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ORIGINAL RESEARCH

Predicting Ventricular Arrhythmias and In-Hospital Mortality in Acute Coronary Syndrome Patients Presenting to the Emergency Department

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Abstract

Background: Ventricular arrhythmias (VA) after acute coronary syndrome (ACS) is associated with a higher risk of mortality. This study sought to examine the incidence, predictors and outcome of VA in ACS patients. **Material and methods:** A prospective cross-sectional study was conducted at the emergency department (ED), Universiti Kebangsaan Malaysia Medical Centre (UKMMC) in Kuala Lumpur, Malaysia. Patients with acute coronary syndrome (ST-segment elevation myocardial infarction [STEMI] and non-ST-segment elevation acute coronary syndrome [NSTEACS]) were continuously monitored for the occurrence of VA. **Results:** A total of 144 patients were recruited (67 STEMI and 77 NSTE-ACS). The total rate of VA was 18.8% (n = 27) and 14.6% (n = 21) experienced malignant ventricular arrhythmias (MVA) (8 ventricular fibrillation, 11 sustained ventricular tachycardia and 2 torsades de pointes). In-hospital mortality was reported in 11.1% of the subjects (n = 16). Factors predicted the occurrence of VA was Killip class IV (OR 8.67, 95% confidence interval [CI] 2.08-36.70, $p < 0.05$). Meanwhile, occurrence of MVA (OR 86.37, 95% CI 4.16 - 1792.70, $p < 0.05$) and blood sugar level (OR 1.30, 95% CI 1.01 - 1.67, $p < 0.05$) independently predicted in-hospital mortality. **Conclusion:** Incidence of VA was higher than the global estimate and the development of malignant forms of VA during hospitalization for ACS was associated with higher in-hospital mortalities.

Keywords

Acute coronary syndrome, Risk factor, Arrhythmias, Emergency, Mortality

1. Introduction

Ventricular arrhythmia (VA) increases the risk of death by sixfold, and it is a well-recognized complication following an acute myocardial infarction [1]. Ventricular fibrillation (VF), ventricular tachycardia (VT), and torsade de pointes (TdP) are forms of cardiac VAs, and their occurrence can be life-threatening [2]. The possible mechanisms for VA occurrence are associated with multiple factors, which include cardiac cell ischemia, scarring, electrolyte disturbances, medications, and advancing age [3–6].

VA is independently associated with an increased risk of in-hospital mortality among patients with acute ST segment elevation myocardial infarction (STEMI) [7], while, in the non-ST-segment elevation acute coronary syndrome (NSTE-ACS), the occurrence is much less, with the incidence being 10% and 2.6%, respectively, [8, 9]. Early detection of high-risk patients will guide clinicians in the emergency department (ED) to institute early corrective measures to prevent VA occurrence and to guide appropriate ward disposition [10]. Furthermore, VA is more likely to occur during the first 12 – 48 hours of ACS onset [10], highlighting the significance of early detection and preventive measures.

Despite being an established malignant complication for ACS, limited data are available regarding the incidence,

TABLE 1. Demographic and clinical characteristics of the subjects (n = 144).

