ORIGINAL ARTICLE

Electrocardiographic measures of ventricular repolarization dispersion and arrhythmic outcomes among ST elevation myocardial infarction patients with pre-infarction angina undergoing primary percutaneous coronary intervention

Tarek A. N. Ahmed | Amr A. Abdel-Nazeer | Ayman K. M. Hassan |
Hosam Hasan-Ali | Amr A. Youssef

Department of Cardiovascular
Medicine, Asyut University Hospital, Asyut,
Egypt

Correspondence

Tarek A. N. Ahmed, Department of
Cardiovascular Medicine, Asyut University
Hospital, Asyut, Egypt.
Email: tarek.a.n.ahmed@med.aun.edu.eg

Abstract

Background: Arrhythmias are considered one of the major causes of death in ST elevation myocardial infarction (STEMI), particularly in the early in-hospital phase. Pre-infarction angina (PIA) has been suggested to have a protective role.

Objectives: To study the difference in acute electrocardiographic findings between STEMI patients with and without PIA and to assess the in-hospital arrhythmias in both groups.

Material and Methods: We prospectively enrolled 238 consecutive patients with STEMI. Patients were divided into two groups: those with or without PIA. ECG data recorded and analyzed included ST-segment resolution (STR) at 90 min, corrected QT interval (QTc) and dispersion (QTD), T-peak-to-T-end interval (Tp-Te), and dispersion and Tp-Te/QT ratio. In-hospital ventricular arrhythmias encountered in both groups were recorded. Predictors of in-hospital arrhythmias were assessed among different clinical and electrocardiographic parameters.

Results: Of the 238 patients included, 42 (17%) had PIA and 196 (83%) had no PIA. Patients with PIA had higher rates of STR ($p < 0.0001$), while patients with no PIA had higher values of QTc ($p = 0.006$), QTD ($p = 0.001$), Tp-Te interval ($p = 0.001$), Tp-Te dispersion ($p < 0.0001$), and Tp-Te/QT ratio ($p = 0.01$) compared to those with angina preceding their incident infarction (PIA). This was reflected into significantly higher rates of in-hospital arrhythmias among patients with no PIA (20% vs. 7%, $p = 0.04$). Furthermore, longer Tp-Te interval and higher Tp-Te/QT ratio independently predicted in-hospital ventricular arrhythmias.

Conclusion: Pre-infarction angina patients had better electrocardiographic measures of repolarization dispersion and encountered significantly less arrhythmic events compared to patients who did not experience PIA.

1 | INTRODUCTION

In patients with acute myocardial infarction (MI), the presence of transient periods of symptomatic ischemia before the onset of the

infarction proves to have beneficial effects. This, so-called preinfarction angina (PIA), appears to be associated with smaller infarct size (Andreotti et al., 1996; Papadopoulos, Karvounis, Parharidis, & Louridas, 2005; Rezkalla & Kloner, 2004; Shiraki et al., 1998), more

myocardial viability (Iglesias-Garriz et al., 2001), better regional and global left ventricular function (Cortina et al., 1985; Hirai et al., 1992; Matsuda et al., 1984), and better improvement in left ventricular function at short- to mid-term follow-up (Iglesias-Garriz, Rodriguez, Garrote, Corral, & Pascual, 2002; Noda et al., 1999). Previous studies have shown that patients with myocardial infarction preceded by angina have smaller infarcts and a better in-hospital outcome after thrombolytic therapy than patients without pre-infarction angina (Kloner, Gibson, Cannon, & Braunwald, 1996). More recent studies have shown that this phenomenon extends to patients undergoing primary percutaneous coronary intervention (PPCI) (Iglesias-Garriz et al., 2005). The reason for this finding is unclear, although myocardial preconditioning by the ischemic episodes associated with angina has been proposed (Kloner et al., 1996). While some studies showed benefit of PIA in terms of surrogate markers of reperfusion as well as in hard clinical endpoint (Ishihara et al., 1997; Taniguchi et al., 2014), other studies have questioned the beneficial effect of PIA in this specific subset of patients (Pryds et al., 2016; Tomoda & Aoki, 1999; Zahn et al., 2001). Recent studies have identified dispersion of repolarization as the principal substrate and the most common trigger for the development of lethal arrhythmias among STEMI patients (Shenthara, Deora, Rai, & Nanjappa, 2015; Tatlisu et al., 2014; Yu et al., 2018). Attempts to identify measures of dispersion of repolarization have been intriguingly challenging. Moreover, inconclusive evidence exists about its relation to arrhythmic risk and sudden cardiac death in the general population, with some conflicting data about this issue (Panikkath et al., 2011; Porthan et al., 2013). In this study, we try to explore the potential value of some electrocardiographic parameters as possible indices of repolarization dispersion in STEMI patients. Moreover, we attempt to assess whether PIA would be associated with better electrocardiographic measures of repolarization dispersion and hypothetically better in-hospital arrhythmic outcomes.

