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Original article

Prediction of AF in ACS Patients Using Different Antiplatelets by Tissue Doppler Derived Atrial Dyssynchrony

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Abstract:

Background: Acute coronary syndromes (ACS) are one of the major causes of mortality and morbidity worldwide. Current guidelines recommend dual antiplatelet therapy in patients with ACS. This study aimed to predict AF in ACS patients using ticagrelor or clopidogrel by tissue Doppler derived atrial Dyssynchrony and to assess the outcome morbidity and mortality in each group. **Methods:** This was an observational, case series, single center study, was carried out at coronary care unit at "Benha University hospital" on 200 patients with ACS (STEMI & NSTE-ACS), 100 of the patients used ticagrelor and the other 100 patients used clopidogrel, in the period from June 2022 to December 2022. **Results:** The incidence of AF was insignificantly different between the studied groups. LAVI max and Mitral regurgitation was significantly higher in New-onset AF patients (P value=0.024, 0.001 respectively). Tissue Doppler imaging data (Lateral mitral P-A' interval, septal mitral P-As interval, tricuspid P-A' interval, LA Dyssynchrony and Inter-atrial Dyssynchrony) were significantly higher in New-onset AF patients (P value<0.05). LA Dyssynchrony can significantly predict the incidence of AF with AUC 0.704 (95% CI: 0.636 - 0.766) and P value = 0.008, at cut off value >7.792 ms, with 68.2 % sensitivity, 63.5 % specificity, 18.7 PPV and 94.2 NPV. LV GLS was significantly lower in New-onset AF patients (P value =0.035). **Conclusion:** Our study showed that there was no significant difference in electro-echocardiographic AF predictors such as PWD, LAVI max, left atrial dyssynchrony and interatrial dyssynchrony in ACS patients who received ticagrelor or clopidogrel.

Keywords: Acute Coronary Syndrome; Atrial Fibrillation; Antiplatelets; Tissue Doppler; Atrial Dyssynchrony.

Introduction

Acute coronary syndromes (ACS) are one of the major causes of mortality and morbidity worldwide. Current guidelines recommend dual antiplatelet therapy in patients with ACS [(1)].

Ticagrelor, one of the relatively new drugs used in ACS, is a reversible and direct-acting oral antagonist of adenosine diphosphate receptor P2Y12, and it was found superior over clopidogrel in the PLATO trial [(2)].

Although the benefit of ticagrelor has been attributed mostly to its faster, greater, and more consistent P2Y12 inhibition compared to clopidogrel, continuity of growing benefits of ticagrelor and its effect on reduction of cardiovascular mortality in the PLATO trial make it different from other P2Y12-ADP receptor blockers [(3)].

These differences led to the hypothesis that ticagrelor has pleiotropic properties and nonplatelet directed mechanisms of action. These effects of ticagrelor have been mostly attributed to increased half-life and plasma concentration of adenosine [(4)].

Adenosine is a purine nucleoside primarily produced by endothelial cells. and it has a number of effects, such as coronary vasodilation, inhibition of platelet aggregation, modulation of inflammation. Reduced ischemia/reperfusion injury and reduced atrioventricular conduction [(5)].

Besides some positive effects, it is also known that adenosine has the potential to cause atrial fibrillation (AF) [(6)].

In addition, there is a case report in the literature suggesting that ticagrelor could cause AF, a possible mechanism of which is increased plasma adenosine level [(7)].

However, there are no studies in the literature investigating the risk of AF in patients treated with ticagrelor. In this study, we aimed to determine whether ticagrelor predisposes to AF in ACS patients by using surrogate electro and echocardiographic parameters.

Therefore, this study aimed to predict AF in ACS patients using ticagrelor or clopidogrel by tissue Doppler derived atrial Dyssynchrony.

Patients and methods

This was an observational, case series, single center study that included all 200 patients with acute coronary syndrome (STEMI & NSTE-ACS) who were admitted at coronary care unit at “Benha University hospital” in the period from June 2022 to December 2022. All the 200 patients had complete revascularization 100 of the patients used ticagrelor and the other 100 patients used clopidogrel. The study was done after being approved by the institutional ethical committee, Benha University (approval code :) and informed consent was obtained from all participants included.

Study protocol: This study evaluated clinical outcome of each category of patients both in hospital stay and at 3 months follow up. ECG was done at both baseline and 3 months follow up.

Inclusion criteria were patients with acute coronary syndrome, sinus rhythm, age group: adults > 18 years old, sex: both sexes.

