RESEARCH



Factors affecting neurological outcomes of patients with sudden cardiac arrest in the emergency department



Kyeongmin Jang¹, Hye-Min Hwang² and Yon Hee Seo^{3*}

Abstract

Background Little is known about patients with sudden cardiac arrest in the emergency department (ED). This study aimed to identify factors affecting the prognosis of patients with cardiac arrest in the ED.

Methods This retrospective study analyzed patients with sudden cardiac arrest admitted to the ED of a general hospital between January 2016 and July 2020. A total of 153 patients with sudden cardiac arrest were identified, and 149 patients for whom all data could be confirmed were included in the statistical analysis of this study. A good neurological outcome was defined as a Cerebral Performance Category (CPC) scale score of 1 or 2, assessed 6 months after discharge.

Results In the univariate analysis, the characteristics of patients included in the good neurological outcomes group were younger (t = 3.553, p < .001), had shorter low flow time (t = 3.31, p = .019), and had more shockable initial rhythms (χ^2 = 28.038, p = < .001). As a result of multivariate binary logistic regression analysis, among 43 patients alive 6 months after discharge, age 60 years or younger (odds ratio = 32.703, p = .005), low flow time 6 min or less (odds ratio = 38.418, p = .006), and initial shockable rhythm (odds ratio = 31.214, p < .001) were identified as predictors that had a significant impact on good neurological outcomes.

Conclusions Young age, short low-flow-time, and initial shockable rhythm are predictors of good neurological outcomes in patients with acute cardiac arrest in the ED.

Keywords Emergency department, Cardiac arrest, Neurological outcome, Binary logistic regression

Background

Most cardiac arrest studies have been conducted with a focus on out-of-hospital cardiac arrest (OHCA) rather than in-hospital cardiac arrest (IHCA) [1, 2]. Generally,

cardiac arrest is classified into IHCA and OHCA, depending on its location. IHCA is defined as the need for chest compression or defibrillation in hospitalized patients [3]. Contrary to expectations, the prognosis of patients with IHCA can be worse than that of patients with OHCA, and the survival rate (the percentage of patients who achieve sustained return of spontaneous circulation and are discharged from the hospital alive) has been reported to be approximately 10–20% [4, 5]. This poorer prognosis is often due to the fact that many patients who experience IHCA are initially in a more critical condition, which impacts their likelihood of survival compared to those experiencing OHCA [6].



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The emergency department (ED) is staffed by medical staff 24 h a day and has abundant available medical resources, including emergency medical equipment. Therefore, patients with cardiac arrest in the ED have several characteristics associated with more favorable outcomes [7]. That is, they are more likely to have ventricular arrhythmias with an early beat rhythm, start chest compressions earlier, and can be defibrillated more quickly than patients with OHCA or non-ED IHCA patients [7]. Furthermore, cardiac arrest that occurs in the ED has a higher rate of potentially reversible etiology and a higher chance of neurologically intact survival than OHCA and IHCA that occur in places other than the ED [8]. In some studies that retrospectively analyzed more than 60,000 IHCA events, approximately 22% of patients with cardiac arrest in the ED were discharged alive, and approximately 10% survived for more than 6 months. Additionally, patients with cardiac arrest occurring in the ED have a better neurological prognosis than those with IHCA occurring outside the ED [8, 9].

Although cardiac arrests occurring in the ED account for approximately 10% of all patients with IHCA cases [7, 10], only a few studies have investigated the incidence of cardiac arrest in the ED separately. It was also difficult to identify studies that identified factors affecting prognosis. Therefore, this study attempted to determine the characteristics of patients with cardiac arrest in the ED and the factors affecting the survival-discharge rate and neurological prognosis.

Methods

Study design

This retrospective study reviewed and analyzed the electronic medical records (EMR) of patients with cardiac arrest admitted to the ED of a general hospital in Seoul, Korea. The hospital where this study's data was collected is a residency training hospital and the largest public hospital in the Republic of Korea. The ED of this hospital receives approximately 50,000 to 60,000 patients annually, with around 300 OHCA patients being admitted each year. Advanced resuscitation was performed for sudden cardiac arrests occurring within the ED, except in cases where prior consent had been given in a POLST (Physician Orders for Life-Sustaining Treatment) form to not attempt CPR, or where a DNR (Do Not Resuscitate) form had been signed by the next of kin. In the emergency department, a five-level triage tool known as the Korean Triage and Acuity Scale (KTAS) was utilized to categorize patients based on the severity of their condition. The KTAS ranges from Level 1, indicating the most urgent cases requiring immediate resuscitation, to Level 5, which denotes the least urgent, non-emergency situations. This triage system facilitates the prioritization of patient care and the efficient allocation of medical resources.