2 | METHODS

2.1 | Study population

This was a prospective study which enrolled 238 consecutive patients with first acute STEMI who underwent PPCI in the period from October 2015 till September 2016. Patients were recruited from an ongoing registry (operational since October 2015), which evaluates the effects of a well-structured AMI care program (Stent For Life) on short- and long-term outcomes (Sobhy et al., 2012). Our center is a tertiary center providing a round-the-clock service of PPCI with highly experienced PCI physicians and dedicated nurses. Diagnosis of STEMI was made on the basis of typical electrocardiographic changes with clinical symptoms associated with elevation of cardiac biomarkers (Thygesen et al., 2019). Patients were included if they had chest pain for >30 min and relevant ST-segment elevation in at least two contiguous leads, and admission within 12 hr from chest pain onset. Patients were excluded from the study for any of the following reasons: previous myocardial infarction,

inability to describe the pattern of pain, or presence of LBBB or paced rhythm. Patients were divided into two groups according to the occurrence of pre-infarction angina (PIA), first group were patients with PIA, and second group were those without PIA. PIA was defined as one or more episodes of typical chest pain persisting <30 min, either at rest or on exertion, within one week before the onset of acute myocardial infarction. Medical history, symptoms on arrival, electrocardiographic examination, angiographic, laboratory, echocardiography, and clinical follow-up data were recorded in all patients. The study was approved by the institutional review board and complies with the Declaration of Helsinki. A written informed consent was obtained from all patients.

2.2 | Medications

All patients received an equivalent of 300 mg of acetylsalicylic acid, 600 mg clopidogrel, or 180 mg ticagrelor as a loading dose. The use of GP IIb/IIIa inhibitors was considered for bailout in case of no reflow or thrombotic complication and left to the operator's discretion. Heparin was given as 70–100 IU/kg i.v. bolus. After the procedure, all patients received aspirin (75 mg/day) indefinitely and clopidogrel 75 mg/day or ticagrelor 90 mg twice daily for one year. Other medications, including beta-blockers, ACE inhibitors, nitrates, and statins, were prescribed according to standardized protocols.

2.3 | Electrocardiographic and arrhythmic outcome analysis

Standard 12-lead electrocardiogram (ECG) was acquired before, immediately after reperfusion, and 90 min from restoration of flow. The 12-lead ECG was recorded at a paper speed of 25 mm/s and 1 mV/cm standardization. To improve the accuracy of measurements, the ECG was scanned, digitalized, and magnified through computer photo viewer. Then, measurements were performed through ECG Caliper software program (Cardio Caliper 3.3, Iconico). The QT interval was regarded as the onset of QRS complex to the end of T wave and corrected by the Bazett's formula. T-peak-to-T-end (Tp-Te) interval was measured from the peak of T wave to its end in lead V₅, because it best reflects the transmural axis of the left ventricle (Antzelevitch et al., 2007). If V₅ was not suitable, leads V₄ and V₆ in that order were measured (Castro et al., 2006). The end of the T wave was defined as the intersection of the tangent to the downslope of the T wave and the isoelectric line when not followed by a U wave or if distinct from the following U wave. If a U wave followed the T wave, the T-wave offset was measured as the nadir between the T and U waves (Perkiomaki, Koistinen, Yli-Mayry, & Huikuri, 1995). QT dispersion was recorded, defined as the difference between the maximum and minimum QT intervals in all ECG leads. Similarly, Tp-Te dispersion was recorded, defined as the difference between the maximum and minimum T-peak-to-T-end interval in all ECG leads. The Tp-Te-to-QT intervals ratio (Tp-Te/QT) was calculated as well. Premature ventricular complexes (PVCs) were characterized with atrioventricular dissociation and widened QRS complex (>120 ms), whose