Characteristics	Results
Demographic	
Mean age ± SD (hours)	58.8 ± 12.8
Gender, n (%):	
Male	124 (86.1)
Female	20 (13.9)
Race, n (%):	
Malay	71 (49.3)
Chinese	49 (34.0)
Indian	14 (9.7)
Others	10 (6.9)
Clinical	
Vital signs on ED arrival:	
Mean SBP ± SD (mmHg)	134.5 ± 32.9
Mean DBP ± SD (mmHg)	76.7 ± 18.0
Mean heart rate ± SD (beats/minute)	82.3 ± 23.2
Diagnosis, n (%):	
STEMI	67 (46.5)
NSTE-ACS	77 (53.5)
Median time from symptom onset to ED arrival (IQR) (hours)	3.0 (8.0)
Present of comorbidities, n (%):	
Diabetes mellitus	73 (50.7)
Hypertension	100 (69.4)
Kidney disease	26 (18.1)
Hypercholesterolemia	56 (38.9)
Smoking	53 (36.8)
Chronic obstructive pulmonary disease	5 (3.5)
Previous PCI	18 (12.5)
Previous CABG	13 (9.0)
Laboratory:	
Mean blood sugar ± SD (mmol/L)	11.6 ± 6.4
Mean leucocytes ± SD (X 109/L)	11.7 ± 4.5
Mean hemoglobin ± SD (g/dl)	13.5 ± 2.0
Mean potassium ± SD (mmol/L)	4.0 ± 0.4
Electrocardiographic features:	
ST-segment depression, n (%)	92 (63.9)
ST-segment elevation, n (%)	76 (52.8)
T-wave inversion, n (%)	52 (36.1)
Mean heart rate ± SD (msec)	83 ± 25
Mean PR interval ± SD (msec)	172 ± 38
Mean QT interval ± SD (msec)	424 ± 40
Killip classification, n (%):	
I	60 (41.7)
II	16 (11.1)
III	7 (4.9)
IV	18 (12.5)
Treatment options, n (%):	
STEMI patients received thrombolysis	42 (29.2)
STEMI patients with failed thrombolysis	0
Number of patients who had angiogram/PCI (including PPCI)	47 (32.6)

peak time of occurrence, and factors associated with VA in Malaysia. The objectives of this study were to describe the time-based incidence, risk factors, and clinical outcome associated with VA among patients admitted with ACS.

2. Methods

2.1 Study design and setting

This was a prospective single-center study conducted over a period of one year from May 1st, 2014, until May 31st, 2015. The study took place at the ED of Universiti Kebangsaan Malaysia Medical Center (UKMMC), an urban tertiary teaching hospital, in Kuala Lumpur, serving 72,000 patients annually. A cardiology consultation unit was available under the department of internal medicine, which offered cardiac catheterization procedure during working hours (8 am to 5 pm).

2.2 Subjects

The study recruited adult patients, aged 18 years and above, who presented to the ED with a presumptive diagnosis of ACS. The diagnosis was established based on the typical clinical history of ACS, such as angina pain at rest, and the patients were diagnosed as having either STEMI or NSTE-ACS based on the electrocardiographic changes [11–13]. Selection of patients with STEMI was according to the electrocardiographic presence of new ST elevation at the J point in at least two contiguous leads $\geq$ 2 mm in men or $\geq$ 1.5 mm in women in leads V2-V3 and/or of $\geq$ 1mm in other contiguous chest or limb leads or presumed new left bundle branch block at the time of ED admission with likely ischemic chest pain, with or without raised cardiac biomarkers [12, 14]. Meanwhile, the selection of patients with NSTE-ACS, which encompassed non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA), was made based on the absence of ST elevation on the electrocardiogram (ECG) in patients with likely ischemic chest pain, with or without raised cardiac biomarkers. The study excluded patients known to have VA due to conditions such as Brugada syndrome and Wolff–Parkinson–White syndrome. Patients who were brought in dead to the ED and ACS patients who were diagnosed in other centers and transferred to the ED for further treatments were also excluded.

2.3 Study protocol

During the course of the study, patients were treated according to the institutional protocol [15]. All patients received dual antiplatelet therapy with aspirin and clopidogrel in the ED. Patients with STEMI received reperfusion therapy by either primary percutaneous coronary intervention (PPCI) or fibrinolysis. Meanwhile, patients with NSTE-ACS received low-molecular-weight heparins. All patients provided written informed consent. The study received approval from UKMMC research ethics committee (study code: FF-2014-278).

All data were collected using a standardized data collection sheet. Demographic and clinical characteristics were obtained, including comorbidities, smoking history, duration of symptoms, vital signs at presentation, biochemical parameters, electrocardiographic features, and treatment outcome. All cases were categorized into either one of the following diagnosis of ACS: STEMI or NSTE-ACS.

The study determined two main outcomes: the incident of VA and in-hospital mortality. Patients were monitored for occurrence of VA within 72 hours of hospitalization. All types of VA defined as VF, sustained and nonsustained VT, torsade des pointes (TdP) polymorphic VT, and episodes of trigeminy, bigeminy, or couplet premature ventricular complexes (PVCs) [2] were recorded.

