, extracorporeal membrane oxygenator; ROSC, return of spontaneous circulation

Table 3. Clinical characteristics of enrolled patients in the training and test cohorts

Characteristics	Training cohort (n=228)	Test cohort (n=228)	*P* value
Demographic characteristics			
Age – yr, median (IQR)	62 (49–74)	66 (51–76)	0.222
Male sex – no. (%)	152 (66.7)	158 (69.3)	0.547
Characteristics of cardiac arrest			
Location of cardiac arrest – no. (%)			0.449
Place of residence	104 (45.6)	116 (50.9)	
Public place	90 (39.5)	85 (37.3)	
Other	34 (14.9)	27 (11.8)	
Bystander-witnessed cardiac arrest – no. (%)	166 (72.8)	165 (72.4)	0.916
Bystander-performed CPR – no. (%)	107 (46.9)	103 (45.2)	0.707
Prehospital rhythm – no. (%)			
Shockable rhythm	56 (24.6)	60 (26.3)	0.667
Ventricular fibrillation	52 (22.8)	57 (25.0)	
Non-perfusing ventricular tachycardia	1 (0.4)	2 (0.9)	
Unknown rhythm but responsive to shock	3 (1.3)	1 (0.4)	
Non-shockable rhythm	172 (75.4)	168 (73.7)	0.667
Pulseless electrical activity	55 (24.1)	49 (21.5)	
Asystole	90 (39.5)	89 (39.0)	
Unknown first rhythm, not responsive to shock or not shocked	27 (11.8)	30 (13.2)	
Time from cardiac arrest to event – min			
Start of basic life support – median (IQR)	2 (0–7)	2 (0–7.5)	0.415
Start of advanced life support – median (IQR)*	27 (14.5–38)	23 (15–35)	0.164
ROSC – median (IQR)	30.5 (18–45.5)	30 (18–42)	0.318
Prehospital ROSC – no. (%)	47 (20.6)	58 (25.4)	0.221
Characteristics at ED			
Serum pH†	7.0 (6.9–7.1)	7.0 (6.9–7.2)	0.193
Serum lactate – mmol/litre‡	11.9 (8.7–15.2)	11.8 (8.8–15.1)	0.815
ECMO CPR – no. (%)	10 (4.4)	3 (1.3)	0.088
Characteristics after ROSC			
ST-segment elevation on 12-lead ECG – no. (%)	26 (11.4)	22 (9.7)	0.542
Glasgow Coma Scale – median (IQR)	3 (3–3)	3 (3–3)	0.795
Pupillary light reflex after ROSC/ED – no. (%)			0.645
Prompt	64 (28.1)	66 (29.0)	
Sluggish	9 (4.0)	13 (5.7)	
Fixed	155 (68.0)	149 (65.4)	
Presumed cardiac cause – no. (%)	84 (36.8)	87 (38.2)	0.772
Emergent coronary angiography – no. (%)	43 (18.9)	47 (20.6)	0.638
Emergent coronary intervention – no. (%)	27 (11.8)	31 (13.6)	0.574
Coronary angiography during admission – no. (%)	58 (25.4)	69 (30.3)	0.250
Coronary intervention during admission – no. (%)	35 (15.4)	40 (17.5)	0.528
Mortality at 28 days – no. (%)	155 (68.0)	146 (64.0)	0.374
CPC at 28 days – no. (%)			0.894
CPC 1	33 (14.5)	35 (15.4)	

CPC 2	9 (4.0)	9 (4.0)
CPC 3	5 (2.2)	7 (3.1)
CPC 4	26 (11.4)	31 (13.6)
CPC 5	155 (68.0)	146 (64.0)

CPC, cerebral performance category; IQR, interquartile range; CPR, cardiopulmonary resuscitation; ED, emergency department; ECMO, extracorporeal membrane oxygenator; ROSC, return of spontaneous circulation; ECG, electrocardiography;

* Only patients without prehospital ROSC (n=351) were analysed.

† Patients with available results (n=426) were analysed.

‡ Patients with available results (n=407) were analysed.

