

Code blue: Predictors of survival

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Abstract

Background and Aims: Code blue is a rapid response system developed for emergency resuscitation and stabilization of any sudden cardiac arrest (SCA) within a hospital. Literatures on outcome and factors predicting mortality from SCA in the Emergency departments (EDs) of India is scant.

Material and Methods: This retrospective cohort study included all patients above the age of 15 years who had a code blue declared in the ED between the months of January 2018 and June 2019. Factors related to the sustained return of spontaneous circulation (ROSC) and mortality were analyzed using descriptive-analytic statistics and logistic regressions.

Results: This study included 435 patients with a male predominance of 299 (69%). The mean age was 54.5 (SD - 16.5) years. Resuscitation was not attempted for 18 patients because of the terminal nature of the underlying disease. The majority were in-hospital cardiac arrests (74%). The nonshockable rhythm included pulseless electrical activity (PEA) (85.5%) and asystole (14.5%) cases. Shockable rhythms, that is, pulseless ventricular tachycardia/ventricular fibrillation were noted in only 10% (43/417) of cases. ROSC was attained in 184 (44.1%) patients, among which 56 (13.4%) were discharged alive from the hospital. Multivariate logistic regression analysis showed CPR > 10 min (odds ratio [OR]: 13.58; 95% CI: 8.39–22.01; $P < 0.001$) and female gender (OR: 1.89; 95% CI: 1.13–3.17; $P = 0.016$) to be independent risk factors for failure to achieve ROSC in ED.

Conclusion: The initial documented rhythm was nonshockable in the majority of the cases. CPR duration of more than 10 min and female gender were independent risk factors for failure to achieve ROSC in the ED. Nonshockable rhythms have a poorer outcomes than that of shockable rhythms.

Keywords: Cardiac arrest, cardiopulmonary resuscitation, code blue, ROSC

Introduction

Sudden cardiac Arrest (SCA) refers to the abrupt cessation of heart function, resulting in loss of blood flow to all the major organ systems. The pathophysiology of SCA is complex, but in general is believed to be because of electrical instability in the heart leading to fatal ventricular arrhythmias and eventual hemodynamic collapse.^[1,2] Considering the obvious urgent risk to life along with the varied and numerous underlying causes for the same, it is no

surprise that SCA proves to be one of the biggest challenges to emergency physicians all over the world.^[3] Code Blue is a rapid response system developed for emergency resuscitation and stabilization of any SCA within a hospital.^[4] The Emergency Department (ED) within a hospital primarily manages the highest volume of patients with SCA with either out-of-hospital arrests (OHCA) who are brought in or critically unwell patients who go on to arrest while receiving care in the ED.^[5,6]

According to the standard resuscitation guidelines, the immediate management consists of emergency response system activation,

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cardiopulmonary resuscitation (CPR), and defibrillation with an external automated defibrillator (AED). The goal of CPR is to restore and maintain perfusion to the vital organs until the underlying cause of the arrest can be diagnosed and as far as possible, reversed.^[7,8] Despite best efforts however, the survival rate of patients who suffer an SCA remain low even in advanced hospital settings. This survival then depends on a multitude of factors relating to patient demographics as well as nature and cause of the arrest. Age and gender naturally play a role, along with characteristics such as the initial rhythm following arrest,—shockable rhythms seem to offer survival benefit, underlying disease process—cardiac origin of arrest seems to have a more favourable outcome than non-cardiac, response time following arrest and the duration and quality of CPR.^[1,9,10] If performed successfully, the return of spontaneous circulation (ROSC) is achieved. Therefore, it is increasingly important to study pre-arrest and arrest parameters and have a better understanding of their prognostic implications so that high quality CPR can be applied in a rational, productive, and effective manner and on those patients that are most likely to benefit. However, most of the studies done on SCA are hospital-based studies as opposed to solely focusing on the ED. Therefore, this study was done in an Utstein style on SCA in ED, to identify the predictors of survival in such patients.