Concomitant VT and VF were categorized as VF. The three forms of VA associated with poor clinical outcome, VF, sustained VT, and TdP, were categorized as malignant ventricular arrhythmias (MVAs) [16], whilst nonsustained VT and episodes of PVCs were not considered MVAs. All deaths that occurred during hospitalization (in-hospital mortality) were recorded.

VF was defined as irregular ECG waves of inconsistent shape and unidentifiable QRS complexes accompanied by hemodynamic compromise requiring immediate defibrillation.

Sustained VT was defined as a series of consecutive regular broad complex ectopic ventricular beats, at a rate of $>$ 100 beats/min, lasting $>$ 30 seconds, which self-terminated or required pharmacological cardioversion or was accompanied by a hemodynamic instability requiring electrical cardioversion. Nonsustained VT was defined as $\geq$ 3 consecutive broad complex ventricular ectopic beats, at a rate of $>$ 100 beats/min, lasting $<$ 30 seconds, and not accompanied by a hemodynamic compromise. Polymorphic VT TdP was defined as a broad complex QRS of a variable morphology with characteristic twisted points in the setting of a prolonged QT interval.

2.4 Sample size and statistical analysis

Categorical and continuous data were presented as percentages and mean or median, respectively. Baseline characteristics of subjects between groups were compared using chi-square for categorical variables and Student's t-test or Mann–Whitney U test for continuous variables. To identify the statistically significant predictors to VA and in-hospital mortality, statistically significant ($p < 0.1$) variables from univariate analysis were subjected to multivariate logistic regression analysis. The results were presented as odds ratio (OR) with 95% confidence interval (CI), and a p value < 0.05 was considered significant. The Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA, Version 22.0) was used for the statistical analysis.

3. Results

A total of 145 patients were consented for enrollment. The diagnosis of one subject was later revised to be myocarditis,

TABLE 2. Baseline characteristics by VA.

Variables	Occurrence of VA		
	Yes	No	p value
	n = 27 (18.8%)	n = 117 (81.2%)	
Mean age ± SD, years	56.4 ± 14.1	59.3 ± 12.4	0.284
Gender, n (%):			
Male	22 (81.5)	102 (87.2)	
Female	5 (18.5)	15 (12.8)	0.536
Race, n (%):			
Malay	17 (63.0)	54 (46.2)	
Chinese	9 (33.3)	40 (34.2)	
Indian	1 (9.7)	13 (11.1)	
Others	0	10 (8.5)	0.186
Diagnosis, n (%):			
STEMI	18 (66.7)	49 (41.9)	
NSTE-ACS	9 (33.3)	68 (58.1)	0.031
Median time from symptom onset to ED arrival (IQR) (hours)	2.0 (4.0)	4.0 (10.0)	0.036
Mean blood pressure ± SD, mmHg:			
Systolic blood pressure	121.5 ± 33.0	136.7 ± 31.9	0.032
Diastolic blood pressure	71.9 ± 21.6	77.3 ± 17.4	0.179
Mean heart rate ± SD, beats/min	84.5 ± 27.0	80.6 ± 21.4	0.429
Baseline blood laboratory data:			
Blood sugar, mean ± SD, mmol/L	11.4 ± 6.9	11.4 ± 6.2	0.996
Leucocytes, mean ± SD, x109/L	13.3 ± 6.5	11.4 ± 4.1	0.057
Potassium, mean ± SD, mmol/L	4.0 ± 0.4	4.1 ± 0.5	0.81
Hemoglobin, mean ± SD, g/dL	13.2 ± 2.6	13.5 ± 1.8	0.514
Comorbidities, n (%):			
HTN	19 (69.9)	81 (69.8)	1
COPD	1 (3.7)	4 (3.6)	1
DM	11 (40.7)	62 (54.4)	0.282
Kidney disease	6 (22.2)	20 (17.5)	0.586
Hypercholesterolemia	8 (29.6)	48 (41.7)	0.281
Smoking history	10 (37.0)	43 (38.4)	1
History of PCI	5 (18.5)	13 (11.6)	0.345
History of CABG	3 (11.1)	10 (8.8)	0.716
Electrocardiographic features:			
ST-segment depression, n (%)	22 (81.5)	70 (59.8)	0.071
ST-segment elevation, n (%)	18 (66.7)	58 (49.6)	0.198
T-wave inversion, n (%)	8 (29.6)	44 (37.6)	0.507
Mean heart rate ± SD (msec)	87 ± 29	81 ± 23	0.266
Mean PR interval ± SD (msec)	167 ± 50	173 ± 34	0.42
Mean QT interval ± SD (msec)	434 ± 58	421 ± 33	0.144
Killip classification, n (%):			
I	8 (30.8)	52 (69.3)	
II	4 (15.4)	12 (16.0)	
III	3 (11.5)	4 (5.3)	
IV	11 (42.3)	7 (9.3)	0.001
Treatment, n (%):			
Thrombolysis	12 (44.4)	30 (25.6)	0.063
PCI/angiogram	6 (22.2)	41 (35.0)	0.177

