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Speckle Tracking Echocardiography as A Predictor of in Hospital Major Adverse Cardiovascular Events in STEMI Patient Treated with Primary PCI Strategy Versus Pharmacoinvasive PCI Versus Rescue PCI

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ABSTRACT

Background: Primary percutaneous coronary intervention (PCI) is considered the best method of reperfusion in the setting of acute ST elevation myocardial infarction (STEMI). Logistics sometimes make a hindrance to this strategy in developing countries. Thrombolytic therapy strategy, whereby the patient receives a fibrinolytic agent and subsequently taken up for coronary angiogram within 3–24 h of successful thrombolysis or immediately if thrombolytic therapy failed is considered an alternative method for reperfusion. This work aimed to study and assess how speckle tracking can predict in hospital major adverse cardiovascular events (MACE) in patients treated with Primary PCI versus pharmacoinvasive strategy versus rescue PCI. **Methods:** This study was conducted on 90 patients admitted with STEMI within the first 24 hours. Exclusion criteria included previous PCI, patients with history of CABG, patients with cardiogenic shock, and patients with renal or hepatic failure, malignancy, rheumatic or congenital heart disease. Patients were divided into 3 groups: Group I: 40 patients subjected to primary PCI, group II: 30 patients subjected to Rescue PCI, and Group III: 20 patients subjected to Pharmacoinvasive PCI. 2D speckle tracking echocardiography was done to the three groups. **Results:** There was a statistically significant difference between the three groups in MACE, and Global longitudinal strain (GLS). There was a statistically significant association between GLS and MACE in the three groups. In univariate regression analysis: Final TIMI flow< III, ejection fraction (EF), end systolic diameter (ESD)m end diastolic diameter (EDD), GLS, and primary PCI mode of treatment were predictors of MACE. In the multivariate regression analysis, using model adjusted for aforementioned parameters: GLS was a predictor of MACE. Conclusions: It was evident that GLS was a good predictor of MACE. Patients with higher GLS had increased incidence of MACE. It was also evident that GLS was higher in patients with rescue PCI when compared to primary PCI and pharmacoinvasive group.

Keywords: Orange fruit, pomegranate fruit, harvesting machine, picking device, harvesting methods, scissor and toothed disc speed.

1. Introduction

Primary percutaneous coronary intervention (PCI) is considered the best method of reperfusion in the setting of acute ST elevation myocardial infarction (STEMI). Logistics sometimes make a hindrance to this strategy in developing countries. Thrombolytic therapy strategy, whereby the patient receives a fibrinolytic agent and subsequently taken up for coronary angiogram within 3–24 h of successful thrombolysis or immediately if thrombolytic therapy failed is considered an alternative method for reperfusion (Paul and George 2017, Ibanez *et al.,* 2017).

In clinical practice, echocardiography is the modality of choice for the assessment of morphology and function of the left ventricle (LV) as it is noninvasive, widely available, relatively inexpensive, and has no side effects. Most of the studies assessed the LV by 2D echocardiography although LV global longitudinal strain (LV-GLS) was suggested to be a strong indicator of LV

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systolic function and for prognosis after PCI for acute myocardial infarction (MI) (Ibanez *et al.,* 2017, Potter Marwick, 2018).

With the advancement in echocardiography and introduction of layer-specific GLS obtained by speckle tracking, few studies have investigated the clinical value of this measure, and generally found that it can provide additional value when assessing prognosis and major adverse cardiac events (MACE) (Gao *et al.,* 2022).

This work aimed to study and assess how speckle tracking can predict in hospital MACE in patients treated with Primary PCI versus pharmacoinvasive strategy versus rescue PCI.

2. Patients and Methods

This study was conducted on 90 patients admitted with STEMI within the first 24 hours and treated with 1ry PCI, Pharmacoinvasive PCI or rescue PCI at Cardiovascular Medicine Department, Tanta University Hospitals during the period from August 2022 to January 2023.

Exclusion criteria included previous PCI, patients with history of CABG, patients with cardiogenic shock, and patients with renal or hepatic failure, malignancy, rheumatic or congenital heart disease.