Material and Methods

This was a retrospective cohort study. We conducted this study in the ED of a large tertiary care hospital in South India. Our ED is a 49-bed department and tends to about 300 patients per day. Based on the patient's vital signs and physiological parameters at ED arrival, they were further triaged as priority 1, 2, and 3 patients. The study was conducted for a period of 18 months from January 1, 2018 to June 30, 2019. The aim was to study the profile and outcome of patients presenting with SCA to the ED. The primary objective was to determine the percentage of patients attaining ROSC in ED. The secondary objectives were to find the mortality rate after activating code blue in the ED, and factors associated with predictors of ROSC and mortality.

Inclusion criteria: All patients with SCA, either OHCA being brought to the ED or critically unwell patients admitted to the ED who had an SCA while receiving treatment.

Exclusion criteria: Charts with incomplete data, age < 15 years and patients who were declared dead on arrival (had an OHCA and presented with asystole with absent brain stem reflexes).

Based on the percentage of ROSC achieved as 71% from a previous study and a precision of 5%, the sample size was calculated to be 330.^[11]

Data of the patients were obtained from the electronic hospital records, and the details of history and physical examination findings of all patients were recorded on a standard data collection sheet. The following were extracted: age/sex, comorbidities (diabetes mellitus, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, HIV status, chronic liver disease, and cerebrovascular accident), time of cardiac arrest, underlying etiology of SCA, initial rhythm in ECG at presentation, duration of CPR, final rhythm, percentage of patients attaining ROSC.

Outcome of the patients with regards to mortality rate in ED after activation of code blue, admissions after attaining ROSC, those that left against medical advice (LAMA), and hospital outcome were documented.

The data was analyzed using Statistical Package for the Social Sciences (SPSS) for Windows software released 2015, version 23.0, Armonk, New York, USA. Data was summarized using mean along with standard deviation for continuous variables and frequencies along with percentages for categorical variables. Some of the variables such as sex of the patient, age, initial rhythm, time and day of presentation, and duration of CPR was categorized and coded. A bivariate analysis was done to identify the relationship between these variables and the attainment of ROSC and mortality. All possible determinants with $P \leq 0.05$ in the bivariate analysis were used as candidates for multivariate logistic regression analysis to determine their significant association simultaneously.

Prior to the commencement of the study, approval from the Institutional review board ethical committee was obtained (IRB Min no: 12586 dated 29th January 2020). Patient confidentiality was maintained using unique identifiers and by password protected data entry software with restricted users.

Results

A total of 1,10,503 patients attended the ED during the study period of January 2018 to June 2019. Among them, 435 (0.4%) patients had an either OHCA or had a SCA in ED while receiving treatment. Eighteen patients had a standing order “do not resuscitate” with prior consent and hence were excluded from the analysis. The study cohort contained 417 patients who satisfied the inclusion criteria. These patient's charts were screened and included into the study [Figure 1]. Among the 320 (74%), IHCA - 276 (86.3%) were witnessed by a medical personnel.

The mean age of the study population 54.5 (SD: 16.5) years and there was a male preponderance (299: 69%). The number of SCA did not differ much between weekdays and

weekends (0.83/day vs. 0.71/day; $P = 0.31$). It was observed that more arrests happened during the morning shifts, that is, 175 (40%) as compared to the evening, that is, 144 (33%) or night 116 (27%) shifts. However, the number of SCA did not differ much between weekdays and weekends (0.83/day vs. 0.71/day; $P = 0.31$). Diabetes mellitus 174 (40%) and hypertension 162 (37.3%) were the most common comorbidities. The baseline characteristics are given Table 1.

The common presumed etiology was because of underlying cardiac causes seen in 188 (42.2%) cases, non-cardiac causes included sepsis, respiratory etiology, trauma, chronic liver disease related, neurology related, malignancy related, and others as given in Figure 2. Most of the SCA were in-hospital cardiac arrests (IHCA), that is, 74% (320/435) with only 26% (115/435) being OHCA. Bystander CPR was given in 12 (10.4%) cases of OHCA before arriving to ED. Most of the SCA were witnessed either by a medical personnel or relative, that is, 98% (426/435) [Figure 2].