TABLE 3. Multivariate logistic analysis of predictors to VA.

Variable	OR	95% CI	p value
Diagnosis of ACS (STEMI vs. NSTE-ACS)	1.16	0.35–3.81	0.808
Duration of onset (hours)	0.97	0.93–1.01	0.161
Baseline systolic blood pressure, mmHg	0.99	0.98–1.01	0.597
Leucocyte count, X 10^9/L	1	0.90–1.12	0.914
Killip class (reference: class I)			
Killip class II	2.78	0.64–12.10	0.172
Killip class III	3.88	0.67–22.64	0.132
Killip class IV	8.67	2.08–36.70	**0.003**

and the patient was excluded from the study. The final analysis included 144 subjects. The mean age of all subjects was 58.7, ranging from 31 to 90 years. The majority of the subjects were males, 124 (86%), and Malays (49.3%), followed by Chinese (34.0%), Indians (9.7%), and other ethnic groups (6.9%). We diagnosed STEMI in 46.5% of the subjects (n = 67) and NSTE-ACS in 53.5% of the subjects (n = 77). In patients with STEMI, 62.7% received fibrinolytic therapy (n = 42). Table 1 shows the demographic and clinical characteristics of the subjects. The median time from symptom onset of ACS to patient arrival at ED was 3.0 hours (ranging from 1 to 96). Median comparison between STEMI and NSTE-ACS with regard to time from symptom onset to ED arrival showed a significant difference (8H, IQR 13.6 vs 16.0, IQR 26.3 hours, p = 0.037). Hypertension and diabetes were reported in more than half of the subjects, 50.7% and 69.4%, respectively. While the majority of the subjects presented in a stable condition, 12.5% of the patients presented in Killip class IV (n = 18). The study reported that 18.8% (n = 27) of the subjects developed VA within 72 hours from ED admission, and 14.6% (n = 21) experienced MVAs. The median time of VA onset was 2.0 hours (IQR: 4.0). 81.5% (n = 22) of the patients had experienced VA within 24 hours from ED admission. The study reported a total of 16 (11.1%) in-hospital deaths. Figure 1 illustrates the proportion of subjects according to the characteristics of VA and in-hospital mortality.

Table 2 demonstrates the comparison of the baseline characteristics according to the occurrence of VA. Types of ACS, duration of symptoms, baseline systolic blood pressure, and Killip class were statistically significant with the occurrence of VA ($p < 0.05$). Among these variables, Killip class IV was the only variable that significantly predicted the occurrence of VA (OR: 8.67, 95% CI: 2.08–36.70; $p < 0.05$) (Table 3).