Data collection

For this study, patients with cardiac arrest that occurred in the ED of a hospital over a period of approximately 5 years from January 2016 to July 2020 were selected according to the following selection criteria: 1) aged 18 years or older, 2) cardiac arrest occurring in the ED Patients for whom advanced resuscitation was performed, and 3) patients for whom data required for statistical analysis could be collected. However, from August 2020, when the number of confirmed COVID-19 cases began to increase rapidly, the number of patients with respiratory cardiac arrest in the ED increased, and there were changes in advanced resuscitation methods and CPR endpoints; therefore, only data up to July 2020 were collected. The total number of patients who visited the emergency room of one hospital where data was collected during this period was confirmed to be 265,782. The ED where this study was conducted is a residency training hospital staffed by emergency medicine specialists. Therefore, advanced life support (ALS) is primarily administered by emergency medicine personnel. After achieving return of spontaneous circulation (ROSC), patients are admitted to the intensive care unit (ICU) for post-cardiac arrest care. Depending on the cause of the cardiac arrest, patients may then be transferred to departments such as cardiology, neurosurgery, or general surgery. All patients with cardiac arrest that occur outside the hospital are admitted through the ED. OHCA was excluded in this study.

Preexisting conditions according to the utstein style

The preexisting conditions of the patients included in this study were recorded following the Utstein style.

The conditions noted among the patients were as follows: Coronary Artery Disease (CAD): 46 (30.9%) of patients had a history of coronary artery disease, which is a significant risk factor for cardiac arrest.

Heart Failure: 19 (12.8%) of patients had been diagnosed with heart failure prior to the cardiac arrest event.

Hypertension: 51 (34.2%) of patients had a history of hypertension.

Diabetes Mellitus: 29 (19.5%) of patients had diabetes mellitus, which can contribute to cardiovascular complications.

Chronic Obstructive Pulmonary Disease (COPD): 5 (3.4%) of patients had COPD, which can affect respiratory function and overall cardiac health.

Chronic Kidney Disease (CKD): 38 (25.5%) of patients were identified with chronic kidney disease.

Previous Stroke: 63 (42.3%)% of patients had a history of stroke.

Peripheral Artery Disease (PAD): 0% of patients had peripheral artery disease.

Primary outcomes

Primary outcomes were measured according to the Utstein reporting system and included the achievement of sustained Return of Spontaneous Circulation (ROSC) lasting more than 20 min, survival to discharge, and good neurological outcomes. Neurological outcomes were assessed using the Cerebral Performance Category Scale (CPC) at discharge. In this study, neurological outcomes were assessed 6 months after discharge, and a good neurological outcome was defined as a CPC score of 1 or 2.

Secondary outcomes

Secondary outcomes were the factors that influenced good neurological outcomes in patients with sustained ROSC. Among patients with cardiac arrest in the ED, with sustained ROSC, those with good and poor neuro-logical outcomes were compared, and statistically significant variables affecting good neurological prognosis were identified. Poor neurological outcomes in this study were defined as a Cerebral Performance Category (CPC) score of 3, 4, or 5, where a score of 5 indicates death.

Ethical considerations

This study was conducted after being approved by the Clinical Research Review Committee of the hospital to which the researchers belonged (No. 20200916/30–2020-51/089). Informed consent was waived by the Clinical Research Review Committee due to the retrospective nature of the study. The collected medical record data were scientifically and ethically managed in accordance with the standards set by the Clinical Research Review Committee and relevant laws and regulations, including the Personal Information Protection Act. EMR data were obtained from the person in charge of the researcher's institution, without any identifying information. EMR data were stored in separate files under the responsibility of the researcher. The collected data will be encrypted and stored in a separate lock for 3 years.

