ORIGINAL ARTICLE

Predictors of neurologically favorable survival among patients with out-of-hospital cardiac arrest: A tertiary referral hospital experience

Hastane dışında kalp durması olan hastalarda nörolojik iyi durumla hayatta kalımı belirleyen etmenler: Üçüncü basamak hastane tecrübesi

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ABSTRACT

Objective: Despite recent advances in medical support and interventions, only 5% to 10% of patients with out-of-hospital cardiac arrest (OHCA) survive to discharge. In this study, factors related to neurologically favorable survival in patients with OHCA were analyzed.

Methods: A total of 129 patients who were admitted to hospital with OHCA were retrospectively enrolled.

Results: Sustained return of spontaneous circulation (ROSC) (ROSC lasting >20 min) was achieved in 29 (22.4%) patients. Percentage of cardiac arrests with ischemic etiology was significantly higher in successful ROSC group (p<0.001). In multivariate logistic regression analysis, cardiac arrest with ischemic etiology (p=0.004) and cardiopulmonary resuscitation (CPR) duration (p=0.013) were found to be independent predictors for ROSC. One-minute increment in CPR duration was associated with 1.202-fold increase in failure to achieve ROSC. Among patients with ROSC, 7 (5.4%) survived to hospital discharge, and 1-minute increment in CPR duration was associated with a 1.123-fold decrease in neurologically favorable survival (p=0.005).

Conclusion: In patients with OHCA, ischemic etiology is associated with better ROSC rate compared to other reasons for cardiac arrest, and patients with prolonged CPR are less likely to survive.

ÖZET

Amaç: Tıbbi destek ve girişimlerdeki ilerlemelere rağmen hastanede dışında kalbi duran hastaların sadece %5–10'u hastaneden taburcu olmaktadır. Biz bu çalışmada, hastane dışında kalbi duran hastalarda iyi nörolojik durumla taburcu olmayı belirleyen faktörleri araştırdık.

Yöntemler: Hastane dışında kalp durması nedeniyle getirilen 129 hasta geriye dönük olarak taranarak çalışmaya dahil edildi.

Bulgular: Dolaşımın kendiliğinden dönmesi (>20 dakika) 29 (%22.4) hastada gerçekleşti. Spontan dolaşım sağlanan grupta iskemik nedenli kalp durması daha fazla idi (p<0.001). Lojistik regresyon analizinde, iskemik nedenli kalp durması varlığı (p=0.004) ve kalp masajı süresi (p=0.013) spontan dolaşımı sağlamada bağımsız faktör olarak bulundu. Kardiyopulmoner yaşama döndürme (KPR) süresindeki bir dakikalık artış kendiliğinden dolaşım sağlamada 1.202 kat azalmayla ilişkili bulundu. Kendiliğinden dolaşım sağlanan hastalardan 7'si (%5.4) hastaneden taburcu oldu. Kardiyopulmoner yaşama döndürme süresindeki bir dakikalık artışın iyi nörolojik durumla taburcu olmada 1.123 kat azalmayla ilişkili olduğu görüldü.

Sonuç: Hastane dışında kalbi duran hastalarda, kalp durması nedeni iskemi ise kendiliğinden dolaşım sağlanma sıklığı diğer nedenlere bağlı kalp durmasına göre daha fazladır ve uzamış KPR süresi ölümle ilişkili bulunmuştur.