3.3 Training FFT for the Prediction of Neurological Outcomes

Figure 2 shows the accuracy of cues in the ROC curve and highlights the five cues with the highest weighted accuracy values in the training cohort, which were as follows: prehospital ROSC (sensitivity: 0.83, specificity: 0.94, WACC: 0.86), pupillary light reflex of prompt or sluggish (sensitivity: 0.86, specificity: 0.80, WACC: 0.84), cardiac cause (sensitivity: 0.83, specificity: 0.74, WACC: 0.80), any shockable rhythm (sensitivity: 0.71, specificity: 0.84, WACC: 0.75), and prehospital shockable rhythm (sensitivity: 0.69, specificity: 0.85, WACC: 0.74). The cues with the three highest WACC values were selected as nodes for the prediction of neurological outcomes. Forty-two patients (18.4%) experienced good neurological outcomes in the training cohort. Figure 3 shows that, at the root node of the tree (prehospital ROSC), 47 patients who experienced ROSC prior to arriving at the hospital were classified as having good neurological outcomes. At the parent node (pupillary light reflex), 33 patients with prompt or sluggish pupillary light reflex responses were classified as having good neurological outcomes. At the leaf node (cardiac cause), 29 patients with cardiac cause were classified as having good neurologic outcomes, while 119 patients without cardiac cause were classified as having poor neurological outcomes. The sensitivity, specificity, AUC, positive predictive value, negative predictive value, and accuracy of the decision tree for predicting good neurological outcomes were 100%, 64.0%, 0.820, 38.5%, 100%, and 70.6%, respectively (Table 4).

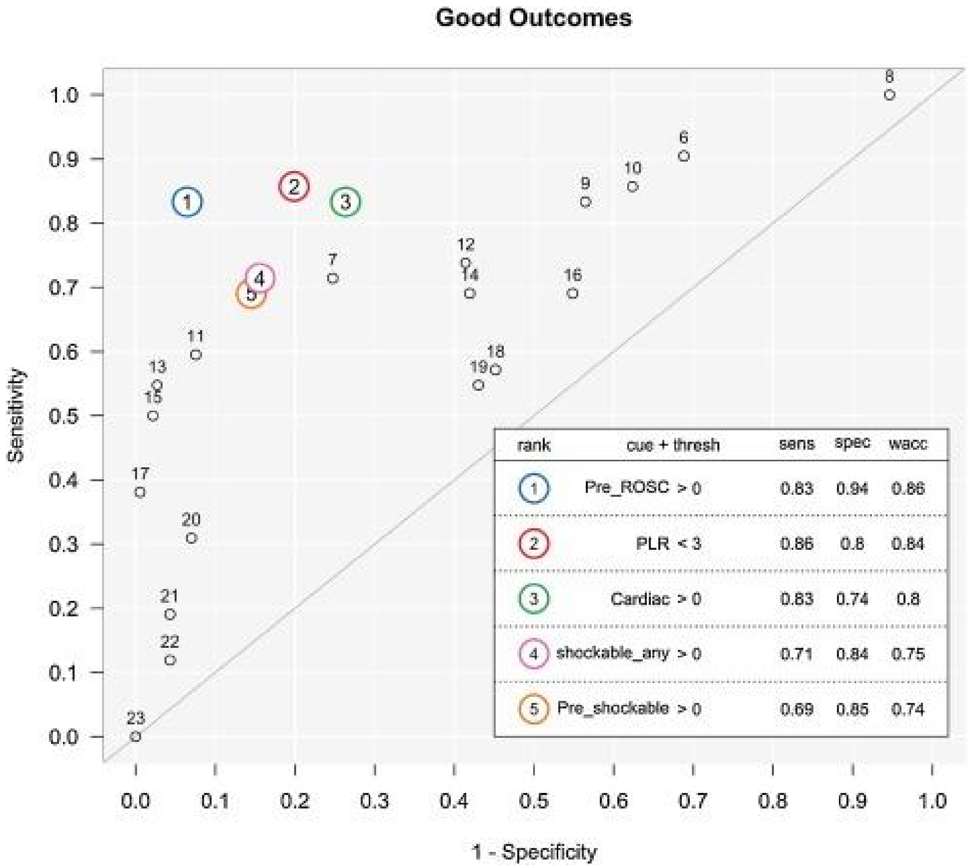

Figure 2. The top five cues with highest WACC are visualised with sensitivity, specificity, and WACC. With the exception of PLR, if the cue value is true, the value is coded as 1. If the value is false, it is coded as 0. The prompt, sluggish, and fixed PLR are coded as 1-3 respectively.

thresh, threshold; sens, sensitivity; spec, specificity; WACC, weighted accuracy; Pre_ROSC, prehospital return of spontaneous circulation; PLR, pupillary light reflex responses; shockable_any, any shockable rhythm; and Pre_shockable, prehospital shockable rhythm.