The initial documented rhythm was nonshockable in majority of the cases, that is, 90% (392/435). Pulseless electrical activities (PEA) were noted in 77% (335/435) and asystole in 13% (57/435) of cases. Shockable rhythms were noted in only 10% (43/435) of cases among which 4% (18/435) cases had pulseless Ventricular Tachycardia (VT) and 6% (25/435) had Ventricular Fibrillation (VF) [Figure 2]. Among the 320 (74%), IHCA - the initial rhythms were as follows: PEA - 241 (75.3%); Asystole 52 (16.3%), VT 18 (5.6%), and VF 9 (2.8%). After CPR, ROSC was attained in 56.1% (234/417) of the study population but was sustained for >20 min in only 44.1% (184/417) of patients.

The mean duration of CPR performed among patients who attained ROSC was 8.23 min compared to 20.91 min among those who did not attain ROSC with significant difference of means of -12.68 (95%CI = -14.33 to - 11.03); $P < 0.001$ as shown in Figure 3. Multivariate logistic regression analysis showed CPR > 10 min (odds ratio [OR]: 13.58; 95% CI: 8.39–22.01; $P < 0.001$) and female gender (OR: 1.89; 95% CI: 1.13–3.17; $P = 0.016$) to be independent risk factors for failure to achieve ROSC in ED [Table 2]. On the contrary patients who received CPR for less than 6 min (OR: 0.28; 95% CI: 0.16–0.50; $P < 0.001$) had a 72% less chance of ED mortality, whereas age more than 70 years (OR: 4.08; 95% CI: 1.22–13.6; $P = 0.023$), and female gender (OR: 2.18; 95% CI: 1.05–4.54; $P = 0.037$) were significant predictors of ED mortality [Table 3]. Among patients with shockable rhythm, ROSC was obtained in 18 (41.9%) patients, and in 166 (42.4%) of those with nonshockable rhythm.

After initial resuscitation, approximately half of the of the study population, that is, 44.1% (184/417) survived the event. However, 94 patients died in the ED because of subsequent SCA. This was because many relatives decided not to continue resuscitation because of grave prognosis. A total of 106 (25.4%) patients were admitted to the medical or surgical intensive care units of our hospital after ED survival. The overall SCA survival to discharge from the hospital rate was 13.4% (56/417).

Discussion

The present study was done to determine the percentage of patients attaining ROSC after a SCA in ED, predictors of