Estimated incidence of out-of-hospital cardiac arrest (OHCA) has been reported to be 50 to 100 per 100,000 person-years.[1,2] Although immediate cardiopulmonary resuscitation (CPR) can provide return of spontaneous circulation (ROSC), survival rates remain low: 5% to 10%, at best.[3] Leading cause of OHCA is coronary artery disease. More than 50% of these patients experience acute myocardial infarc-

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Abbreviations:

CPC	*Cerebral Performance Category*
CPR	*Cardiopulmonary resuscitation*
ECG	*Electrocardiography*
ED	*Emergency department*
OHCA	*Out-of-hospital cardiac arrest*
ROSC	*Return of spontaneous circulation*

tion in out-of-hospital setting and cardiac death typically occurs due to ventricular arrhythmia.[4]

Immediate attempt at CPR and immediate defibrillation for shockable rhythm are crucial for survival in patients with OHCA.[5] Cessation of blood flow to the brain and other organs during cardiac arrest and resulting organ failure have significant effect on survival. After achieving RSOC, every effort is made to maintain neurologically intact survival. During decision-making process having accurate prognosis for these patients may enable avoidance of unnecessary interventions, with related costs and use of medical resources.

This study examines the predictors related to neurologically favorable survival outcomes in patients who experienced non-traumatic OHCA.

METHODS

This is a retrospective review of patients with diagnosis of OHCA who were admitted to Türkiye Yüksek Ihtisas Education and Research Hospital between July 2010 and January 2016. Patients who were age ≥18 years of age and admitted to emergency department with non-traumatic OHCA were included in the present study. Twelve patients who were dead on arrival and those for whom CPR attempt, including defibrillation or cardioversion for shockable rhythm, was not performed were excluded from the study. Patients who were alive when admitted to hospital and experienced in-hospital arrest were also excluded. Detailed demographic information and history of patients, including age, gender, prior history of diabetes, hypertension, hyperlipidemia, smoking, coronary artery disease, previous coronary intervention, pre-arrest symptoms, ambulance data, admission electrocardiogram (ECG) and coronary angiographic data, were obtained from medical records and nurse observation forms.

Study outcomes

Based on data obtained from hospital records, primary outcome of this study was defined as discharge from hospital with favorable neurological outcome. Cerebral Performance Category (CPC) scale was used to assess neurological status; CPC level of 1 or 2 (good recovery or moderate disability, respectively) was accepted as favorable neurological status, whereas CPC level of 3 (severe disability), 4 (vegetative state), and 5 (death) were regarded as unfavorable neurological status.

Statistical analysis

Data analysis was performed using SPSS Statistics for Windows, Version 17.0 (SPSS, Inc., Chicago, IL, USA). Kolmogorov-Smirnov test was used to test distribution pattern. Data were presented as mean±SD or median (minimum-maximum) for continuous variables. Number of cases and percentages were used for categorical data. Mean differences between groups were compared using Student's t-test. Mann-Whitney U test was applied for comparisons of data that were not normally distributed. Categorical data were analyzed using Fisher's exact test when 1 or more cells had expected frequency of 5 or less. Otherwise, chi-square test was applied. The best predictor(s) for ROSC and neurologically favorable survival were determined using forward multiple logistic regression procedure. Any variable whose univariable test had p value <0.25 was accepted as candidate for multivariable model, along with all variables of known clinical importance. Adjusted odds ratios, 95% confidence intervals and Wald statistics for each independent variable were also calculated. P value <0.05 was considered statistically significant.