Table 4 demonstrates the comparison of baseline characteristics of subjects according to in-hospital mortality. Compared with the patients who had survived, the patients who had died had significantly lower baseline blood pressure, higher baseline blood sugar level, and higher baseline leucocyte count ($p < 0.05$). Meanwhile, a predominant in-hospital mortality was present among patients with Killip class IV, 66.7% (n = 10), and the patients had experienced MVAs, 68.8% (n = 11) ($p < 0.05$). The study reported 68.8% (n = 11) of in-hospital mortality occurring among STEMI patients although it was not statistically significant. From the multivariate regression analysis, the occurrence of MVAs (OR: 86.37; 95% CI: 4.16–1792.70; $p < 0.05$) and blood sugar level (OR: 1.30; 95% CI: 1.01–1.67; $p < 0.05$) independently predicted in-hospital mortality among ACS patients presenting to the ED (Table 5).

4. Discussion

4.1 Ventricular arrhythmia

In this single-institution observational study, the incidence of VA was 18.8%, where 14.6% were MVAs. To the best of our knowledge, this study is the first in Malaysia to report on the incidence of VA among ACS patients presenting to the ED. Patients with MVAs had an 86-fold increased risk of in-hospital mortality. Notably, most of the VAs occurred during the first 24 hours of ED admission. Thus, to improve the prognosis of these patients, early corrective measures need to be instituted, and continuous ECG telemetry is crucial in detecting the life-threatening arrhythmias.

The incidence of VA in our study was three times higher than the incidence reported by Avezum et al. based on a huge study from the GRACE registry over 6 years, which recorded a proportion of only 6.9% of VA during hospital stay [16]. This could be due to the fact that the majority of patients with STEMI (62.7%) in our study received thrombolytic therapy as the reperfusion modality, because PCI was only available during office hours.

Before the era of PPCI, VA particularly VT was observed in around 20% of patients with myocardial infarction (MI) [3]. The occurrence of VA is expected to be high in the setting where thrombolytic therapy is still widely used as the main reperfusion strategy as is the case in our setting.

Among the STEMI patients who developed VA, 12 (66.7%) had received thrombolysis in ED before developing the arrhythmia. However, only six (22.2%) of the 27 VA patients had undergone PCI before developing the arrhythmia. MI patients, who underwent PPCI as the main reperfusion strategy, had shown less occurrence of VA than thrombolytics [4, 10, 11]. Similarly, thrombolysis did not show a reduction in the occurrence of VA as shown

TABLE 4. Baseline characteristics according to in-hospital mortality.

	In-hospital mortality		
Variables	**Yes**	**No**	**p value**
	n = 16	**n = 128**	
Mean age ± SD, years	58.7 ± 13.7	58.7 ± 12.7	1
Gender, n (%):			
Male	13 (81.3)	111 (86.7)	
Female	3 (18.8)	17 (13.3)	0.468
Race, n (%):			
Malay	9 (56.3)	62 (48.4)	
Chinese	5 (31.3)	44 (34.4)	
Indian	2 (12.5)	12 (9.4)	
Others	0	10 (7.8)	0.657
Diagnosis, n (%):			
STEMI	11 (68.8)	56 (43.8)	
NSTE-ACS	5 (31.3)	72 (56.3)	0.068
Median time from symptom onset to ED arrival (IQR) (hours)	3.0 (9.0)	4.0 (8.0)	0.167
Mean blood pressure ± SD, mmHg			
Systolic blood pressure	102.1 ± 31.3	137.4 ± 29.4	**0.002**
Diastolic blood pressure	60.8 ± 20.3	79.3 ± 17.0	**0.001**
On arrival heart rate, mean ± SD, beats/min	84.6 ± 28.1	82.8 ± 23.0	0.328
Baseline blood sugar mean ± SD, mmol/L	16.4 ± 9.0	11.1 ± 5.9	**0.001**
Baseline blood laboratory data:			
Leucocytes, mean ± SD, ($x10^9$/L)	14.7 ± 7.4	11.3 ± 3.9	**0.005**
Potassium, mean ± SD, mmol/L	4.1 ± 0.5	4.0 ± 0.4	0.55
Hemoglobin, mean ± SD, g/dL	13.1 ± 2.2	13.6 ± 1.7	0.144
Comorbidities, n (%):			
HTN	12 (75.0)	88 (69.3)	0.777
COPD	2 (12.5)	3 (2.4)	0.101
DM	6 (37.5)	67 (53.6)	0.291
Kidney disease	4 (25.0)	22 (17.6)	0.496
Hypercholesterolemia	7 (43.8)	49 (38.9)	0.788
Smoking history	9 (56.3)	44 (35.8)	0.17
History of PCI	2 (12.5)	16 (13.0)	1
History of CABG	1 (6.3)	12 (9.7)	1
Electrocardiographic features:			
ST-segment depression, n (%)	13 (81.3)	79 61.7)	0.262
ST-segment elevation, n (%)	11 (68.8)	65 (50.8)	0.289
T-wave inversion, n (%)	4 (25.0)	48 (37.5)	0.411
Mean heart rate ± SD (msec)	90 ± 29	82 ± 24	0.188
Mean PR interval ± SD (msec)	167 ± 68	173 ± 32	0.589
Mean QT interval ± SD (msec)	428 ± 54	423 ± 38	0.638
Killip classification, n (%):			
I	2 (13.3)	58 (67.4)	
II	2 (13.3)	14 (16.3)	
III	1 (6.7)	6 (7.0)	
IV	10 (66.7)	8 (9.3)	**< 0.001**
Incidence of MVAs, n (%)	11 (68.8)	10 (7.8)	**< 0.001**