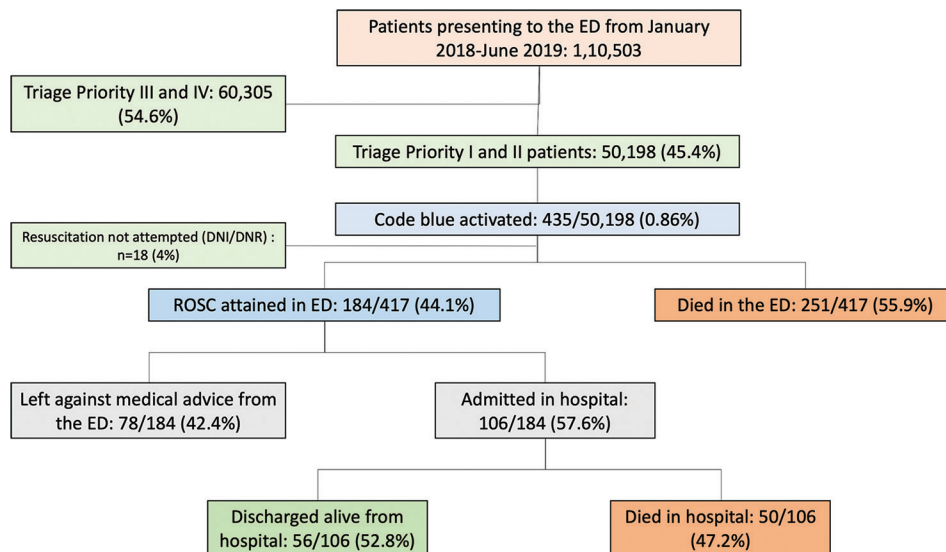


Figure 1: COHORT diagram

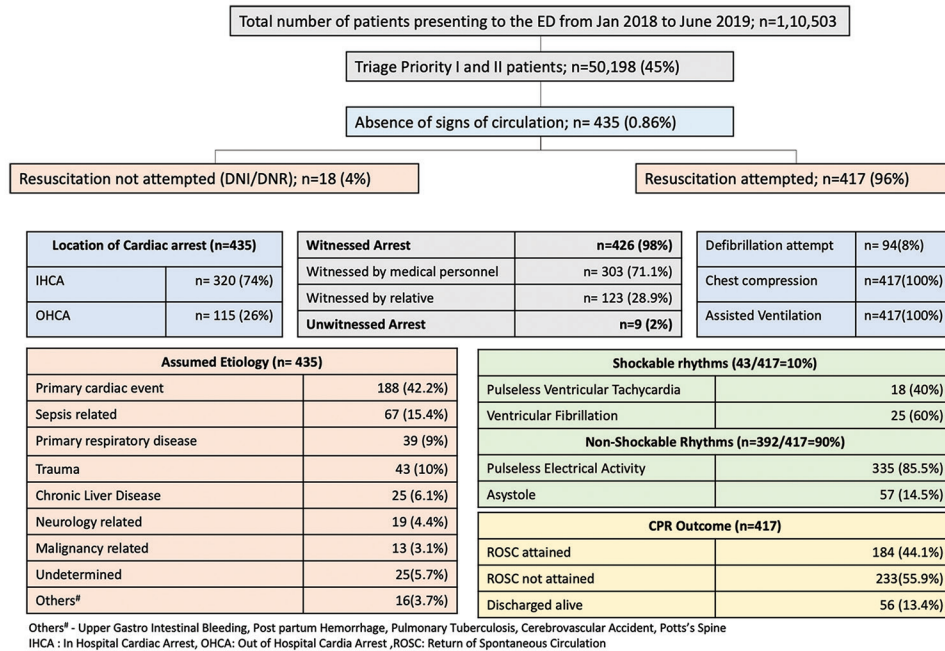


Figure 2: Modified Utstein template

Table 1: Baseline Characteristics (n=435)

Variable	Frequency (%)
Mean age in years (SD)	54.5 (16.5)
Male	299 (69)
Weekdays (Mon-Fri)	325 (75)
Weekends (Sat, Sun)	110 (25)
Time of cardiac arrest	
8 am-5 pm	175 (40)
5 pm-12 am	144 (33)
12 am-8 am	116 (27)
Comorbidities	
Diabetes Mellitus (DM)	174 (40)
Hypertension (HTN)	162 (37.3)
DM + HTN	122 (28.1)
Ischemic Heart Disease (IHD)	56 (12.9)
DM + HTN + IHD	33 (7.6)
Chronic Kidney Disease	16 (3.7)
Chronic Liver Disease	6 (2.5)
Others*	16 (3.7)

Others* - Reactive Airway Disease (Chronic obstructive Pulmonary Disease, Asthma), Pulmonary Tuberculosis, Cerebrovascular Accident, Potts's Spine

ROSC/mortality and finally hospital outcome when ROSC is attained. The mean age of our cohort [54.5 (SD: 16.5) years] with male predominance (69%) is the typical demographic of the bread winner of most families and is hence a cause for worry. It also shows that SCA are becoming more prevalent in the middle aged population, frequently between 45 and 75 years, and this is seen in other recent studies as well.^[12,13] We noted that most of these patients had an arrest in the early hours of the day, the cause of which was identified in earlier studies to be multifactorial. A peak in platelet aggregability at

this time contributing to higher risk of thrombosis correlating with a rise in sympathetic nervous activity causing heart rate variability and blood pressure fluctuations seem to partly explain this finding.^[14] Consistent with other studies, the most common presumed etiology in this study was that of underlying cardiac origin.^[15,16] A study done in the West showed that the Asian Indian population had 2–3 fold increased risk of an atherosclerotic disease than the Caucasian population, which contributes heavily to the development of a SCA.^[17] This is often the result of a number of chronic diseases such as hypertension, diabetes, and hypercholesterolemia, the risk of which is compounded in our population by food habits favoring fat/sugar rich meals and cultural factors that fail to reiterate the importance of incorporating regular exercise into our lives. In fact, recent studies have suggested that the shift to a Mediterranean-style diet pattern, including vegetables, fruits, nuts, whole grains, fish with low intake of red/processed meat may significantly lower the risk of heart disease among the elderly.^[18,19] It should be also noted that earlier studies have demonstrated a higher number of comorbidities in a single patient to be associated with lower likelihood of attaining ROSC.^[9,20] The setting in which this study is done is influenced by the urban lifestyle with its contributing factors such as greater alcohol consumption, obesity, and cigarette smoking, all of which further contribute to the increased risk. Hence, the initiation of lifestyle modifications and early screening for risk factors of atherosclerotic disease may prove to be preventive. Pre-hospital care is another hugely important factor for a favorable outcome in patients with SCA. In this study, approximately a quarter (115) had OHCA, among