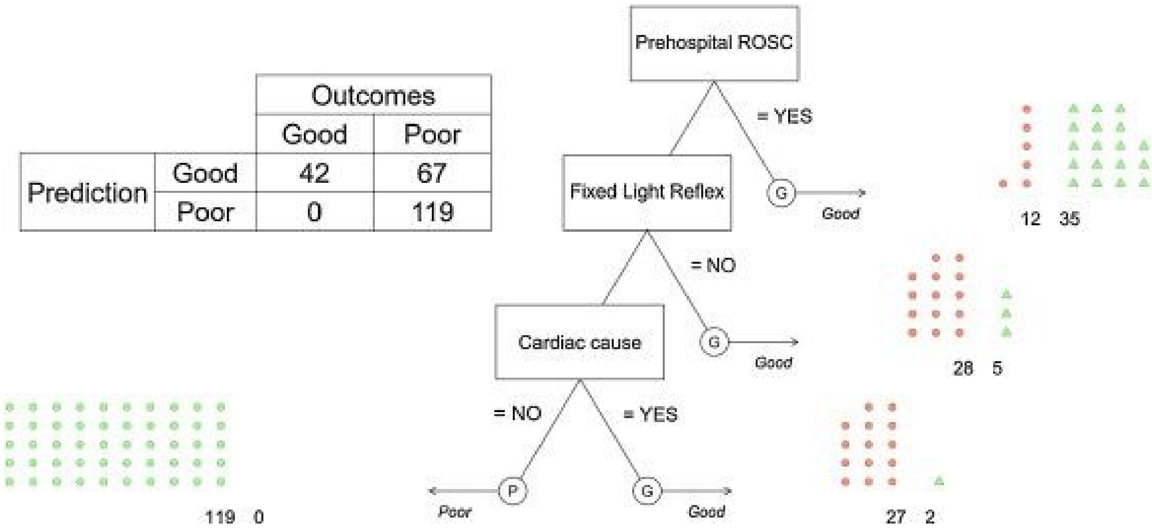

Figure 3. A training tree shows true-positive, true-negative, false-positive, and false-negative cases classified at each node. Forty-seven patients with prehospital ROSC were classified as having good neurologic outcomes. Of these, 12 had a poor outcome and 35 had a good outcome. Thirty-three patients without fixed light reflex were classified as having good neurologic outcomes. Of these, 28 had a poor outcome and 5 had a good outcome. Twenty-nine patients with cardiac cause were classified as having good neurologic outcomes. Of these, 27 had a poor outcome and 2 had a good outcome. One hundred and nineteen patients without cardiac cause were classified as having poor neurologic outcomes and all had a poor outcome.

ROSC, return of spontaneous circulation.

Table 4. Diagnostic performance of fast-and-frugal tree model in training and test cohorts*

	Training cohort	**Test cohort**
Sensitivity	100% (91.6%–100%)	95.5% (84.5%–99.4%)
Specificity	64.0% (56.6%–70.9%)	57.6% (50.1%–64.8%)
ROC area	0.820 (0.785–0.854)	0.765 (0.718-0.813)
Positive predictive value	38.5% (29.4%–48.3%)	35.0% (26.5%–44.2%)
Negative predictive value	100% (96.9%–100%)	98.1% (93.5%–99.8%)

ROC, receiver operating characteristics.

* Data were presented as value (95% confidence intervals).

3.4 Testing the FFT for the prediction of neurological outcomes

Forty-four patients (19.3%) in the test cohort experienced good neurological outcomes. Figure 4 shows that 58 patients who experienced ROSC prior to arriving at the hospital were classified as having good neurological outcomes. Thirty-six patients with prompt or sluggish pupillary light reflex responses were classified as having good neurological outcomes. Then, 108 patients without cardiac causes were classified as having poor neurological outcomes, while 26 patients with cardiac cause were classified as good poor neurological outcomes. Sensitivity, specificity, AUC, positive predictive value, and negative predictive value of the decision tree for predicting good neurological outcomes were 95.5%, 57.6%, 0.765, 35.0%, and 98.1%, respectively (Table 4).