Patients were divided into 3 groups: Group I: 40 patients subjected to primary PCI, group II: 30 patients subjected to Rescue PCI, and Group III: 20 patients subjected to Pharmacoinvasive PCI.

The privacy of all data was guaranteed and there was code number for every patient and included all of the investigations. Informed written consent was obtained from all patients after full explanation of benefits, risks and complications of the study. The study was approved by the institutional review board.

All patients were subjected to through history taking, complete clinical examination, 12 lead Electrocardiogram (ECG), routine laboratory investigations, primary PCI, pharmacoinvasive procedure or rescue PCI, 2D echocardiography within the first 24 hours after PCI, and speckle tracking echocardiography within the first 24 hours after PCI.

In pharmacoinvasive group, the patient received fibrinolytic therapy as alteplase or streptokinase intravenous infusion followed by PCI within 2 to 24 hours. In rescue PCI group, patients underwent PCI after failure of fibrinolytic therapy either alteplase or streptokinase intravenous infusion. This failure is determined by persistent chest pain and persistent STEMI.

Primary percutaneous intervention for Infarct related artery (IRA)
Preparation before primary PCI

A loading dose of dual anti platelet (Aspirin 300mg chewable) plus P2Y12 inhibitor (Ticagrelor 180 mg or Clopidogrel 600mg), plus IV unfractionated heparin (UFH) or low molecular weight heparin (LMWH) were used before the procedure. Glycoprotein IIb IIIa inhibitors (Tirofiban) were used during or after the procedure in selected cases.

Pharmacoinvasive and rescue techniques: patients receive thrombolytic therapy followed by coronary angiography either immediately in case of failed thrombolytic (rescue PCI) or within 3-24 hours after sign of successful reperfusion (pharmacoinvaseve PCI).

The used type of thrombolytic in Tanta university hospital CCU is
Streptokinase or alteplase according to availability in CCU.

The accepted time for starting the infusion: According to ESC guidelines 2017 IV bolus of thrombolytic therapy should start within 10 minutes, however thrombolytic therapy can be given within 12 hrs. from onset of chest pain.

Preparation of patient before starting Thrombolytic infusion (Hausenloy and Yellon, 2013)

A loading dose of dual anti-platelets; Aspirin (300 mg) & Clopidogrel (300 mg) was given if the patient's age was below 75 years old and half-loading dose if the patient's age was ≥75 years old was given (Grove *et al.,* 2021; Thygesen *et al.,* 2018).

Dose of Streptokinase: 1.5 million units IV over 30-60 minutes (Grove *et al.,* 2021; Thygesen *et al.,* 2018).

Preparation of Streptokinase

This should be infused over 60 minutes; Patients were monitored for the first few hours for signs of anaphylaxis or major bleeding. Infusion was slowed or terminated if allergic symptoms or major bleeding appeared (Lassen *et al.,* 2013).

Dose and preparation of alteplase

Patients received a bolus of 15 mg followed by weight-based 30-minute infusion of 0.75 mg/kg and a 60-minute infusion of 0.5 mg/kg. The total dose should not exceed 100 mg. Patient were followed for signs of major bleeding or anaphylaxis after which alteplase was stopped or slowed down.

Assessment of thrombolytic success: Chest pain relief, decrease in ST segment elevation by ≥ 50% compared to the initial ECG, reperfusion arrhythmia, and shooting of cardiac enzymes.

Percutaneous coronary angiography was performed either immediately after failed thrombolytic therapy or within 3 -24 hours after criteria of successful thrombolysis.

Major adverse cardiac events (MACE)

The three studies group were compared regarding in hospital MACE which include mortality, heart failure symptoms, re-infarction, bleeding complication and stroke.

Statistical analysis

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and were compared by paired Student's t- test for the same group. Qualitative variables were presented as frequency and percentage (%). Evaluation of diagnostic performance sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Agreement: Measurements of TTE and EC were compared by paired Student's T test. Calculation of Bias and its SD between TTE and EC were calculated. Modified Bland Altman plots of TTE and EC measurements were done A two tailed P value < 0.05 was considered significant.