Table 2: Bivariate and multivariate logistic regression analysis for factors associated with failure to achieve ROSC in ED (n=417)

Variable	ROSC not attained n=236	ROSC attained n=181	Bivariate analysis		Multivariate analysis	
			P	Unadjusted OR	P	Adjusted OR
Out of hospital arrest	72 (30.5)	39 (21.5)	0.04	1.59 (1.01-2.50)	0.052	1.72 (1.00-2.99)
CPR# duration >10 min	201 (85.2)	51 (28.2)	<0.05	14.6 (9.03-23.74)	<0.001	13.58 (8.39-22.01)
VF/VT*	25 (10.6)	18 (9.9)	0.83	1.07 (0.57-2.03)		
Age >60 years	93 (39.4)	62 (34.3)	0.28	1.25 (0.83-1.87)		
Female gender	86 (36.4)	47 (26)	0.023	1.64 (1.07-2.5)	0.016	1.89 (1.13-3.17)
8 pm-8 am	125 (53)	101 (55.8)	0.56	0.89 (0.60-1.32)		
Week end (Sat, Sun)	55 (23.3)	51 (28.2)	0.26	0.77 (0.49-1.20)		

*CPR - Cardio pulmonary resuscitation, *VF/VT - Ventricular Fibrillation/Ventricular Tachycardia

Table 3: Bivariate and multivariate logistic regression analysis for factors associated with mortality in the ED (n=417)

Variable	Died in hospital n=361	Alive n=56	Bivariate analysis		Multivariate analysis	
			P	Unadjusted OR	P	Adjusted OR
Out of hospital arrest	100 (27.7)	11 (19.6)	0.20	1.56 (0.78-3.15)		
CPR# duration <6 min	87 (24.1)	30 (53.6)	<0.05	0.27 (0.15-0.49)	<0.001	0.28 (0.16-0.50)
VF/VT*	34 (9.4)	9 (16.1)	0.13	0.54 (0.24-1.20)		
Age >70 years	61 (16.9)	3 (5.4)	0.03	3.59 (1.09-11.87)	0.023	4.08 (1.22-13.66)
Female gender	123 (34.1)	10 (17.9)	0.01	2.38 (1.16-4.87)	0.037	2.18 (1.05-4.54)
8 pm-8 am	191 (52.9)	35 (62.5)	0.18	0.67 (0.39-1.20)		
Weekends (Sat, Sun)	93 (25.8)	13 (23.2)	0.68	1.15 (0.59-2.23)		

*CPR - Cardio pulmonary resuscitation, *VF/VT - Ventricular Fibrillation/Ventricular Tachycardia