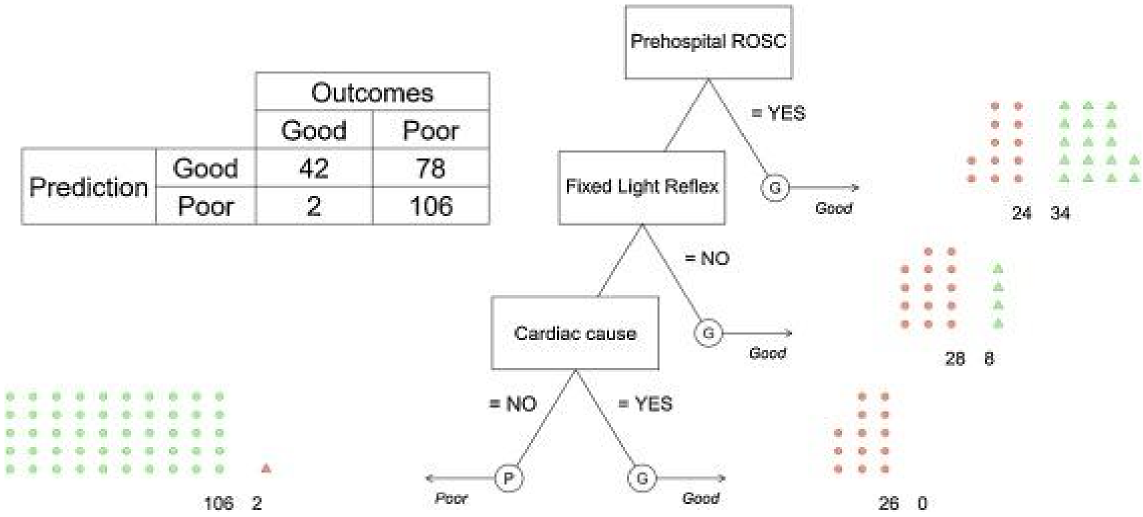

Figure 4. A test tree shows true-positive, true-negative, false-positive, and false-negative cases classified at each node.

Fifty-eight patients with prehospital ROSC were classified as having good neurologic outcomes. Of these, 24 had a poor outcome and 34 had a good outcome. Thirty-six patients without fixed light reflex were classified as having good neurologic outcomes. Of these, 28 had a poor outcome and 8 had a good outcome. Twenty-six patients with cardiac cause were classified as having good neurologic outcomes and all had a poor outcome. One hundred and eight patients without cardiac cause were classified as having poor neurologic outcomes. Of these, 106 had a poor outcome and 2 had a good outcome.

ROSC, return of spontaneous circulation.

IV. Discussion

In the present study, we constructed and validated a simple FFT prediction model for patients with OHCA who have experienced ROSC. Our findings indicated that patients with favourable neurological outcomes can be identified based on three simple variables in the early period following ROSC (prehospital ROSC, light reflex responses, and cardiac cause). Performance analysis in the test cohort revealed that the FFT model had a sensitivity of 95.5% and negative predictive value of 98.1%. It is notable that, although the FFT model is simple, its accuracy was comparable to that of other complex classification algorithms [7-9]. Thus, our findings suggest that the FFT model is not only fast and frugal, but also helpful for predicting neurological outcomes in patients with OHCA during early post-resuscitation period.

As briefly described above, multivariate logistic regression analysis has disadvantage over tree-based model, especially for the binary decision making like this study. Multivariate logistic regression model requires both complex formulas to calculate probabilities and the specific cut-off value of the predicted probability to make a clinical decision. Even though researchers usually provide the simplified scoring system and the specific cut-off values for the risk stratification, those scoring systems are not widely used in the clinical practice [7-9].

Several studies have employed decision tree-based models to predict outcomes following cardiac arrest. These tree-based methods rely on recursive partitioning algorithms to determine predictor nodes with high discriminating ability [16]. CART, one of the most popular classification tree algorithms, has been widely investigated for its ability to identify patients with high or low likelihood of discharge with good neurological function [10-12]. CART models do not make any assumptions regarding the values of classifiers and are able to handle any type of data. However, one of the major limitations of CART is that, as a regression-based algorithm, it is susceptible to overfitting during the training phase. That is, noise in the data may lead to different trees, and a large amount of data is thus required to calibrate for such fluctuation and instability [16]. In contrast, FFTs are robust against overfitting, and can make good predictions based on a small amount of relatively noisy data [13, 15, 17].

In the present study, we used FFT analysis to select for three variables that can be used to predict which patients will attain discharge CPC values of 1 or 2. The most crucial factor for predicting favourable neurological outcomes was prehospital ROSC status, followed by the presence of a prompt light reflex and arrest due to cardiac aetiology, respectively. Our findings are consistent with those of previous studies, which have demonstrated that prehospital ROSC is among the most important factors for predicting survival from OHCA [2, 8, 11, 18]. Careful neurological examination is essential for predicting neurological outcomes following cardiac arrest. Previously, Greer et al. reported that the pupillary reflex can be used for predicting outcomes as early as day 0 [19]. In addition, one recent study has reported that quantitative pupillary light reflex values are highly accurate in predicting long-term neurological prognosis following cardiac arrest [20]. Taken together, these finding indicate that simple bedside evaluation of the pupillary light reflex can aid in predicting neurological outcomes during the early post-resuscitation period. Furthermore, it is well known that cardiac causes of OHCA are associated with hospital survival and good neurological outcomes [11, 21]. However, the decision for determining cardiac aetiology was at the discretion of the attending physician. A previous study reported that the accuracy of such assumptions is approximately 89% [22].