in a huge landmark Global Utilization of Streptokinase t-PA for Occluded Coronary Arteries (GUSTO-I) trial [7]. Therefore, it is not surprising that the occurrence of VA is still relatively high in our study.

Killip classification has been associated with VA occurrence in ACS patients [1, 16, 17]. Henkel et al. reported the

TABLE 5. Multivariate regression analysis of predictors to in-hospital mortality.

Variables	OR	95% CI	p value
Diagnosis of ACS (STEMI vs. NSTE-ACS)	0.62	0.06–6.05	0.683
MVAs vs. non-MVAs	86.37	4.16–1792.70	**0.004**
Baseline systolic blood pressure, mmHg	0.95	0.89–1.02	0.167
Baseline diastolic blood pressure, mmHg	0.98	0.88–1.09	0.716
Baseline blood sugar, mmol/L	1.3	1.01–1.67	**0.04**
Leucocyte level, X 10^9/L	1.04	0.85–1.28	0.721
Killip class (reference: class I)			
Killip class II	6.54	0.21–203.33	0.284
Killip class III	0.29	0.01–11.86	0.518
Killip class IV	13.96	0.72–269.45	0.081

association of VA with Killip III and IV classifications [1], which was supported by Newby et al. [7] and in agreement with our findings that indicated that the larger the area of MI, the higher the risk of MVAs [18]. Killip classification, which was introduced in 1967, risk-stratified patients with MI [19] and had also shown a significant association with mortality [20–22]. However, it did not show a statistical significance for the prediction of in-hospital mortality in our study.

Several factors had been previously investigated, which significantly predict the occurrence of VA, such as STEMI diagnosis [23], age [16], biochemical parameters such as leukocytosis [9, 24], glucose level [24], acidosis [25], potassium level [9, 26], and electrocardiographic features [27]. However, none of these factors predict the occurrence of VA in our study.

4.2 In-hospital mortality

The in-hospital mortality rate was extremely high in patients with MVA in our study. One potential explanation for the high in-hospital mortality rates reported in this observational study is the severity level. The patients that died were most likely be of the higher Killip class and had higher leucocyte level with poor glycemic control (Table 4). As VA predicts in-hospital and long-term deaths [16], it is crucial to identify ACS patients at risk of developing VA to improve the short- and long-term outcome.

Arguably, STEMI diagnosis has been implicated with a more severe clinical outcome than NSTE-ACS [28]. In previous studies, VA occurrence was significantly higher in the STEMI than the NSTE-ACS group as reflected from the pathophysiology of STEMI in which coronary vessels that are fully occluded cause an infarction involving all the layers of the heart which are suitable substrates for reentry circuit formation, rendering the heart prone to arrhythmia [27]. Nevertheless, in our study, STEMI diagnosis did not show a significant association as well as predictive value for VA and in-hospital mortality. The mean time of arrival to ED was significantly earlier among STEMI patients compared with NSTE-ACS patients, possibly resulting in timely definitive therapy. Furthermore, none of the thrombolyzed patients showed failed thrombolysis, indicating possible successful reperfusion therapy, hence limiting the damage and scar formation.