Statistical analysis

The data collected in this study were statistically processed using the SPSS/WIN 29.0 program (IBM Corp., Armonk, NY, USA) and the MedCalc 22.016 program (MedCalc Softwase Ltd., Oostende, Belgium), and the specific methods are as follows. To identify general characteristics, categorical variables were analyzed using descriptive statistics and presented as frequencies and percentages. Continuous variables were presented as means and standard deviations. For comparisons between groups, continuous variables were analyzed using the independent sample Student's t-test, and categorical variables were analyzed using the chi-square test. Binary logistic regression analysis was used to identify the factors affecting sustained ROSC and good neurological outcomes. If the independent variable was continuous, the cutoff value was obtained through receiver operating characteristic (ROC) curve analysis and divided into dichotomous types. The level of statistical significance was set at p < 0.05.

Results

Characteristics of patients with cardiac arrest occurring in the ED

A total of 153 patients experienced cardiac arrest in the ED between January 2016 and July 2020. Excluding 4 patients with insufficient or unclear data for statistical analysis, including 3 patients who transferred to another hospital after ROSC and 1 patient with no record of cardiac arrest rhythm, 149 patients were included in the statistical analysis (Fig. 1).

The characteristics of the patients with cardiac arrest in the ED are shown in Table 1. Around 44.3% were male, the average age was 67.8 years, 53.7% had CPC 1–2 before cardiac arrest, and 45% had CPC 3. The average low flow time was 18.6 min, the advanced airway was endotracheal intubation in 59.7%, I-gel, a supraglottic airway in 14.1%, and an advanced airway was not secured in 26.2%. The initial cardiac arrest rhythm was shockable in 21.5% of cases, and sustained ROSC lasting > 20 min was observed in 55.7%. Most patients who acquired ROSC in the ED were admitted to the ICU, and 22.8% of all patients with ED cardiac arrest survived. As a result of evaluating CPC after 6 months, CPC 1–2 was 14.1%.

Factors influencing ROSC among patients with cardiac arrest in the ED

Among patients with cardiac arrest in the ED, 83 (55.7%) in the sustained ROSC group lasting > 20 min were compared with 66 (44.3%) in the no ROSC group. The results showed that the sustained ROSC group was younger than the no ROSC group (p < 0.001, t=4.944), the initial rhythm was often shockable (p < 0.001, X2=17.049), and the low flow time was shorter (p < 0.001, t=9.993) (Table 2). There were no significant differences between the groups in terms of sex, availability of an advanced airway, or precardiac arrest CPC.

Among the independent variables, the continuous variables age and low flow time were analyzed using the ROC curve to confirm the Youden index, which can predict a





Fig. 1 Flowchart of the study patients follow-up

emergency department (ED)			
Variable	Categories	Mean (SD) or n (%)	
Sex	Male sex	66 (44.3)	
Age	Years	67.8 (14.44)	
CPC before cardiac arrest	CPC 1	4 (2.7)	
	CPC 2	76 (51.0)	
	CPC 3	67 (45.0)	
	CPC 4	2 (1.3)	
	CPC 5	0 (0)	
CPR duration	Minutes	18.6 (15.93)	
Advanced airway	Endotracheal tube	89 (59.7)	
	l-gel	21 (14.1)	
	No	39 (26.2)	
Initial rhythm	Shockable	32 (21.5)	
	Non-shockable	117 (78.5)	
CPR results	Sustained ROSC	83 (55.7)	
	Any ROSC	22 (14.8)	
	No ROSC	44 (29.5)	
Disposition of ED	Transfer to ICU	60 (40.2)	
	Death in ED	89 (59.8)	
	CPC 1	4 (2.7)	
CPC after 6 months	CPC 2	17 (11.4)	
	CPC 3	12 (8.1)	
	CPC 4	19 (12.8)	
	CPC 5	97 (65.1)	

 Table 1
 Characteristics of patients with cardiac arrest in the emergency department (ED)

SD Standard deviation, CPC Cerebral performance category scale,

CPR Cardiopulmonary resuscitation, ROSC Return of spontaneous circulation, ED Emergency department, ICU Intensive care unit good neurological prognosis. The results showed that the age was 70 years (p < 0.001, AUC=0.720) and low flow time was 8 min (p < 0.001, AUC=0.823). To identify factors affecting sustained ROSC lasting more than 20 min in patients with cardiac arrest in the ED, continuous variables were converted to dichotomous variables and analyzed using binary logistic regression. The variables that significantly influenced sustained ROSC were age <70 years (p=0.029, OR=3.044), low flow time <8 min (p<0.001, OR=55.443), and initial shockable rhythm (p=0.001, OR=10.493) (Table 3).