morphology was different from the sinus' one. Documentation of high-risk PVCs was recorded, and patients were classified according to Lown grading score (high-risk PVC: Lown score ≥ 3 ; Lown & Wolf, 1971). Ventricular tachycardia (VT) was defined as sustained VT (≥ 30 s), and ventricular fibrillation (VF) as an irregular fibrillation wave. Location of MI was defined by ST elevation on related leads in ECG (V_1 – V_3 with or without V_4 – V_6 referring to the anterior wall; I, aVL, or V_4 – V_6 referring to lateral wall; II, III, aVF referring to the inferior wall). In-hospital death related to cardiac arrhythmias was reported. All ECGs were double-checked, and the final results were established by consensus of two independent cardiologists (A.A. and A.H.) who were blinded to the clinical and angiographic data. The inter-observer agreement was calculated with weighted kappa statistics and showed good agreement ($k = 0.96$, $p = 0.001$). All patients were provided continuous ECG monitoring until discharge.

2.4 | Primary PCI and angiographic analysis

Immediately after established STEMI diagnosis, PCI was performed via the femoral or radial access route. Culprit vessel in MI was verified by selective coronary angiography (CAG). Coronary arteries were divided into four systems: left main artery system (LM), left anterior descending artery system (LAD), left circumflex artery system (LCX), and right coronary artery system (RCA). CAG characteristics included culprit artery, acute occlusive segment, and multivessel disease, regarded as having at least another vessel with $\geq 75\%$ stenosis besides culprit artery occlusion. Initial and postprocedural TIMI flow grade of the IRA was routinely assessed (TIMI Study Group, 1985).

Interventional techniques, thrombus aspiration, and administration of platelet glycoprotein IIb/IIIa receptor inhibitors were left to the operator's discretion and according to rigorously standardized protocols strictly adopted at our hospital.

2.5 | Statistical analysis

Categorical variables were compared using the chi-square test or Fisher's exact test. Continuous, normally distributed data were tested by Student's *t* test or, in the case of a non-Gaussian distribution, by a nonparametric test for independent samples (Mann-Whitney *U* test). A probability level of *p* value < 0.05 was considered as statistically significant in all tests. The inter-observer agreement was calculated using weighted kappa statistics. Relevant variables that at univariate analysis had a *p*-value ≤ 0.05 were included in a multiple logistic regression model for the outcome of in-hospital ventricular arrhythmias. All statistical analyses were performed using IBM SPSS statistics 21 software.

3 | RESULTS

3.1 | Baseline characteristics

This was a prospective study involving 238 patients referred to Assiut University Hospital for primary PCI in the setting of STEMI

over a period of 12 months. Among those, 42 (17%) had PIA and 196 (83%) had no PIA. Demographics and clinical data are presented in Table 1. There was no significant difference in the baseline clinical characteristics between both groups. There was a trend toward higher rates of DM in PIA group (38% vs. 24%, $p = 0.07$).

3.2 | Acute electrocardiographic characteristics

Table 2 shows the acute electrocardiographic characteristics of the study population.

Patients with PIA had higher rates of ST-segment resolution at 90 min (83% vs. 51%, $p < 0.0001$), while patients with no PIA had higher values of QTc (445.3 ± 50.3 vs. 422.3 ± 41.2 ms, $p = 0.006$), QTD (70 ± 25.6 vs. 56.1 ± 20.7 ms, $p = 0.001$), Tp-Te interval (91.7 ± 20.2 vs. 81.2 ± 12.6 ms, $p = 0.001$), Tp-Te dispersion (17.9 ± 6.2 vs. 13.6 ± 4.3 ms, $p < 0.0001$), and Tp-Te/QT ratio (0.205 ± 0.03 vs. 0.193 ± 0.02 , $p = 0.01$) compared to those with PIA.