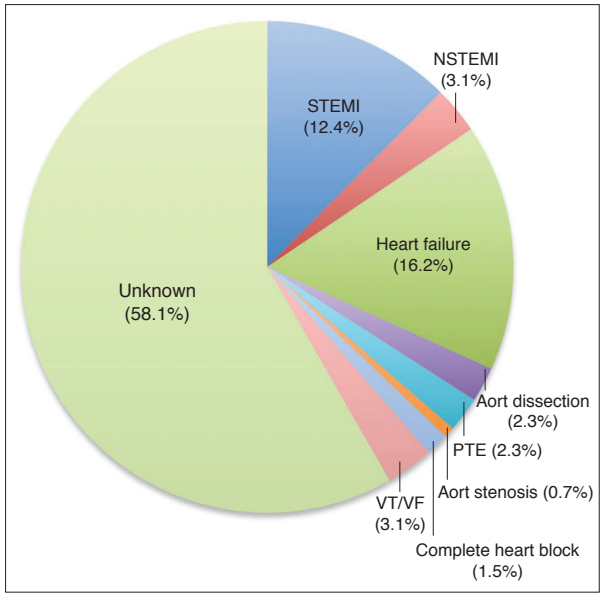

Figure 1. Distribution of the etiology of OHCA. STEMI: ST elevation myocardial infarction; NSTEMI: Non-ST elevation myocardial infarction; PTE: Pulmonary thrombo-embolsm; VF: Ventricular fibrillation; VT: Ventricular tachycardia.

RESULTS

Total of 129 patients (mean age: 67.2±13.7 years; 65.9% male) were included in the study of the patients had previously been treated by our outpatient clinic: 18 had heart failure, 6 had coronary artery disease, and 1 patient had significant aortic stenosis. Etiology of OHCA was identified in 54 (41.8%) of patients (Figure 1). Twelve-lead electrocardiography (ECG) was recorded for all patients. In total, 97 had asystole, 17 were in sinus rhythm, 8 had either ventricular fibrillation or ventricular tachycardia, 4 had atrial fibrillation, 2 had pulseless electrical activity, and 1 had bradycardia (heart rate <40 bpm). Of these patients, ROSC (sustained ROSC lasting >20 min) was achieved in 29 (22.4%) cases. Table 1 illustrates com-

Table 1. Comparison of baseline characteristics according to ROSC

Variables	ROSC-achieved (n=29)	ROSC-failure (n=100)	*p*
Age, years (Mean±SD)	68.1±14.4	67.0±13.7	0.687†
Male, n (%)	17 (58.6)	68 (68.0)	0.348‡
Diabetes mellitus, n (%)	7 (24.1)	29 (29.0)	0.607‡
Hypertension, n (%)	16 (55.2)	58 (58.0)	0.786‡
Smoking, n (%)	10 (34.5)	56 (56.0)	0.041‡
Coronary artery disease, n (%)	13 (44.8)	55 (55.0)	0.334‡
Coronary bypass grafting, n (%)	3 (10.3)	13 (13.0)	>0.999¶
Cerebrovascular accident, n (%)	1 (3.4)	2 (2.0)	0.537¶
Chronic kidney disease, n (%)	8 (27.6)	15 (15.0)	0.119‡
Etiology of cardiac arrest, n (%)			
Ischemia (STEMI/NSTEMI)	12 (41.4)	8 (8.0)	<0.001¶
Heart failure	5 (17.2)	16 (16.0)	>0.999¶
Other reason (PTE, atrioventricular block)	2 (6.9)	11 (11.0)	0.731¶
Unknown reason	10 (34.5)	65 (65.0)	0.003‡
Baseline electrocardiogram, n (%)			
Asystole	15 (51.7)	82 (82.0)	<0.001‡
STE/ST depression	12 (41.4)	9 (9.0)	<0.001‡
Direct admission	17 (58.6)	78 (78.0)	0.037‡
Transport duration, minutes	50 (40–95)	45 (20–100)	0.007§
Cardiopulmonary resuscitation duration, minutes	45 (5–65)	45 (25–100)	0.005§
Pre-arrest symptoms, n (%)			
Chest pain	11 (37.9)	29 (29.0)	0.360‡
Dyspnea	6 (20.7)	17 (17.0)	0.648‡
Palpitation	2 (6.9)	17 (17.0)	0.240¶
Unknown	10 (34.5)	37 (37.0)	0.804‡
Witnessed arrest	25 (86.2)	61 (61.0)	0.011‡
Glucose (mg/dL)	168 (47–516)	130 (30–500)	0.097§
Creatinine (mg/dL)	1.32 (0.47–5.00)	1.19 (0.24–5.87)	0.473§
Sodium (mmol/L)	139 (127–156)	140 (122–150)	0.762§
Potassium (mmol/L)	4.4 (2.6–7.6)	4.5 (2.8–7.8)	0.910§
Hemoglobin (g/dL)	12.4±1.9	12.7±2.1	0.407†
Troponin (ng/mL)	0.9 (0.01–95.0)	0.5 (0.01–187.0)	0.028§