Occurrence of MVA is a strong predictive factor for in-hospital and long-term mortality in ACS patients [16, 23]. The identified causative factors that include scar formation, reentry pathway, and hyperinnervation of myocardium following MI have been attributed to the pathogenesis of VA [29, 30]. Following MI, necrosis of cardiomyocytes ensues, which subsequently undergoes a reparative process to maintain the structural integrity of the myocardium. The myocardium undergoes a complex phase of remodeling and ventricular healing, where alterations of the structure, morphology, and biochemical processes occur [31]. The most prominent in the remodeling phase is the formation of scar with fibrosis, which is vulnerable to the generation of VA [31].

In different development, Kostin et al. discovered, from a molecular study, that alterations in cell-to-cell coupling following the redistribution of connexins may contribute to the occurrence of reentrant tachycardias in the infracted zone [32]. The *nerve-sprouting hypothesis* is one of the most interesting theories regarding the pathogenesis of VA, particularly for VF. Increased sympathetic innervation preceded by nerve regeneration and myocardial hyperinnervation following an infarct was suggested to play crucial roles in the development of cardiac arrhythmia. Immediately after an infarct, the myocardium sustains nerve damage and regional denervation [33]. This is subsequently followed by neurilemma cell proliferation and axonal regeneration *(nerve sprouting)* [34], which consequently results in a global increase in adrenergic nerve density (*sympathetic hyperinnervation)*, hence amplifying the risk and propensity for VA [35].

Systolic failure secondary to acute MI correlates well with left ventricular ejection fraction, which is a known prognostic parameter for short- and long-term risk of mortality and sudden cardiac death [36]. The patients who died had a significantly lower mean systolic and diastolic blood pressure on presentation to the ED. Although both parame-