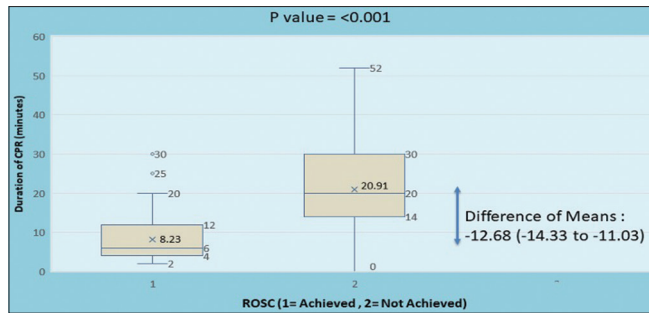


Figure 3: Box- plot of CPR duration

which only 10.4% (12/115) received bystander CPR, showing little to no education or understanding among the general Indian population about the potentially lifesaving act of chest compressions. Many ambulances in India are under equipped with under trained paramedical personnel. This humbling statistic emphasizes the need for widespread awareness along with BLS training programs in the general population, as well as revamping of ambulance healthcare all over our country. Another factor that had far-reaching implications in the outcome of these patients was the type of initial rhythm found following SCA. Nonshockable rhythms (asystole/PEA) are regarded as agonal rhythms and multiple investigations done in different settings in the past showed a poorer outcome when compared to shockable (VT/VF) rhythms.^[10,21] Kayser *et al.*, after analyzing the AHA sponsored—National Registry of Cardiopulmonary Resuscitation (NRCPR) confirmed the same.^[22] The initial documented rhythm in the majority of our study population was a nonshockable rhythm (asystole/PEA)

which is similar in incidence to studies done in the West.^[3,6,22] A similar study done in an ED setting of Thailand by Sittichanbuncha *et al.* showed 83.3% of the study population to have a nonshockable rhythm that was also associated with poorer outcomes.^[23]

Furthermore, analysis of our data revealed that the longer the duration of the CPR, less was the likelihood of survival. The inability to achieve ROSC rapidly leading to longer CPR increases the likelihood of tissue hypoxia and the risk of death. Bivariate and multivariate logistic regression analysis showed CPR duration, age, and female gender to be independent predictors of outcome in these patients. Our ED SCA survival to hospital admission rate of 25.4% was better than the survival rates described by Rajaram R. *et al.*, that is, 18.4% cases but less than that seen in the study done at our centre in 2016 is (29.5%) cases.^[11,24] The overall survival to discharge rate in our study population was 13.4%, with survival rates varying from 12.5% for IHCA and 15.6% for OHCA. The purpose of this observational study is to add to the plethora of research already available on this subject, and build on it further with important statistics and valuable insights into sustainable solutions that can decrease the frightening mortality from this condition.

Clinical implication

Owing to the comparatively larger study population, our analysis can contribute meaningfully to further understanding the risks associated with deaths from SCAs as well as aid in

highlighting country-specific needs that are to be met in order to alleviate some of this burden.

Research implication

Despite a large amount of data present regarding SCAs in our country, there are certain variables that require deeper investigation. Statistics regarding survival rate with early intubation of patient's versus with intubation following ROSC are required to make concrete guidelines for the same. Similarly, the benefit of obtaining an ABG during an SCA in Indian population and its relation to decision making and outcome must be reviewed. While there are numerous studies in the west that have examined the morbidity following survival after CPR—usually related to cerebral hypo-perfusion, there seems to be a dearth of the same in our country. Further characterization of the etiology and risks for OHCA/SCA as well as arrests in young adults could also constructively contribute to our knowledge.

Limitations

The presence of a separate chest pain unit diverted some likely patients with an SCA (probably due to myocardial infarctions) away from our ED and hence could be not included in our study. Of the patients recruited, the origin of the SCA was classified to be of cardiac or non-cardiac based solely on a thorough history, examination findings and clinical acumen and the presumption could not be confirmed with investigations or an autopsy.

Conclusion

This study was undertaken to look for predictors of survival in patients presenting with SCA or who had an SCA following admission in ED. Middle aged males were most commonly affected. The initial documented rhythm was nonshockable in majority of the cases and were associated with a poorer outcome than that of shockable rhythms. CPR duration of more than 10 min and female gender were independent risk factors for failure to achieve ROSC in the ED. Approximately a quarter of the study population could be resuscitated in ED, and admitted in different surgical and medical ICUs; of which more than half of them got discharged stable from hospital.

Research quality and ethics statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting, and reproducibility guidelines set forth by the EQUATOR Network. The authors also attest that this clinical investigation was determined to require Institutional Review Board/Ethics Committee review, and the corresponding protocol/approval number is (IRB Min no: 12586 dated 29th January

2020). We also certify that we have not plagiarized the contents in this submission and have done a Plagiarism Check.

Declaration of patient consent

This was a retrospective study approved by the Institution Review Board and waiver of patient's consent was obtained.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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