Factors influencing good neurological outcome among patients with sustained ROSC

Among the 43 patients with survival discharged, 21 (25.3%) out of 83 patients with ROSC had a good neurological prognosis as CPC 1 or 2 in the neurological prognosis evaluation 6 months after discharge, and 22 patients did not (26.5%). The results showed that younger age (p < 0.001, t=3.553), shorter low flow time (p = 0.019, t=3.310), early shockable rhythm (p < 0.001, 28.038), and CPC score of 1 or 2 before cardiac arrest (p < 0.001, X²=19.507) were found to have a statistically significantly better prognosis (Table 4).

Among the independent variables, the continuous variables age and Low flow time were analyzed using the ROC curve to confirm the Youden index, which can predict a good neurological prognosis. The results showed that the age was 60 years (p < 0.001, AUC = 0.759) and the Low flow time was 6 min (p = 0.005, AUC = 0.798). To identify the factors that affect the neurological outcomes of patients with cardiac arrest occurring in the

Variables	Categories	Sustained ROSC (n = 83) n (%) or mean (SD)	Non-ROSC (n = 66) n (%) or mean (SD)	t or X ²	р
Sex	male sex	37 (45.1)	29 (43.3)	0.006	.535
Age	years	63.36 (14.168)	74.11 (11.806)	4.944	<.001
Advanced airway	intubation	49 (59.0)	40 (60.6)	0.278	.87
	I-gel	11 (13.3)	10 (15.2)		
	none	23 (27.7)	16 (24.2)		
Defibrillation	yes	28 (33.7)	7 (10.6)	10.943	<.001
Initial rhythm	VF	20 (24.1)	3 (4.5)	17.049	<.001
	pulseless VT	8 (9.6)	1 (1.5)		
	PEA	49 (59.0)	53 (80.3)		
	asystole	6 (7.2)	9 (13.6)		
Low flow time	minutes	9.32 (8.435)	30.39 (15.389)	9.993	<.001
CPC before arrest	CPC 1	7 (8.4)	0 (0)	6.044	.11
	CPC 2	42 (50.6)	34 (51.5)		
	CPC 3	33 (39.8)	31 (47)		
	CPC 4	1 (1.2)	1 (1.5)		
Outcomes	Survival discharged	51 (61.4)			
	Survival six months	43 (51.8)			

Table 2 Comparison between Sustained ROSC and non-ROSC groups

ROSC Return of spontaneous circulation, SD Standard deviation, VF Ventricular fibrillation, VT Ventricular tachycardia, PEA Pulseless electrical activity, ALS Advanced life support, CPC Cerebral performance category scale

Predictors	В	OR	p	Lower 95%	Upper 95%
Female sex	0.911	2.485	.076	0.91	6.785
Age: below 70 years	1.113	3.044	.029	1.119	8.282
CPC 1 or 2 before cardiac arrest	0.235	1.265	.643	0.468	3.421
Low flow time: 8 min or less	4.015	55.443	.001	13.839	222.13
Advanced airway	0.505	1.546	.187	0.383	6.242
Initial shockable rhythm	2.351	10.493	<.001	2.55	43.186

Summary statistics Model $X^2 = 26.756$, p < .001 Hosmer–Lemeshow test $X^2 = 4.272$ (DF=7, p = .968) Nagelkerke $R^2 = 0.624$

ROSC Return of spontaneous circulation, ED Emergency department, OR Odds ratio, CPC Cerebral performance category scale, ALS Advanced life support

ED, continuous variables were converted into dichotomous variables and analyzed using binary logistic regression. As a result, if the age was below 60 years (p=0.005, OR=32.703), if the Low flow time was less than 6 min (p=0.001, OR=38.418), and if the initial rhythm was shockable rhythm (p<0.001, OR=351.214), they were found to have a significant impact on good neurological prognosis (Table 5). Sex and whether an advanced airway was obtained before ROSC did not appear to have significant effects on good neurological outcomes.

Discussion

Few studies have investigated the prognosis of cardiac arrest patients in the ED [5] (see also Wiberg et al. 2020 [11]). Our study was limited to patients with cardiac

arrest admitted to the ED of a single general hospital. However, it is significant in that it identifies the characteristics of patients with sudden cardiac arrest that occurred over a period of approximately 5 years and the factors that affect their prognosis. To summarize the main results, first, the prevalence of cardiac arrest among patients who visited the ED was 0.72 per 1,000; second, approximately 55% of these patients acquired ROSC; and third, among patients with cardiac arrest in the neurological prognosis evaluation after 6 months, approximately 14.1% showed good neurological prognosis. By comparing these key results with those of previously published studies, we aimed to help predict the prognosis of patients with cardiac arrest in the ED.