The most recent guidelines recommend that registries and researchers report the outcomes of all EMS-treated patients with cardiac arrest and continue to record the pathogenesis of cardiac arrest as medical (presumed cardiac or unknown, other medical causes), traumatic, drug overdose, drowning, or asphyxia [23]. In this study, cardiac aetiology was presumed in the absence of non-cardiac causes such as asthma, pneumonia, subarachnoid haemorrhage, gastrointestinal haemorrhage, or advanced malignancy [24]. Although cardiac aetiology did not provide a discriminating ability in the test cohort, presumed cardiac cause exhibited a higher accuracy than shockable rhythm when predicing neurological outcomes in the training cohort.

The present study possesses several limitations of note. First, our model classified two patients with good neurological outcomes into the poor outcome group in the test cohort. Although the negative predictive value of the FFT model in training cohort was 100%, current guidelines recommend that the false-positive rate should be close to 0% when predicting poor outcomes [6]. Therefore, this model should not be used as a sole basis for the withdrawal of life-sustaining treatment. Second, number of patients with a good outcome in test cohort was only 44. Consequently, the 95% confidence intervals were quite wide in table 3. Third, the validity of the FFT model was tested internally. Neurologic prognosis of patients with cardiac arrest, especially long-term prognosis, may vary depending on the subsequent care provided. Further studies using heterogenous cohorts with more patients are required to determine the validity and generalisability of the model.

Despite these limitations, the FFT model is advantageous due to its frugality, as it utilises a maximum of three cue values for classification. Also, relative to CART models, FFT models are heuristic, enabling accurate prediction based on small amounts of noisy data. We believe that this simple model will be particularly helpful for physicians working in the ED. Taken together, our findings demonstrated that a simple decision rule developed via FFT analysis can aid clinicians in predicting neurological outcomes following ROSC in patients with OHCA.

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요약(국문초록)

목표

병원 밖의 심정지 환자의 신경학적 예후를 예측하기 위해 다양한 정량적 방법이 개발되었지만 임상적으로 사용하기에는 너무 복잡하다. 본 연구는 Fast-and-Frugal tree 분석을 이용하여 병원 밖 심정지 환자에서 자발 순환 회복 후 신경학적 예후를 예측하기 위한 간단한 의사 결정 규칙을 개발하고자 하였다.

방법

본 연구에서는 3개 병원의 레지스트리에 보관된 전향적으로 수집된 데이터에 대해 후향적 분석을 시행하였다. 양호한 신경학적 예후는 퇴원 후 28일에 뇌 기능 수행 범주(cerebral performance category, CPC) 점수 1 또는 2 점으로 정의되었다. Fast-and-Frugal tree 분석에 사용 된 변수에는 나이, 성별, 심정지 목격자 여부, 현장 심폐소생술 여부, 초기 쇼크 리듬, 병원 전 제세동, 병원 전 자발 순환회복, 무관류 시간(no flow time), 저관류 시간(low flow time), 심정지 원인, 동공 빛 반사, 자발 순환 후 Glasgow Coma Scale 점수가 있다.

결과

등록 된 456명의 환자 중 86명(18.9%)이 양호한 신경학적 예후가 예측되었다. 병원 전 자발순환 회복 여부, 자발 순환 직후 즉각적인 동공 빛 반사, 심장 원인에 의한 심정지, 이 세 가지 요인이 의사결정 트리의 노드로 선택되었다. 좋은 신경학적 결과를 예측하기 위한 결정 트리의 민감도, 특이도, 양성 예측도, 음성 예측도는 100 % (42/42), 64.0 % (119/186), 38.5 % (42/109), 100 % 119/119), 시험 세트(test set)에서는 95.5 % (42/44), 57.6 % (106/184), 35.0 % (42/120), 98.1 % (106/108)이었다.

결론

Fast-and-Frugal tree 분석을 통하여 개발 된 간단한 의사결정 규칙은 임상의가 병원 밖 심정지 환자의 자발순환 후에 따른 신경학적 결과를 예측하는데 도움이 될 수 있다.

주요어: 심정지, 신경학적 예후, 예측, 병원 밖 심정지, 의사결정트리

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