3.3 | Angiographic and procedural data

Most of patients presented with anterior STEMI. In 141 (59%) patients, LAD was the culprit, while RCA in 81 (34%) patients and LCx in 16 (7%) patients. Baseline TIMI flow was significantly worse among patients with no PIA ($p < 0.0001$). However, the final TIMI flow was not significantly different between both groups ($p = 0.2$). Procedural data were quite similar between both groups with no statistically significant difference (Table 3).

TABLE 1 Baseline patients' characteristics

Parameter	PIA <i>n</i> = 42	No PIA <i>n</i> = 196	<i>p</i> Value
Age (years)	56.6 ± 11	55 ± 13	0.4
Male	32 (76%)	150 (77%)	0.9
Hypertension	14 (33%)	45 (22%)	0.2
DM	16 (38%)	48 (24%)	0.07
Previous IHD	10 (23%)	30 (15%)	0.2
Smoker	24 (57%)	120 (61%)	0.6
Infarction site			
Anterior	28 (66%)	113 (57%)	0.3
Nonanterior	14 (34%)	83 (43%)	
Killip class			
I	39 (94%)	176 (90%)	0.3
II	0 (0%)	12 (6%)	
III	1 (2%)	4 (2%)	
IV	2 (4%)	4 (2%)	

Note. DM: diabetes mellitus; IHD: ischemic heart disease; PIA: pre-infarction angina; SD: standard deviation. Data are presented as mean $\pm$ SD or number (%) of patients.

TABLE 2 Electrocardiographic findings in the study groups

Parameter	PIA N = 42	No PIA N = 196	p Value
ST-segment resolution	35 (83%)	100 (51%)	<0.0001
Corrected QT interval	422.3 ± 41.2	445.3 ± 50.3	0.006
QT dispersion	56.1 ± 20.7	70 ± 25.6	0.001
Tp-Te interval	81.2 ± 12.6	91.7 ± 20.2	0.001
Tp-Te dispersion	13.6 ± 4.3	17.9 ± 6.2	<0.0001
Tp-Te/QT	0.193 ± 0.02	0.205 ± 0.03	0.01

Note. F.QRS: fragmented QRS complex; PIA: pr-infarction angina; SD: standard deviation; Tp-Te: T peak-T end. Data are presented as mean ± SD or number (%) of patients.

TABLE 3 Procedural and angiographic characteristics of the study population

Parameter	PIA (n = 42)	No PIA (n = 196)	p-Value
Total ischemic time (hr)	4.8 ± 3.5	5.3 ± 3.4	0.4
Stent length (mm.)	24.4 ± 8	27.2 ± 7	0.06
Stent diameter (mm.)	3 ± 0.3	3.1 ± 0.4	0.2
Thrombus aspiration	7 (17%)	47 (24%)	0.5
Predilatation	34 (81%)	156 (79%)	0.9
GP IIb/IIIa inhibitors	13 (31%)	71 (36%)	0.5
Culprit artery			
LAD	28 (67%)	113 (58%)	0.3
RCA	10 (24%)	71 (36%)	
LCX	4 (9%)	12 (6%)	
Baseline TIMI flow			
0	30 (71%)	172 (87%)	<0.0001
I	0 (0%)	10 (5%)	
II	7 (17%)	9 (5%)	
III	5 (12%)	5 (3%)	
Final TIMI flow			
<III	7 (17%)	52 (27%)	0.2
III	35 (83%)	144 (73%)	

Note. GP: glycoprotein; LAD: left anterior descending; LCX: left circumflex artery; PIA: p-infarction angina; RCA: right coronary artery; TIMI: thrombolysis in myocardial infarction. Data are presented as mean ± SD or number (%) of patients.

Bold indicates significant *p*-values.