Variables	Categories	Good outcome	Poor outcome	t or X ²	p
		(<i>n</i> =21)	(n=22)		r
Sex	male sex	12 (57.1)	12 (54.8)	0.74	.854
Age	years	54.48 (11.111)	66.37 (13.892)	3.553	<.001
Advanced airway	intubation	14 (66.7)	12 (54.5)	4.324	.115
	I-gel	0 (0)	4 (18.2)		
	none	7 (33.3)	6 (25.8)		
Initial shockable rhythm	yes	17 (81.0)	3 (13.6)	28.038	<.001
Initial rhythm	VF	13 (61.9)	3 (13.6)	17.049	<.001
	pulseless VT	4 (19.0)	0 (0)		
	PEA	4 (19.0)	14 (63.6)		
	asystole	0 (0)	2 (9.0)		
Low flow time	minutes	5.62 (4.364)	10.58 (9.114)	3.31	.019
CPC before arrest	CPC 1 or 2	21 (100)	9 (40.9)	19.507	<.001

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lable 4	Comparison	between	the good and	l boor neurolog	aical prognosis groups

VF Ventricular fibrillation, VT Ventricular tachycardia, PEA Pulseless electrical activity, ALS Advanced life support, CPC Cerebral performance category scale

Table 5 Predictors of good neurological outcomes in patients

 with cardiac arrest in the ED
 ED

Predictors	В	OR	р	Lower 95%	Upper 95%
Female sex	1.183	3.266	.215	0.502	21.237
Age: below 60 years	3.487	32.703	.005	2.851	375.066
Low flow time: 6 min or less	3.649	38.418	.006	2.844	518.935
Advanced airway	1.835	6.262	.095	0.728	53.891
Initial shockable rhythm	5.861	31.214	<.001	15.503	795.668

Summary statistics

Model $X^2 = 52.052, p < .001$

Hosmer and Lemeshow test $X^2 = 4.033$ (DF = 7, p = .776)

Nagelkerke R²=0.540

ED Emergency department, OR Odds ratio, CPC Cerebral performance category scale, ALS Advanced life support

EDs are staffed 24 h a day and have abundant medical resources available [12]. Therefore, if sudden cardiac arrest occurs in the ED, the prognosis is expected to be good because immediate action is possible. However, contrary to this expectation, the results were not significantly different from the prognosis of patients with cardiac arrests that occurred in a hospital rather than in an ED. In one study [13], approximately 49% of patients with cardiac arrest in the ED acquired ROSC. In another study [14], the survival-discharge rate of patients with cardiac arrest in the ED was 5.6%, and the neurological outcome evaluated at 6 months was CPC 1 or 2 in 4.5%. In another study [15], the survival rate of patients with cardiac arrest in the ED was 25.6%, and the neurological outcome was a CPC score of 1 or 2 in 19% of the patients. The incidence of ROSC in patients with cardiac arrest occurring in the ED varies from approximately 25 to 50%, and the incidence of good neurological outcomes 6 months after evaluation varies from approximately 5 to 19%. These results are not significantly different from those of our study. Therefore, the question arises regarding what factors are associated with a good neurological prognosis. Previous studies have shown that the time required to start the first CPR, whether cardiac arrest was witnessed, the initial beat of the cardiac arrest, and whether ALS was approaching were related to whether cardiac arrest patients acquired ROSC and good neurological outcomes [15]. In a study conducted in Thailand to identify factors associated with survival after cardiac arrest, the likelihood of acquiring ROSC was 10.8 times higher when the pre-cardiac arrest CPC scores were 1 and 2 [16].

First, if the initial rhythm at the time of cardiac arrest was found to be shockable, such as VF or pulseless VT, it was shown to be a strong predictor of good neurological outcome. Patients with OHCA have a good prognosis if the initial rhythm is shockable rhythm [17, 18]. Patients with cardiac arrest in an ED are more likely to be detected earlier than in patients with cardiac arrest in a hospital rather than in an ED; the success rate may be high if the patient has a shockable rhythm. In the present study, approximately 33% of the initial rhythms that occurred in the ED were shockable rhythms, VF, or pulseless VT. In another study [19], among the cardiac arrest rhythms that occurred in the ED, systole accounted for the most, at approximately 50%, and the shockable rhythm, VF, or pulseless VT, was approximately 16%. In this study, the ROSC acquisition rate of approximately 50% in the ED was believed to be due to the high rate of nonshockable rhythm in the initial rhythm. Even in patients with cardiac arrest admitted in the hospital rather than in the ED,

the survival rate is high if the initial rhythm is shockable [18, 20].