Exclusion criteria were any rhythm other than sinus rhythm, history of any arrhythmia, history of use of anti-arrhythmic drugs other than beta-blockers, permanent pacemaker, cerebrovascular disease, patients who needed coronary bypass surgery, history of significant valvular heart disease or prosthetic valve, other comorbidities as (mental diseases, pregnancy, breast feeding, severe renal impairment, or advanced live disease) and history of congenital heart disease.

Methods: the included patients were subjected to the following: Baseline evaluation: All patients had review of medical history including Age, sex, Risk Factors of coronary artery disease (DM-HTN-Dyslipidemia- smoking), prior history of coronary artery disease, prior

history of intervention, other comorbidities, drugs.

Full clinical examination: With particular emphasis on the pulse and blood pressure of the patients, as well as auscultation of the back to elicit the presence of any clinically detectable pulmonary venous congestion, auscultation of the heart for the presence of third heart sounds or audible murmurs.

Baseline Electrocardiography: Twelve leads ECG was done for each patient at rest for assessment of heart rate, rhythm, P-max, P-min, PWD, PR interval and P wave axis

Cardiac biomarkers and other Laboratory investigations: Venous blood was obtained from the patients to estimate 24th hour troponin, high-sensitive troponin levels and other laboratory investigations like CBC , RBS , serum creatinine , TSH , serum K , serum Ca , lipid profile to exclude other causes of morbidity and mortality.

Baseline Echocardiography: Complete comprehensive transthoracic echocardiographic examination was performed using a Philips EPIQ 7C machine with the S5-1 probe with simultaneous ECG signal. When performing transthoracic echocardiography, the patient was in a left decubitus position. This allowed the heart to fall closer to the anterior thoracic wall, making sonography easier. The probe was positioned in the intercostal spaces to avoid the scattering effects of bone. Subjects were examined for the assessment of regional wall abnormalities and overall left ventricular systolic function. Left ventricular EF was measured by Simpson method, while resting segmental wall motion abnormalities assessed in the parasternal long axis (PSLAX), parasternal short axis (PSSAX), apical 2 chambers and apical 4 chambers views. Mitral valve was assessed for presence and severity of mitral regurgitation. LAVI max, LAVI min, LAVI-pre, E/A ratio were also obtained by conventional echocardiography.

Tissue Doppler imaging: The pulsed wave tissue Doppler sample volume was placed on the lateral mitral annulus, septal mitral annulus, and tricuspid annulus in the apical four chamber view. The first negative wave, E′, represents early diastolic myocardial relaxation. A′ was an abbreviation for the second negative wave that represents active atrial contraction. Electromechanical delay was measured for each location on the mitral annulus as the time interval between the beginning of the P-wave on the ECG and the beginning of the A′-wave **(P-A′ interval)**. The difference in P-A′ intervals at lateral and septal mitral locations was defined as left atrial dyssynchrony. The difference in P-A′ intervals at the lateral mitral and tricuspid locations was used to define interatrial dyssynchrony. A three-beat average was taken. In addition, the peak E′ was measured at each location, the E/E′ ratio was calculated, and the average of the three locations was used for analysis.

Follow up: the second end point was 3 months follow up included assessment of patients of both groups to assess their rhythm and detect patients who developed AF using 12 leads ECG and assessment of clinical variables among males and female patients including all-causes of mortality, myocardial infarction, stroke, heart failure, revascularization. 3 months follow up with echocardiography using tissue doppler derived atrial Dyssynchrony as described above.

Statistical analysis:

Statistical analysis was done by SPSS v28 (IBM Inc., Armonk, NY, USA). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate. Evaluation of Diagnostic Performance was performed

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using diagnostic sensitivity, specificity, PPV and NPV. Receiver Operating Characteristic curve (ROC-curve) analysis: The overall diagnostic performance of each test was assessed by ROC curve analysis, a curve that extends from the lower left corner to the upper left corner then to the upper right corner is considered a perfect test. The area under the curve (AUC) evaluates the overall test performance (where the area under the curve >50% denotes acceptable performance and area about 100% is the best performance for the test). A two tailed P value < 0.05 was considered statistically significant

Research ethics committee: Ms.21.9.2021

Results

Baseline characteristics and Vital signs were presented int Table 1. Troponin was significantly higher in Clopidogrel group compared to Ticagrelor group (P value = 0.001). Table 1