3.4 | In-hospital ventricular arrhythmic outcome

Table 4 shows the patterns and overall in-hospital ventricular arrhythmic events and fatalities among the study groups. There were significantly higher ventricular arrhythmic events in the no PIA

TABLE 4 Patterns and overall in-hospital ventricular arrhythmic events among the study groups

Parameter	PIA N = 42	No PIA N = 196	p Value
High-risk PVCs	0 (0%)	11 (5.6%)	0.2
NSVT	1 (2.4%)	13 (6.6%)	0.7
Sustained VT	2 (4.8%)	14 (7.1%)	0.8
VF	0 (0%)	2 (1%)	0.5
Overall in-hospital VA	3 (7%)	40 (20.4%)	0.04
Fatal arrhythmias	0 (0%)	7 (3.6%)	0.5

Note. NSVT: nonsustained ventricular tachycardia; PIA: pre-infarction angina; PVCs: premature ventricular complexes; VA: ventricular arrhythmias; VF: ventricular fibrillation; VT: ventricular tachycardia. Data are presented as number (%) of patients.

Bold indicates significant *p*-values.

group compared to the PIA group (3 [7.1%] vs. 40 [20.4%], *p* = 0.04). Seven (3.6%) of the 16 VT/VF events in the no PIA group were fatal while none were in the PIA group (*p* = 0.5).

3.5 | Predictors of in-hospital ventricular arrhythmias

Univariate binary logistic regression analysis was performed for each of the relevant clinical and electrocardiographic parameters to identify potential predictors of in-hospital ventricular arrhythmias. Multivariate binary logistic regression analysis was conducted to determine which variables independently predicted the occurrence of in-hospital ventricular arrhythmias (Table 5). To avoid multicollinearity, which occurs when independent variables in a regression model are correlated, each of the individual electrocardiographic parameters was included in a separate model. After adjusting for significant covariates, it was observed that QTc (OR = 1.1, 95% CI = 1.05–1.11, *p* < 0.0001), longer Tp-Te interval (OR = 1.2, 95% CI = 1.11–1.21, *p* < 0.0001), and higher Tp-Te/QT ratio (OR = 2.1, 95% CI = 1.7–2.6, *p* < 0.0001) independently predicted the occurrence of dangerous in-hospital ventricular arrhythmias.

4 | DISCUSSION

This study adds further evidence to the pre-existing likely protective benefits of PIA in the setting of STEMI. Patients with PIA had significantly better electrocardiographic measures of repolarization dispersion, in the form of shorter QTc, QTD, Tp-Te interval, Tp-Te dispersion, and Tp-Te/QT ratio. This was reflected on hard clinical endpoints, with less in-hospital ventricular arrhythmias among patients with PIA compared to those without. Eventually, fatal in-hospital arrhythmias were more encountered among patients without PIA (seven patients [3.6%] vs. 0 patients [0%], *p* = 0.7).

Pre-infarction angina has been shown in several studies to be associated with better clinical outcome and significant myocardial protection in the setting of PPCI during STEMI (Reiter, Henry, &

TABLE 5 Univariate and multivariate logistic regression analysis to predict in-hospital ventricular arrhythmias

Predictors	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Age	0.9	0.96–1.01	0.5	–	–	–
Male gender	0.9	0.45–2.14	0.9	–	–	–
DM	0.6	0.31–1.27	0.2	–	–	–
HTN	1.3	0.58–2.91	0.5	–	–	–
Total ischemic time	1.0	0.91–1.10	0.9	–	–	–
Infarct site	1.9	0.96–4.11	0.06	–	–	–
PIA ^a	3.3	1.01–11.3	<0.05	2.1	0.3–13.5	0.4
				2.6	0.4–15.2	0.3
				1.0	0.2–4.5	0.9
STR ^a	2.6	1.33–5.22	<0.01	2.5	0.8–7.2	0.09
				1.2	0.4–3.7	0.8
				2.2	0.9–5.4	0.08
QTc interval ^a	1.07	1.05–1.10	<0.0001	1.1	1.05–1.11	<0.0001
Tp-Te ^a	1.15	1.11–1.25	<0.0001	1.2	1.11–1.21	<0.0001
Tp-Te/QT ^a	2.12	1.71–2.64	<0.0001	2.1	1.7–2.6	<0.0001

Notes. Data are displayed as odd's ratio (OR), 95% confidence interval (CI), and p value. DM: diabetes mellitus; HTN: hypertension; PIA: pre-infarction; QTc: corrected QT interval; STR: ST resolution; Tp-Te: T-peak-to-T-end interval. Infarct site: anterior versus non-anterior.