3. Results

There was no statistically significant difference between the three groups regarding demographic data (age, and gender), risk factors, and STEMI location. (Table 1)

Table 1: Demographic data, risk factors, and location of STEMI of the three study groups

	Group I (n = 40)		**Group II (n = 30)**		**Group III (n = 20)**		**p**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Sex							
Male	31	77.5	23	76.7	15	75.0	0.977
Female	9	22.5	7	23.3	5	25.0	
Age (years)							
Mean ± SD.	56.73 ± 8.17		60.07 ± 7.17		58.35 ± 13.04		0.324
Risk factors	**Group I (n = 40)**		**Group II (n = 30)**		**Group III (n = 20)**		**p**
	No.	**%**	**No.**	**%**	**No.**	**%**	
Diabetes	23	57.5	17	56.7	11	55.0	0.983
Hypertension	21	52.5	13	43.3	10	50.0	0.745
Smoking	28	70.0	19	63.3	9	45.0	0.168
Family history	19	47.5	18	60.0	6	30.0	0.115
	STEMI location						
Anterior	19	47.5	11	36.7	8	40.0	
Inferior	20	50.0	17	56.7	12	60.0	0.740
Lateral	1	2.5	2	6.7	0	0.0	
Combined	3	7.5	2	6.7	2	10.0	1.000

There was no statistically significant difference between the three groups regarding vital signs but there was a statistically significant difference regarding symptoms duration. (Table 2)

Table 2: Vital signs and duration of symptoms in the study groups

Vital sings	Group I (n = 40)	Group II (n = 30)	Group III (n = 20)	p
Systolic blood pressure (mmHg)				
Mean ± SD.	119.0 ± 20.23	123.67 ± 25.29	122.0 ± 24.41	0.692
Diastolic blood pressure (mmHg)				
Mean ± SD.	76.50 ± 12.31	74.0 ± 13.61	76.50 ± 14.61	0.702
Pulse				
Mean ± SD.	76.13 ± 12.01	79.67 ± 12.99	81.50 ± 12.04	0.237
Symptoms duration (hours)				
Mean ± SD.	6.98 ± 4.85	7.43 ± 1.74	5.0 ± 2.43	0.006*

There was a statistically significant difference between the three groups regarding EF, ESD, EDD, and GLS while there was no difference between them regarding RSWMA. (Table 3)

Table 3: Echocardiographic data of the studied groups

Echo	Group I (n = 40)	Group II (n = 30)	Group III (n = 20)	p
EF (%)				
Mean ± SD.	47.05 ± 6.21	40.83 ± 4.69	47.60 ± 5.63	<0.001*
ESD (mm)				
Mean ± SD.	37.60 ± 3.14	39.30 ± 2.34	38.70 ± 2.81	0.044*
EDD (mm)				
Mean ± SD.	54.60 ± 4.65	58.10 ± 2.59	54.10 ± 3.63	<0.001*
RSWMA				
Anterior	20(50.0%)	11(36.7%)	7(35.0%)	0.407
Inferior	20(50.0%)	19(63.3%)	13(65.0%)	
GLS	**Group I (n = 40)**	**Group II (n = 30)**	**Group III (n = 20)**	**p**
Mean ± SD.	-11.95 ± 3.27	-10.17 ± 1.72	-12.70 ± 2.39	0.002*

EF: ejection fraction, ESD: end systolic diameter, EDD: end diastolic diameter, RSWMA: resting segmental wall motion abnormalities, GLS: global longitudinal strain

There was a statistically significant difference between the three groups in MACE. (Table 4)

Table 4: In hospital major adverse cardiovascular events (MACE) of the study groups.