Lipid profile (Cholesterol, Triglycerides, LDL and HDL) was insignificantly different between the studied groups. ECG data (P-max, P-min, PWD, PR interval and P wave axis) were insignificantly different between the studied groups. Table 2

Affected lesion (LAD lesion, LCX lesion, RCA lesion and Multivessel disease), No. of stents and Final TIMI flow were insignificantly different between th estudied groups. Figure 1

According to the type of acute coronary syndrome, in STEMI population, electrocardiographic data were insignificantly different between Ticagrelor group and Clopidogrel group except PR interval which was significantly higher in Clopidogrel group compared to Ticagrelor group (P value= 0.046). Also, in NSTE-ACS population, electrocardiographic data were insignificantly different between Ticagrelor group and Clopidogrel. Table 3

The incidence of AF was insignificantly different between the studied groups. Figure 3A) Incidence of complications between the studied groups were illustrated in Figure 3 B).

A) **B)**

Figure 1: A) Affected lesion of the studied groups and B) No of stents between the studied groups.

A) **B)**

Figure 2: A) GLS between the studied groups and B) Mitral regurgitation > mild between the studied groups.

Table 1: Baseline characteristics and Vital signs of the studied patients

		Total (n=200)	Ticagrelor group (n=100)	Clopidogrel group (n=100)	P value
Age (years)		64.7± 9.64 45-85	65.77± 9.31 45-83	63.62± 9.89 48-85	0.115
Sex	**Male**	147 (73.5%)	75 (75%)	72 (72%)	0.748
	Female	53 (26.5%)	25 (25%)	28 (28%)	
BMI (Kg/m^2)		27.95± 3.17 22.41-35.47	28.15± 3.36 22.41-35.47	27.76± 2.98 22.66-34.78	0.384
DM		60 (30%)	28 (28%)	32 (32%)	0.539
HTN		103 (51.5%)	49(49%)	54(54%)	0.571
Smoking		105 (52.5%)	54 (54%)	51 (51%)	0.777
History of CAD		61(30.5%)	30 (30%)	31 (31%)	1
BB		62(31%)	32(32%)	30(30%)	0.878
CCB		52 (26%)	25 (25%)	27 (27%)	0.872
Killip class	**I**	116 (58%)	58 (58%)	58 (58%)	0.678
	II	36 (18%)	20 (20%)	16 (16%)	
	III	48 (24%)	22 (22%)	26 (26%)	
ACS type	**STEMI**	113 (56.5%)	58 (58%)	55 (55%)	0.775
	NSTE-ACS	87 (43.5%)	42 (42%)	45 (45%)	
Vital signs					
SBP (mmHg)		140.5± 12.47 120-160	141.1± 12.46 120-160	139.9± 12.51 120-160	0.498
DBP (mmHg)		83.2± 8.37 60-90	83.8± 7.63 60-90	82.6± 9.06 60-90	0.312
HR (beats/min)		75.26± 10.03 56-96	76.52± 10.52 56-96	73.99± 9.4 58-96	0.075
Lab. investigations					
Hb (g/dL)		12.57± 1.66 9.9-15.5	12.49± 1.61 9.9-15.5	12.65± 1.72 9.9-15.5	0.474
PLT (*10^{3}cells/µL)		247.07± 59.71 150-350	246.1± 60.71 150-350	248.04± 58.99 150-349	0.819
Creatinine (mg/dL)		1.07± 0.15 0.8-1.37	1.08± 0.14 0.8-1.33	1.06± 0.17 0.8-1.37	0.235
TSH (mIU/L)		1.23± 0.09 1.07-1.43	1.23± 0.09 1.07-1.42	1.23± 0.09 1.08-1.43	0.920
Potassium (mmol/L)		4.16± 0.32 3.55-4.87	4.17± 0.3 3.55-4.81	4.14± 0.33 3.59-4.87	0.562
Calcium (mg/dL)		4.16± 0.32 3.55-4.87	4.17± 0.3 3.55-4.81	4.14± 0.33 3.59-4.87	0.562
Troponin (ng/mL)		14.92± 2.47 10.3-21.2	14.33± 2.22 10.3-19.55	15.51± 2.58 11.04-21.2	**0.001***
Peak HsTnT (ng/L)		9870.5±3120.8 6003-14944	9760.9±2977.4 6003-14792	9980.1± 3269.2 6026-14944	0.621
Hs CRP (mg/L)		31.42± 9.55 12.85-52.36	30.54± 9.59 13.93-50.68	32.3± 9.48 12.85-52.36	0.193
HbA1c (%)		6.21± 0.85 5.26-9.1	6.21± 0.89 5.4-9.1	6.21± 0.82 5.26-8	0.963

BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, ACS: acute coronary syndrome, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate. Hb: Hemoglobin, PLT: platelet count, TSH: thyroid stimulating hormone, HsTnT: high-sensitive Troponin T, Hs CRP: high-sensitivity C-reactive protein, Data presents as mean ± SD, *: statistically significant as P value <0.05.