^aTo avoid multicollinearity, each of the marked parameters was included individually in separate multivariate models, along with other statistically significant clinical parameters (*). *OR, 95% CI, and p value of PIA and STR, in different models, are displayed in the same order of the marked ECG parameters as shown in table.

Bold indicates significant p-values.

Traverse, 2013; Taniguchi et al., 2014). Other studies have shown that PIA is associated with a better prognosis (Andreotti et al., 1996; Kloner et al., 1995; Nakagawa et al., 1995; Ottani et al., 1995), including reduced infarct size and in-hospital ventricular arrhythmias. In a study performed by Lorgis et al. (2012) on 1541 patients, it was observed that patients with PIA developed fewer ventricular arrhythmias and heart failure during the hospital admission.

Dangerous cardiac arrhythmias (VT/VF) are encountered in about 5%–10% of STEMI cases (Bloch Thomsen et al., 2010; Henkel et al., 2006; Zorzi et al., 2014). Nevertheless, reliable methods to predict VT/VF in the setting of acute STEMI are still not fully elucidated. Prolonged QT interval is considered the conventional risk factor for VT/VF (Arisha et al., 2013; Yu et al., 2012). However, this factor is not that reliable in the acute phase of STEMI.

In our study, univariate logistic regression analysis of various clinical and electrocardiographic parameters showed that PIA, ST-segment resolution, QTc interval, QTD, Tp-Te interval, Tp-Te dispersion, as well as Tp-Te/QT ratio were individual predictors of dangerous in-hospital arrhythmias. However, when adjusted for other covariates in a multivariate logistic regression model, only prolonged QTc, prolonged Tp-Te interval, and higher Tp-Te/QT ratio independently predicted in-hospital ventricular arrhythmias.

Myocardial ischemia induces electrophysiological alterations in action potentials, causing repolarization dispersion between normal and ischemic fibers and between epicardium and endocardium, which can be detected on the surface 12-lead ECG (Lukas, 1993;

Nash, Bradley, & Paterson, 2003). This means that more precise examination of ST-T waveforms with closer look at measures of repolarization dispersion (rather than ST segment alone) is more promising in prognostication and risk stratification in the acute phase of STEMI.

QRS complex and T wave represent cardiomyocyte depolarization and repolarization, respectively. QTc interval, Tp-Te interval, and Tp-Te/QT ratio are widely known as ECG parameters to reflect cardiac repolarization. Because QT interval already includes QRS duration, which is an indicator of cardiac depolarization, it might not be precise enough to reflect cardiac repolarization. On the other hand, Tp-Te interval specifically represents the degree of dispersion of cardiac repolarization from the epicardium to endocardium (Xia et al., 2005; Yagishita et al., 2015). Increased transmural dispersion of cardiac repolarization is prone to elicit VT/VF underlying reentrant mechanism (Akar, Laurita, & Rosenbaum, 2000; Chauhan et al., 2006). Accordingly, it would be reliable to consider Tp-Te interval and Tp-Te/QT ratio as noninvasive parameters to predict VT/VF in the acute phase of STEMI.

In a study on coronary artery disease patients, it was concluded that prolonged Tp-Te interval was independently associated with SCD, particularly in situation where QTc is either normal or uninterpretable due to prolonged QRS duration (Panikkath et al., 2011), thus extending the value of repolarization beyond the traditional QTc. However, in a large adult general population study, although T-wave morphology parameters predicted SCD, there was no association between Tp-Te interval and SCD (Porthan et al., 2013). Subsequently, it

could be inferred that the prognostic value of Tp-Te might be more reliable when myocardium is vulnerable as in case of STEMI.

Using a canine ventricular wedge preparation model, a bench study explored the genesis of Tp-Te as well as the potential mechanisms that may link Tp-Te prolongation to increased risk of arrhythmias (Diego et al., 2013). The potassium current is the most involved among outward currents, leading to delayed repolarization, which in turn renders the myocardium electrically unstable. Myocardial infarction is associated with transmural dispersion of repolarization, which leads to malignant ventricular arrhythmias that may cause sudden cardiac death, undermining the benefits of reperfusion therapy.