	Group I (n = 40)		Group II (n = 30)		Group III (n = 20)		χ^2	p
	No.	%	No.	%	No.	%		
Death	0	0.0	0	0.0	0	0.0	–	–
Stroke	0	0.0	1	3.3	0	0.0	1.957	0.549
Rein fraction	0	0.0	1	3.3	0	0.0	1.957	0.549
CHF	8	20.0	8	27.6	1	5.0	3.946	0.139
Major bleeding	1	2.5	5	16.7	2	10.0	4.307	0.093
CIN	2	5.0	3	10.0	1	5.0	0.863	0.757
MACE	11	27.5	18	60.0	4	20.0	10.873*	0.004*

There was a statistically significant association between GLS and MACE in the three groups (Table 5)

Table 5: Relation between major adverse cardiovascular events (MACE) and global longitudinal strain (GLS) in each group

GLS	MACE		p
	No	Yes	
Group I	**(n= 29)**	**(n= 11)**	
Mean ± SD.	-12.86 ± 3.25	-9.55 ± 1.86	0.002*
Group II	**(n= 12)**	**(n= 18)**	
Mean ± SD.	-11.42 ± 1.62	-9.33 ± 1.24	0.001*
Group III	**(n= 16)**	**(n= 4)**	
Mean ± SD.	-13.56 ± 1.75	-9.25 ± 0.96	<0.001*

GLS: global longitudinal strain, MACE: major adverse cardiovascular events

In univariate regression analysis: Final TIMI flow< III, ejection fraction(EF), end systolic diameter (ESD)m end diastolic diameter (EDD), GLS, and primary PCI mode of treatment were predictors of MACE. In the multivariate regression analysis, using model adjusted for aforementioned parameters: GLS was a predictor of MACE. (Table 6)

Table 6: Univariate and multivariate Logistic regression analysis for the parameters affecting MACE

	Univariate		#Multivariate	
	p	OR (LL – UL 95%C.I)	P	OR (LL – UL 95%C.I)
Sex (male)	**0.718**	1.209(0.432 – 3.386)		
Age (years)	**0.299**	0.975(0.930 – 1.023)		
Diabetes	**0.895**	1.060(0.446 – 2.521)		
HTN	**0.953**	0.975(0.413 – 2.298)		
Smoking	**0.268**	1.673(0.673 – 4.155)		
Family history	**0.589**	1.267(0.537 – 2.990)		
Chest pain duration (hours)	**0.465**	1.044(0.929 – 1.174)		
Systolic blood pressure (mmHg)	**0.198**	1.013(0.994 – 1.032)		
Diastolic blood pressure (mmHg)	**0.641**	1.008(0.975 – 1.041)		
Pulse	**0.328**	0.982(0.948 – 1.018)		
STEMI location				
Anterior	**0.027***	2.714(1.122 – 6.564)	0.982	1.017(0.228 – 4.534)
Inferior	**0.084**	0.463(0.194 – 1.108)		
Lateral	**0.999**	–		
Number of diseased vessel (Multivessel)	**0.671**	0.830(0.351 – 1.962)		
Final TIMI flow (<3)	**0.013***	15.077(1.763 – 128.955)	0.066	22.941(0.811 – 648.587)
EF (%)	**<0.001***	0.744(0.653 – 0.847)	0.424	0.885(0.657 – 1.193)
ESD (mm)	**<0.001***	1.586(1.254 – 2.007)	0.621	0.874(0.513 – 1.490)
EDD (mm)	**<0.001***	1.441(1.216 – 1.708)	0.878	0.972(0.680 – 1.391)
RSWMA	**0.074**	0.450(0.188 – 1.080)		
GLS	**<0.001***	0.399(0.263 – 0.604)	0.005*	0.427(0.235 – 0.776)
Treated with Pharmacoinvasive PCI	**0.109**	0.483(0.198 – 1.177)		
Treated with primary PCI	**0.002***	4.500(1.766 – 11.467)	0.371	2.146(0.402 – 11.451)
Treated with Rescue PCI	**0.088**	0.353(0.107 – 1.167)		

OR: Odd`s ratio
C.I: Confidence interval LL: Lower limit UL: Upper Limit

4. Discussion

Regarding clinical data on presentation with STEMI, in the current study we reported a significant variation between the three groups regarding symptom duration where we found that rescue PCI group showed longest duration of chest patient and more patient delay which explain the failure of thrombolytic therapy. This came in accordance with different reports analyzing predictors of successful thrombolytic therapy in STEMI patients. Khalifa *et al.* (2020) reported the four hours as a predictor of success of thrombolytic therapy.