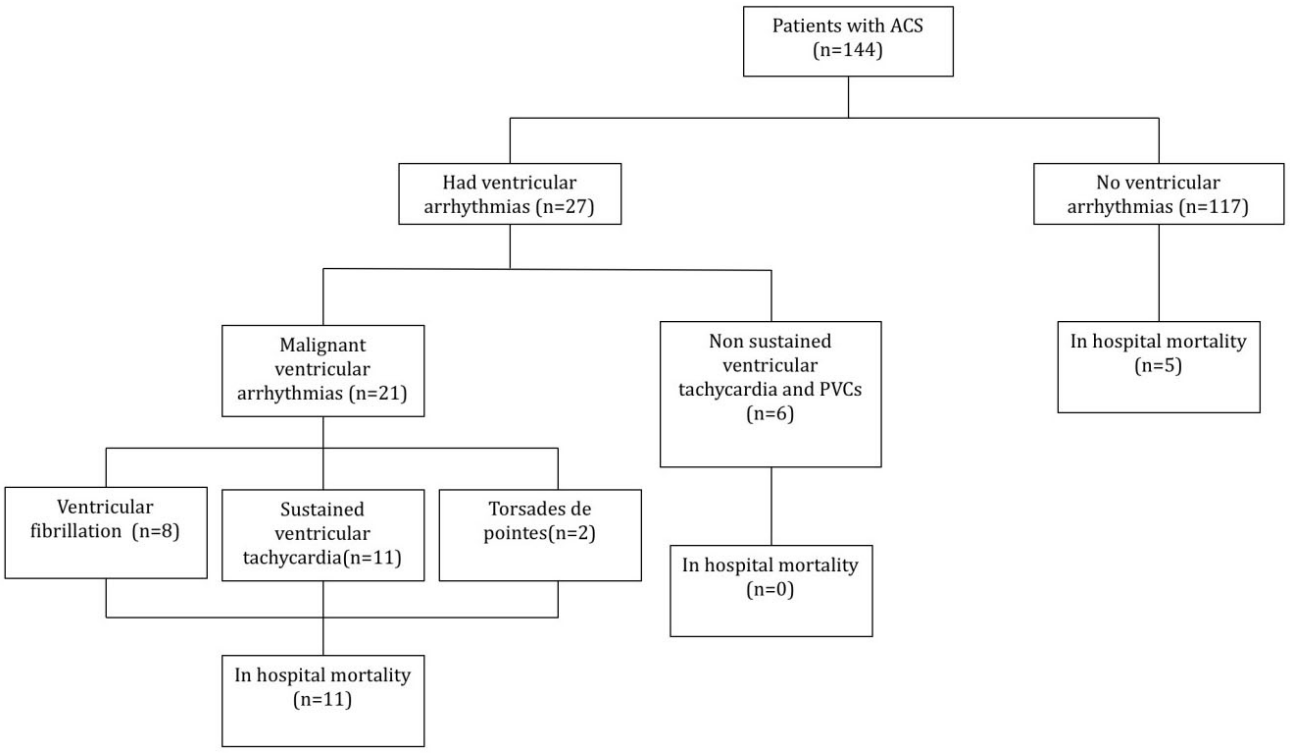

FIGURE 1. The characteristics of VA and in-hospital mortality.

ters did not show a statistical significance predictive value regarding the development of VA and in-hospital mortality, they may correlate with the severity of MI, considering that lower blood pressure is a marker of cardiogenic shock. From the clinical practice standpoint, this finding supports the need for clinicians to be more vigilant regarding blood pressure changes among ACS patients during the early course of ED stay.

The mean glucose level at presentation was significantly higher among ACS patients who died in our study. This finding was supported by Sanjuan et al. that highlighted the impact of stress hyperglycemia as an independent risk factor for VA and death among STEMI patients [37]. Glucose level above 140mg/dL (7.8 mmol/L) was associated with a twofold increase of in-hospital mortality risk, regardless of the diabetic status [37, 38]. This finding further emphasizes the need for aggressive glycemic control among MI patients, independent of the diabetic background.

Time-based risk assessment showed that 81.5% of VA occurred within the first 24 hours from the onset of symptoms. This finding was consistent with previous studies that also demonstrated early VA occurrence among ACS patients [4, 10, 23], which signifies a higher risk of mortality [23]. The findings further reiterate the current recommendations of 24 to 48 hours of continuous electrocardiographic monitoring in patients with MI [39]. However, in-hospital settings with backlog issues, this group of patients may end up in the ED longer than 24 hours. Close monitoring and continuous telemetry should be made compulsory to avoid missing the life-threatening arrhythmia, and priority should be given for coronary rehabilitation ward, coronary care unit, or intensive care unit admission.

5. Conclusion

One major finding from this observational study was the 86-fold increased risk of in-hospital mortality among ACS patients who developed VA, with most arrhythmias occurring during the first 24 hours from ED admission. Recognition of risk factors for VA is crucial in aiding the treating physicians to institute early corrective measures. Our study indicates the need for a predictive scoring model to be formulated to systematically identify the high-risk patients. With such events being difficult to treat and detect, our study also reiterates the recommendations of continuous ECG monitoring for 24 to 48 hours in high-risk groups. It is recommended that a larger prospective study be conducted to further determine the possible variables associated with the occurrence of VA and in-hospital mortality.

6. Limitation

This study has a relatively small sample size and was conducted in a single center. A larger prospective multicenter study may provide a better representation of our population. In addition, the study sample was inclusive of all types of ACS: UA, NSTEMI, and STEMI. In this study, UA and NSTEMI were grouped together as NSTE-ACS. As some of the NSTE-ACS patients were admitted to the general ward without continuous ECG telemetry, the true incidence of MVA in the NSTE-ACS group may have been underreported. The study had to exclude the troponin levels

in the analysis due to a sudden change in the hospital policy for troponin use. Therefore, the association of troponin with the outcome under study cannot be ascertained.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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