Our study concludes that electrocardiographic markers of repolarization dispersion in the acute phase of STEMI, namely QTc interval, Tp-Te interval, and Tp-Te/QT ratio, could predict the occurrence of potentially fatal cardiac arrhythmias. Topilski et al. (2007) found that QT, QTc, and Tp-Te intervals were strong predictors of torsade de pointes, with the best single discriminator being prolonged Tp-Te, which was in concordance with our results. Watanabe et al. (2004) demonstrated that prolonged Tp-Te was associated with inducibility as well as spontaneous development of ventricular tachycardia (VT) in high-risk patients with organic heart disease.

In accordance with our results, a smaller study conducted on 50 STEMI patients showed that Tp-Te interval and Tp-Te/QT ratio predicted in-hospital malignant ventricular arrhythmias (Shenthar et al., 2015). They showed that Tp-Te >0.1 s and Tp-Te/QT ratio >0.3 predicted primary VF with a sensitivity of 100%. However, the Tp-Te/QT ratio had a higher specificity (82.9% for Tp-Te/QT ratio vs. 44.7% for Tp-Te) and overall accuracy (84% for Tp-Te/QT ratio vs. 48% for Tp-Te) as compared with Tp-Te. Recently, a study by Yu and colleagues demonstrated similar findings, showing that Tp-Te interval >100 ms. and Tp-Te/QT ratio >0.253 independently predicted VT/VF in the acute phase of STEMI. Moreover, they showed that PVC characteristics not only predicted VT/VF in the acute phase, but also predicted LVEF decrease on long term (Yu et al., 2018).

Although the association of prolonged Tp-Te and Tp-Te/QT ratio to arrhythmias in STEMI patients has been tackled by several investigators, this is the first study, to our knowledge, that shows an additive protective effect of PIA based on these measures of repolarization dispersion.

5 | CLINICAL IMPLICATIONS

The issue of risk stratification and arrhythmia prediction, during the in-hospital course of STEMI, remains a challenging subject, particularly in STEMI patients with vulnerable myocardium that was not preconditioned by PIA. Future approach to ECG interpretation should focus on analysis of such simple, non-invasive, bedside parameters of ventricular repolarization dispersion.

Looking at new repolarization parameters beyond the traditional QTc might be an important risk stratification tool, thus determining the group of potentially high-risk patients for whom special attention should be paid. The latest guidelines of management of

STEMI patients have recommended 24 hr of ECG monitoring (Ibanez et al., 2018). Our data suggest that some ECG parameters, often overlooked, might warrant a longer period of close monitoring and watchful expectancy.

6 | LIMITATIONS

The study has some limitations. This study was a single-center study with limited number of patients and limited number of events with possibility of by chance findings. The sample size was relatively small, although it was powered enough to detect the pre-specified endpoints. Still, the findings need to be validated in larger cohorts. Besides, long-term follow-up of VT/VF occurrence in STEMI patients was not performed. Accordingly, the present findings are only appropriate for predicting VT/VF in the acute phase of STEMI. The prediction models do not take into account simultaneous assessment of QTc, Tp-Te, and Tp-Te/QT. It is well known that Tp-Te and Tp-Te/QT correlate well with each other and they correlate to some extent with QTc. Therefore, claiming that all three parameters are independent predictors must be cautiously interpreted. Moreover, in our prediction models, it is possible that some potentially important variables lacked significance, which might be due to relatively small sample size.

7 | CONCLUSION

PIA patients had better electrocardiographic measures of ventricular repolarization dispersion and encountered significantly less in-hospital arrhythmic events compared to patients who did not experience PIA. Among the different clinical and electrocardiographic parameters, QTc, Tp-Te interval, and Tp-Te/QT ratio were significantly and independently associated with increased odds of in-hospital ventricular arrhythmias.

ORCID

Tarek A. N. Ahmed <https://orcid.org/0000-0003-4986-4849>

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