Regarding STEMI location in the current study, 38 patients of the study population presented with anterior STEMI (42.2%),49 patients presented with inferior STEMI (54.4%), and 3 patients presented by Lateral STEMI represent 3.3% of the study population. There was no significant difference between the three groups.

Regarding TIMI flow in the current study, in group I, 38 patients had TIMI III flow (95%), and 2 patients had TIMI <III (5 %). In group II,26 patients had TIMI III flow (86.7 %), and 4 patients had TIMI <III (13.3 %). In group III, 18 patients had TIMI III flow (90%), and 2 patients had TIMI <III (10 %). This came in agreement with Paul and George (2017). in which patients with TIMI III flow were higher (93.3%) in the primary PCI group when compared to pharmacoinvasive group (88.3%).

Regarding Ejection Fraction (EF) within the current study, in Group I, EF ranged between 35.0-62.0% with a mean of 47.0 ±6.21. In group II, it ranged between 30.0- 52.0% with a mean of 40.83±4.69. In group III, it ranged between 38.0-56.0% with a mean of 47.6±5.63. There was statistically significant difference between the three groups (P value < .001) being lowest in the rescue PCI group with no significant difference between the primary PCI and pharmacoinvasive groups. These findings came to disagreement with Paul and George (2017). which reported that the outcome of left ventricular ejection fraction (LVEF) was better in the primary PCI group as compared to the pharmacoinvasive group (45.1 (36–49) % vs. 40.7 (33.9–44.5), P = 0.02).

Regarding GLS of the current study groups, in group I, GLS ranged between -19.0 - -8.0% with a mean of -11.95±3.27. In group II, it ranged between -15.0 - -8.0% with a mean of -10.17±1.72. In group III, it ranged between -16.0- -8.0% with a mean of -12.9±2.22 There was statistically significant difference between the three groups (P value =0.001). GLS of the three groups is lowest in patients who did not develop MACE when compared to those who developed MACE. The results of the current study came in agreement with Paul and George (2017). that reported GLS of primary PCI group was lower -11 (-8.5 to- 14) when compared to GLS of pharmacoinvasive group was -9 (-8 to -12). Results of the current study came in agreement with Abushabana *et al.,* (2023) that assessed GLS with 2D speckle-tracking (mean - 13.6 ± 1.4 vs. -10.3 ± 1.2, P ≤ 0.001) were significantly lower in the primary PCI group as compared to the thrombolytic group.

Regarding MACE, none of our current study groups reported in hospital death. Similar data was reported by Paul and George (2017). whose reported mortality was zero. In the study conducted by Abushabana *et al.* (2023) one patient died in the thrombolytic group (4%).

Regarding ischemic stroke, in group I, none of the study population reported ischemic stroke. In group II, 1 patient reported from ischemic stroke (3.3%). Meanwhile, group III, none of the study population reported ischemic stroke. There was no statistically significant difference between the three groups (P value =1.0). In the study conducted by Paul and George (2017). no patient reported ischemic stroke in both groups. Meanwhile, Abushabana *et al.* (2023) reported that one patient developed stroke in the thrombolytic group (4%).

Regarding reinfarction, in group I, none of the study population reported reinfarction. In group II, 1 patient reported reinfarction (3.3%). In group III, none of the study group reported reinfarction. There was no statistically significant difference between the three groups (P value =0.549). Paul and George (2017) reported that one patient developed reinfarction in pharmacoinvasive group (1.6%). While Abushabana *et al.* (2023) reported that no patient developed reinfarction in both groups.