†Student's t-test; ‡Pearson's chi square test; ¶Fisher's exact test; §Mann-Whitney U test. STEMI: ST elevation myocardial infarction; NSTEMI: Non ST elevation myocardial infarction; PTE: Pulmonary thromboembolism; ROSC: Return of spontaneous circulation; SD: Standard deviation.

Table 2. Results of multiple logistic regression analysis

	Odds ratio	95% CI	Wald	*p*
Dependent variable: Return of spontaneous circulation				
Ischemic etiology	0.003	0.00005–0.146	8.437	0.004
Cardiopulmonary resuscitation duration	1.202	1.040–1.388	6.206	0.013
Dependent variable: Neurologically favorable survival				
Cardiopulmonary resuscitation duration	1.123	1.036–1.217	7.958	0.005

CI: Confidence interval.

parison of patient characteristics according to ROSC status. Presence of diabetes mellitus, hypertension, prior history of coronary angiogram and coronary artery bypass grafting, or pre-arrest symptoms did not differ between groups (p>0.05). However, percentage of cardiac arrests with ischemic etiology was significantly higher in successful ROSC group (p<0.001). When admission ECGs were compared, presence of asystole was significantly higher among patients who died in the emergency department (ED) compared to the patients who achieved ROSC. Also, presence of ischemic ECG markers (ST elevation/depression) was significantly higher in the ROSC-achieved group (ROSC-achieved group:11 ST elevation, 1 ST depression; ROSC-failure group: 7 ST elevation, 2 ST depression; p<0.001). Number of witnessed arrest events was significantly higher in successful ROSC group (p=0.011). Number of current smokers and of patients transported from other hospitals was significantly higher in ROSC-failure group (p=0.041 and p=0.037, respectively). Compared to ROSC-achieved group, transport duration was significantly longer among patients with ROSC failure (p=0.007). Blood parameters, with exception of troponin, did not differ between groups. In multivariate logistic regression analysis, cardiac arrest with ischemic etiology (p=0.004) and CPR duration (p=0.013) were found to be independent predictors regarding ROSC in ED (Table 2). Among all patients, 1-minute increment in CPR duration was associated with 1.202-fold increase in ED ROSC failure.

Among patients who achieved ROSC, 18 (62%) patients underwent coronary angiogram. In 1 patient with inferior ST elevation myocardial infarction, fibrinolytic therapy was administered at peripheral hospital preceding transport to our hospital. Seven patients (5.4%) survived to hospital discharge. Of these patients, 1 experienced severe neurological disability (CPC level 3), 3 had implantable cardioverter defibrillator inserted, 2 had stent implanted in culprit lesion, and 1 patient had pacemaker implantation performed due to complete heart block. Other than transport and duration of CPR and hospitalization, other variables did not differ with respect to survival (Table 3). Among patients who survived, both median transport (45 vs 50 minutes; p=0.015) and CPR duration (15 vs 45 minutes; p<0.001) were significantly shorter. There was no significant difference between groups with respect to in-hospital interventions (p>0.05) (Table 4). After excluding the 1 patient with severe neurological disability, among patients who achieved ROSC, 1-minute increment in CPR duration was associated with 1.123-fold decrease in neurologically favorable survival (p=0.005) (Table 2).

DISCUSSION

Results of this study demonstrate that despite current CPR routines and aftercare of patients with OHCA, survival rates remain low. In our study cohort, survival rate was 5.4%. Cardiac arrest with ischemic etiology was determined to be related to greater ROSC success, but not to neurologically favorable survival. Early response to CPR may also be related to better outcomes after cardiac arrest.