Age is one of the most important variables for predicting the prognosis of patients with in-hospital cardiac arrest [5, 21]. In an observational study including 234,767 IHCA patients from 2000 to 2016, those aged below 50 years showed the highest ROSC achievement rate, survival rate, and good neurological outcomes, followed by those aged under 50–60 years, and showed good neurological outcome. However, as age increases, the rate of achieving ROSC, survival, and likelihood of good neurological outcomes appear to decrease [11]. In most studies, younger age was associated with a higher resuscitation rate, survival rate, and good neurological outcomes. In our study, younger age was more advantageous for acquiring ROSC, and age was highly correlated with a good neurological prognosis.

Low-flow-time is an important variable for predicting prognosis in all patients with cardiac arrest. In the United States, more than 290,000 in-hospital cardiac arrest cases occur annually, and their prognosis is favorable when the low flow time is short [4]. In a correlation study that confirmed the relationship between low flow time and ROSC in 311 patients with in-hospital cardiac arrest [22], the results showed that there was a high risk of being declared dead if low flow time exceeded 15 min. Only few studies have been conducted on low flow time in patients with cardiac arrest in the ED. In a study [23] that investigated 78 patients with cardiac arrest that occurred in the ED of a single hospital over a period of approximately 2 years found that the average low flow time of patients who acquired ROSC was shorter than that of non-ROSC patients. Our study also found that the low flow time was shorter in the ROSC group and in the group with good neurological prognosis than in the group without a good neurological prognosis. In particular, binary logistic regression analysis showed that the likelihood of a good neurological prognosis was 38 times higher when the low flow time was 6 min or less. These results may be because as low flow time increases, perfusion pressure to cerebral blood flow decreases and brain damage increases accordingly. Another reason is that, because the low flow time was short, ROSC could be achieved quickly, which would increase the likelihood of a good neurological prognosis.

However, this study has several limitations. First, because this was a retrospective study conducted in the ED of a teaching hospital, the number of participants was small, making it difficult to generalize the study results. Second, this study did not investigate the subjects' chief complaint or principal diagnosis. Third, there may be potential biases in data collection and patient selection inherent in retrospective studies. Lastly, the study did not account for all possible confounding factors that could influence patient outcomes, such as differences in post-resuscitation care.

Conclusions

Few studies have investigated the prognosis of patients with cardiac arrest in the ED. Our results showed that 55.7% of patients with cardiac arrest in the ED achieved ROSC, and 25.3% of these patients had good neurological outcomes at 6 months. Factors affecting good neurological outcomes in patients with cardiac arrest occurring in the ED were young age (less than 60 years), short low flow time (less than 6 min), and initial shockable rhythm. These results were not significantly different from those of factors affecting the prognosis of patients with in-hospital cardiac arrest.

Abbreviations

IHCA	In-hospital cardiac arrest
OHCA	Out-of-hospital cardiac arrest
ED	Emergency department
EMR	Electronic medical records
CPC	The Cerebral Performance Category Scale
ROSC	Return of Spontaneous Circulation
ROC	Receiver operating characteristic
ICU	Intensive care unit
ALS	Advanced life support
CPR	Cardiopulmonary resuscitation
VF	Ventricular fibrillation

- VT Ventricular tachycardia
- PEA Pulseless electrical activity

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Authors' contributions

KJ contributed to the concept and design of the study, the collection and analysis of data, and the drafting of the manuscript. YHS and H-M Hwang contributed to the concept and design of the study, statistical analysis, and interpretation of results. All the authors have read and approved the final version of this manuscript.

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Availability of data and materials

The datasets used and/or analyzed in this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the SMG-SNU Boramae Medical Center Institutional Review Board (IRB approval number: 20200916/30–2020-51/089). As a result of the research ethics review, the need for Informed Consent was waived off by a the SMG-SNU Boramae Medical Center Institutional Review Board. All the steps/ methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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