Regarding Congestive heart failure (CHF) in the current study, in group I, 8 patients reported CHF (20.0 %), and in group II, 8 patients reported CHF (26.7 %). In group III, 1 patient reported CHF (5.0%). There was no statistically significant difference between both groups (P = 0.139). In the study conducted by Paul and George (2017). one patient developed heart failure in primary PCI group (3.3%). Meanwhile Abushabana *et al.* (2023) reported that 4 patients developed CHF in primary PCI group (16%) while 4 patients developed CHF in thrombolytic group (16%).

Concerning major bleeding in the current study, in group I, 1 patient reported major bleeding (2.5%). In group II, 5 patient reported major bleeding (16.7 %). In group III, 1 patient reported major bleeding (5.0%). There was no statistically significant difference between both groups (P =0. 093). In the study conducted by Paul and George (2017), no patient developed major bleeding in both groups. Meanwhile, Abushabana *et al.* (2023) study reported that One patient developed major bleeding in thrombolytic group (4%).

Regarding Contrast induced nephropathy (CIN) in the current study, in group I, 2 patients developed CIN (5%). In group II, 3 patients developed CIN (10%). In group III, 1 patient developed

CIN (5%). There was no statistically significant difference between the three groups (P =0.757). In the study conducted by Paul and George (2017). one patient developed CIN in the primary PCI group (1.6%) while 6 patients developed CIN in the pharmacoinvasive PCI group (10%) which was statistically significant difference (P=0.5) but was not explained by the author.

Regarding MACE in the current study, in group I, 11 patients reported MACE (27.5%). In group II, 18 patients reported MACE (60.0%). In group III, 4 patients reported MACE (20.0%). There was statistically significant difference between both groups (P =0. 004). Paul and George (2017) study reported that 5% of the primary PCI group developed MACE (3 patients) while 11.6% of pharmacinvasive group developed MACE (7 patients). Regarding Abushabana *et al.* (2023) study, 16% of the primary PCI group developed MACE (4 patients) while 25% of thrombolytic group developed MACE (6 patients).

Regarding the relation between GLS and MACE, In Group I, in patients who developed MACE, GLS ranged between -13 - -8% with a mean of -9.55±1.86 %. In patients who did not develop MACE, GLS ranged between -19- -8% with a mean of -12.86±3.25%. There is significant statistical difference between the two groups (P=0.01). In group II, in patents who developed MACE, GLS ranged between -11- -8% with a mean of -9.33±1.24. In patients who did not develop MACE, GLS ranged between -15- -9% with a mean of -11.42±1.62%. There is significant statistical difference between the two groups (P=0.012). In group III, in patents who developed MACE, GLS ranged between -10 - -8% with a mean of -9.25±0.96. In patients who did not develop MACE, GLS ranged between -16- -11% with a mean of -13.56±1.75. There is significant statistical difference between the two groups (P=0.042).

In patients who developed MACE, it's evident that mean of GLS is lower in the primary PCI group (-9.7±1.89) than pharmacoinvasive group (-9.44±1.26) which is lower than rescue PCI group (-9.25±0.96). Regarding Paul and George. [1] study which reported 5% of the primary PCI group whose GLS range was -11 (-8.5 to- 14) % developed MACE while 11.6% of pharmacinvasive group whose GLS range was -9 (-8 to -12) % developed MACE. It is noteworthy that despite a statistically significant difference in LV GLS and ejection fraction, pharmacoinvasive strategy was similar to primary angioplasty in most of the other outcome variables except for increased incidence of CIN in the pharmacoinvasive group.

The study had some potential limitations such as: small size of study population, which was due to short study duration and a single-center experience. The mechanism of reinfarction was not evaluated whether in stent thrombosis or other vessel thrombosis. Another limitation was the short period assigned for follow up which didn't allow the appearance of results for mortality, re-infarction & re-hospitalization. We recommend that speckle tracking should get more opportunity as a tool for assessment of cardiac function and estimation of infarct size which will subsequently will help us to assess clinical outcome of the patients.

Conclusions

It was evident that GLS was a good predictor of MACE. Patients with higher GLS had increased incidence of MACE. It was also evident that GLS was higher in patients with rescue PCI when compared to primary PCI and pharmacoinvasive group.

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