Although predicting which patients will survive after OHCA is challenging, greater ability to do so would help clinicians to determine treatment and when informing the family of the victim. In this population, several predictors, including time between cardiac arrest and ROSC, shockable rhythm on admission, and witnessed arrest event have been identified as prognostic markers.[6] As in previously published data, we observed that witnessed OHCA was related to better recovery of cardiac function, probably due to immediate call for health professionals. Also, not surprisingly,

Table 3. Comparison of baseline characteristics according to survival

Variables	Survivors (n=7)	Deceased (n=22)	*p*
Age, years (Mean±SD)	70.1±17.1	67.5±13.8	0.680†
Male, n (%)	4 (57.1)	13 (59.1)	>0.999‡
Diabetes mellitus,n (%)	1 (14.3)	6 (27.3)	0.646‡
Hypertension, n (%)	4 (57.1)	12 (54.5)	>0.999‡
Smoking, n (%)	2 (28.6)	8 (36.4)	>0.999‡
Coronary artery disease, n (%)	4 (57.1)	9 (40.9)	0.667‡
Coronary bypass grafting, n (%)	2 (28.6)	1 (4.5)	0.136‡
Cerebrovascular accident, n (%)	1 (14.3)	0 (0.0)	0.241‡
Chronic kidney disease, n (%)	2 (28.6)	6 (27.3)	>0.999‡
Etiology of cardiac arrest, n (%)			
Ischemia (STEMI/NSTEMI)	2 (28.6)	10 (45.5)	0.665‡
Heart failure	2 (28.6)	3 (13.6)	0.569‡
Other reason (PTE, atrioventricular block)	1 (14.3)	1 (4.5)	0.431‡
Unknown reason	2 (28.6)	8 (36.4)	>0.999‡
Baseline electrocardiogram, n (%)			
Asystole	3 (42.9)	12 (54.5)	0.682‡
STE/ST depression	2 (28.6)	10 (45.5)	0.665‡
Direct admission	6 (85.7)	11 (50.0)	0.187‡
Transport duration, minutes	45 (40–50)	50 (40–95)	0.015¶
Cardiopulmonary resuscitation duration, minutes	15 (5–40)	45 (10–65)	<0.001¶
Pre-arrest symptoms, n (%)			
Chest pain	2 (28.6)	9 (40.9)	0.677‡
Dyspnea	1 (14.3)	5 (22.7)	>0.999‡
Palpitation	0 (0.0)	2 (9.1)	>0.999‡
Unknown	4 (57.1)	6 (27.3)	0.193‡
Witnessed arrest	5 (71.4)	20 (90.9)	0.238‡
Intubation duration (hours)	24 (1–360)	24 (1.5–1488)	0.784¶
Hospitalization duration (days)	9 (5–49)	1 (0–62)	0.004¶
Glucose (mg/dL)	131 (109–312)	188.5 (47–516)	0.709¶
Creatinine (mg/dL)	1.06 (0.59–2.79)	1.40 (0.47–5.0)	0.438¶
Sodium (mmol/L)	138 (134–145)	139.5 (127–156)	0.901¶
Potassium (mmol/L)	4.1 (2.6–7.4)	4.6 (2.7–7.6)	0.258¶
Hemoglobin (g/dL)	13.0±2.1	12.2±1.9	0.366†
Troponin (ng/mL)	2.1 (0.13–95)	0.6 (0.01–93.0)	0.181¶

†Student's t-test; ‡Fisher's exact test; ¶Mann-Whitney U test. STEMI: ST elevation myocardial infarction; NSTEMI: Non ST elevation myocardial infarction; PTE: Pulmonary thromboembolism; SD: Standard deviation.

shorter interval between arrest and ROSC may identify patients who have greatest possibility of survival. ED data indicated that mortality was related to longer CPR attempt. Recovery of sustained circulation in early responders to CPR may provide more opportunity to utilize interventional therapies and make other efforts.