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Table 2: Lipid profile and ECG data of the studied groups

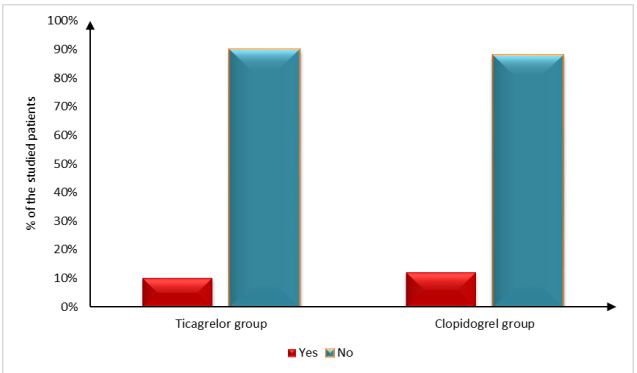
	Total (n=200)	**Ticagrelor group (n=100)**	**Clopidogrel group (n=100)**	**P value**
Cholesterol (mg/dL)	230.65± 18.24 200-260	231.24± 17.36 201-260	230.05± 19.15 200-260	0.646
LDL (mg/dL)	122.27± 10.4 105-155	122.92± 10.49 105-155	121.62± 10.31 106-150	0.378
HDL (mg/dL)	42.77± 7.24 29.64-65	43.65± 7.04 31.66-57.76	41.88± 7.37 29.64-65	0.084
ECG data				
P-max (ms)	112.65± 11.19 87.86-136.89	114.1± 9.79 95.74-136.89	111.21± 12.31 87.86-136.76	0.067
P-min (ms)	72.93± 10.74 50.63-99.68	73.57± 11.87 52.42-99.68	72.29± 9.49 50.63-99.68	0.400
PWD (ms)	42.08± 9.51 27-58	41.95± 8.79 27-58	42.21± 10.23 27-58	0.847
PR interval (ms)	170.56± 22.32 128.99-225.11	169.52± 21.3 128.99-213.94	171.6± 23.36 128.99-225.11	0.511
P wave axis (degree)	53.58± 6.69 42-65	53.04± 6.79 42-65	54.12± 6.59 42-65	0.255

LDL: low-density lipoprotein, HDL: high-density lipoprotein, ECG: electrocardiogram, PWD:P Wave Dispersion, Data presents as mean ± SD, *: statistically significant as P value <0.05.

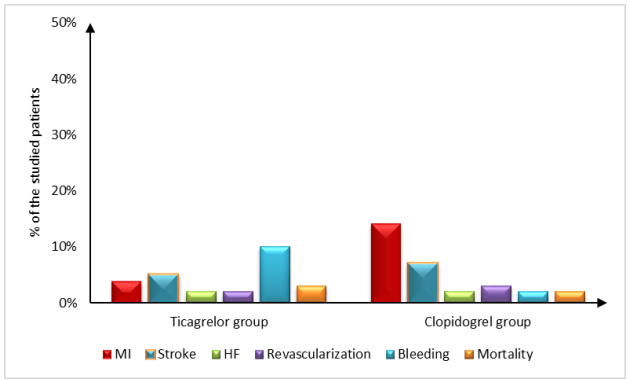
Table 3: Comparison of electrocardiographic data by type of acute coronary syndrome

	STEMI			NSTEMI		
	Ticagrelor group (n=100)	**Clopidogrel group (n=100)**	**P value**	**Ticagrelor group (n=100)**	**Clopidogrel group (n=100)**	**P value**
P-max (ms)	114.7±10.2	110.5 ± 14.1	0.075	113.6 ± 9.2	111.8 ± 9.8	0.390
P-min (ms)	75.1±13.2	71.6 ± 6.01	0.072	71.3 ± 9.9	73.1 ± 12.4	0.464
PWD (ms)	42.9 ± 8.4	43.9 ± 9.9	0.547	40.2 ± 8.9	40.5 ± 10.5	0.903
PR interval (ms)	169.5 ± 22.9	178.4 ± 23.8	**0.046***	169.6 ± 19.2	163.4±19.8	0.144
P wave axis (degree)	53.2 ± 7.4	53.7 ± 6.1	0.725	52.6 ± 5.9	54.7 ± 7.1	0.151

Data presented as mean ± SD, *: statistically significant as P value <0.05.



A)



B)

Figure 3: A) Incidence of atrial fibrillation between the studied groups and B) Incidence of complications between the studied groups

LA Dyssynchrony can significantly predict the incidence of AF with AUC 0.704 (95% CI: 0.636 - 0.766) and P value = 0.008, at cut off value >7.792 ms, with 68.2 % sensitivity, 63.5 % specificity, 18.7 PPV and 94.2 NPV. Inter-atrial Dyssynchrony can significantly predict the incidence of AF with AUC 0.704 (95% CI: 0.694 - 0.817) and P value <0.001, at cut off value >7.9, with 81.82% sensitivity, 44.94% specificity, 15.5 PPV and 95.2 NPV. LAVI $_{max}$ can significantly predict the incidence of AF with AUC 0.656 (95% CI: 0.585-0.721) and P value = 0.039, at cut off value >41.26, with 68.18 % sensitivity, 44.38 % specificity, 13.2 PPV and 91.9 NPV. The new onset AF group has statistically significant dyssynchrony. Table 4

Tissue Doppler at baseline and at follow-up was insignificantly different between the studied groups. Only 173 patients were followed-up and analyzed as 22 cases developed AF and 5 cases were excluded due to mortality. Table 5

After 3 months follow up, we found 22 patients developed New-onset persistent atrial fibrillation (12 cases in ticagrelor group and 10 cases in clopidogrel group).

On comparing the baseline characteristics between groups HTN was significantly higher in New-onset atrial fibrillation (77.2% vs. 48.3%, P value =0.012) and LDL significantly higher in New-onset atrial fibrillation (127.5 ± 10.2 vs. 121.6 ±10.263, P value=0.012). Other parameters were insignificantly different between both groups. ECG data were insignificantly different between both group except PWD was significantly higher in New-onset atrial fibrillation patients (40.3 ± 10.5 vs. 45.5 ± 9.4, P value =0.027). Conventional echocardiography data were insignificantly different between both groups except LAVI max which was significantly higher in New-onset atrial fibrillation (43.1 ± 5.5 vs. 47.0 ± 7.8, P value=0.024). Mitral regurgitation was significantly higher in New-onset atrial fibrillation (72.7% vs. 35.4%, P value=0.001).

Tissue Doppler imaging data (Lateral mitral P-A' interval (45.9 ± 2.6 vs. 49.4 ± 4.1, P value=0.001), septal mitral P-As interval (38.9 ± 2.1 vs. 40.1 ± 2.5, P value=0.022), tricuspid P-A' interval (36.9 ± 1.4 vs. 37.5 ± 1.1, P value= 0.043), LA Dyssynchrony (6.9 ± 2.8 vs. 9.3 ± 3.6, P value =0.006) and Inter-atrial Dyssynchrony (8.93± 4.72 vs. 12.36± 5.04, P value = 0.001)) were significantly higher in New-onset atrial fibrillation (P value<0.05) whereas E/E' ratio was insignificantly different between both groups. It was found that LV GLS was significantly lower in New-onset atrial fibrillation patients (-16.6 -2.5 vs. -17.8-2.6, P value =0.035). Table 6.

On multiple regression analysis, LDL, mitral regurgitation, LA dyssynchrony, Inter-atrial dyssynchrony and LAVI max were significant predictors for AF development (P value =0.046, 0.022, <0.001, <0.001, 0.008 respectively). Table 7

Table 4: Diagnostic performance of LA Dyssynchrony, inter-atrial Dyssynchrony, and LAVI $_{max}$ for prediction of AF

	Cut off	Sensitivity %	Specificity %	PPV	NPV	AUC	95% CI	P value
LA Dyssynchrony	>7.79	68.2	63.5	18.7	94.2	0.704	0.636 - 0.766	**0.008***
Interatrial Dyssynchrony	>7.9	81.82	44.94	15.5	95.2	0.704	0.694 - 0.817	**<0.001***
LAVI $_{max}$	>41.26	68.18	44.38	13.2	91.9	0.656	0.585-0.721	**0.039***