While the most important priority is achieving spontaneous circulation as soon as possible, the second aim is to clarify etiology of cardiac arrest in order to determine post-ROSC care. However, in real life, etiology of OHCA may not be established for every patient. Etiology was ascertained in 41.8% of cases

Table 4. Comparison of in-hospital events and interventions according to survival

Variables	Survivors (n=7)		Deceased (n=22)		$p^{\dagger}$
	n	%	n	%	
Neurological deficit	1	14.3	0	0.0	0.241
Coronary angiogram	6	85.7	12	54.5	0.202
Stent	2	28.6	5	22.7	>0.999
Fibrinolytic drug	0	0.0	1	4.5	>0.999
Culprit lesion					
Left anterior descending	1	14.3	5	22.7	>0.999
Circumflex	0	0.0	1	4.5	>0.999
Right coronary artery	1	14.3	4	18.2	>0.999

†Fisher's exact test.

in our study cohort. It has been speculated that clinical features and ECG are not always reliable indications acute coronary syndrome as trigger of OHCA in a comatose patient.[7,8] Whittaker et al. reported that 21% of the patients who had occluded coronary artery on coronary angiogram did not have ST elevation on post-ROSC ECG, which raised uncertainty about use of ECG markers to predict OHCA etiology,[8] but we observed that all of the patients with ST elevation on admission ECG who achieved ROSC and underwent coronary angiography had acutely occluded coronary artery. Therefore, ST elevation on admission ECG does seem to be reliable clue for etiology of OHCA. As stated in present guidelines,[9,10] victims of OHCA with ST elevation should undergo coronary angiogram for immediate myocardial salvage.

Our study indicated that every increment in CPR duration was related to lower survival rate in patients who achieved ROSC. Similarly, 2 trials reported that duration of CPR had impact on survival.[11,12] This finding probably reflects population who were unlikely to survive after OHCA due to ongoing lack of circulation and subsequent failure of organs. In comparison with earlier studies, we found significantly longer median CPR duration (45 minutes) in ROSC-failure group. Earlier trials reported median of 17.5 minutes and 28 minutes.[11,12] Regardless of having favorable characteristics (younger age, witnessed event, shockable rhythm), CPR duration may be influenced, and it has been reported that poorer baseline characteristics were related to shorter CPR attempts.[11,13] In contrast, we observed that CPR attempt duration was significantly longer in ROSC-failure group, even though most often asystole was seen on baseline ECG. We found that longer transport duration was related to failed ROSC and lower survival. The reasonable explanation for this finding is that during transport, CPR quality and performance deteriorates.[14,15] Mechanical CPR, Hypothermia, ECMO, and Early Revascularization (CHEER) trial demonstrated that after prolonged CPR attempt, survival with good neurological condition is likely;[16] however, in that trial, CPR efforts were supported by mechanical CPR devices, therapeutic hypothermia, and extracorporeal life support, which might have affected the results.[16,17] Therefore, with conventional CPR procedures, longer duration may indicate both failing body and patients with poorer baseline characteristics who may not survive.

Study limitations

Although the present study provides valuable information about patients who were admitted to our tertiary referral hospital with OHCA, the number of patients included was relatively small, which probably lowered the statistical power of the study. In some patients, pre-hospital data were limited; confounders may not have been interpreted. Inclusion of patients who were transported from other centers might have created selection bias due to possible need for advanced care and worse prognosis. Also, there is no information about extent of brain injury in study participants, which certainly affects survival. The present study represents a specific patient population; however, definitive, broad conclusions cannot be made due to small sample size and retrospective design.

Conclusion

Patients with ischemic cardiac arrest may be more likely to achieve ROSC after CPR. However, prolonged CPR duration seems to be related to lower survival rate among victims of OHCA.

Conflict-of-interest issues regarding the authorship or article: None declared

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