LA: left atrium, LAVI: left atrial volume index, PPV: positive predictive value, NPV: negative predictive value, AUC: area under the curve, CI: confidence interval, *: statically significant as P value <0.05

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Table 5: Tissue Doppler of the studied patients

		Total (n=200)	**Ticagrelor group (n=100)**	**Clopidogrel group (n=100)**	**P value**
Baseline	E/E' ratio	14.17± 3.71 6.61-26.91	13.94± 3.79 6.96-26.91	14.4± 3.64 6.61-26.26	0.381
	Lateral mitral P-A' interval (ms)	46.29± 2.99 42.5-56.80	46.52± 3.05 42.46-56.016	46.07± 2.93 42.568-56.796	0.290
	Septal mitral P-A' interval (ms)	39.11± 2.23 35.7-46.4	39.25± 2.21 35.66-46.404	38.96± 2.25 35.66-46.404	0.353
	Tricuspid P-A' interval (ms)	36.97± 1.43 34.4- 40.1	36.98± 1.42 34.396-40.128	36.95± 1.44 34.396-39.912	0.880
	LA Dyssynchrony (ms)	7.19± 2.56 1.65-16.01	7.26± 2.46 2.5-14.804	7.11± 2.67 1.65-16.01	0.669
	Inter-atrial Dyssynchrony (ms)	9.98± 4.78 2.5-19.8	9.66± 4.91 2.5-19.8	10.31± 4.64 2.7-18.9	0.336
		Total (n=173)	**Ticagrelor group (n=87)**	**Clopidogrel group (n=86)**	
Follow-up	E/E' ratio	11.74± 2.78 6.39-22.61	11.57± 3 6.39-22.61	11.91± 2.55 6.8-19.48	0.424
	Lateral mitral P-A' interval (ms)	37.99± 1.79 35.38-45.25	38.18± 1.84 35.38-44.3	37.79± 1.73 35.47-45.25	0.148
	Septal mitral P-As interval (ms)	32.38± 1.62 29.72-38.29	32.44± 1.56 29.72-37.98	32.33± 1.69 29.9-38.29	0.656
	Tricuspid P-A' interval (ms)	30.75± 1.2 28.66-33.44	30.8± 1.2 28.66-33.44	30.7± 1.21 28.66-33.26	0.591
	LA Dyssynchrony (ms)	8.73± 4.64 1.5-17.5	8.43± 4.32 1.5-17.3	8.95± 5 1.6-17.5	0.432
	Inter-atrial Dyssynchrony (ms)	10.58± 4.7 2.3-18.4	10.09± 4.96 2.3-18.4	11.08± 4.39 2.4-18.4	0.136

LA: left atrial, Data presents as mean ± SD or frequency.

Table 6: Multiple regression analysis for prediction of AF development.

Independent variables	**Coefficient**	**Std. Error**	**t**	**P**	$r_{partial}$	$r_{semipartial}$
Age	0.002	0.002	0.669	0.504	0.050	0.046
DM	0.015	0.049	0.302	0.763	0.023	0.021
HTN	0.065	0.046	1.399	0.164	0.104	0.096
History of CAD	-0.031	0.050	-0.632	0.528	-0.047	0.044
Troponin	0.002	0.009	0.167	0.868	0.013	0.012
Hs CRP	0.001	0.002	0.506	0.613	0.038	0.035
Peak HsTnT	0.000	0.000	-0.440	0.660	-0.033	0.030
Cholesterol	0.000	0.001	0.385	0.701	0.029	0.027
TG	-0.002	0.002	-0.895	0.372	-0.067	0.062
LDL	0.004	0.002	2.009	**0.046***	0.149	0.139
HDL	0.000	0.003	-0.140	0.889	-0.011	0.010
GLS	-0.010	0.024	-0.400	0.689	-0.030	0.028
Mitral regurgitation	0.113	0.049	2.314	**0.022***	0.171	0.160
LA dyssynchrony	0.029	0.008	3.583	**<0.001***	0.248	0.232
Inter-atrial dyssynchrony	0.020	0.004	4.585	**<0.001***	0.340	0.309
E/A ratio	0.051	0.073	0.694	0.488	0.052	0.048
LAVI max	0.009	0.003	2.674	**0.008***	0.187	0.178
LAVI min	0.003	0.004	0.859	0.392	0.064	0.059
LAVI pre	0.001	0.003	0.181	0.856	0.014	0.013
LVEF	-0.007	0.008	-0.861	0.390	-0.064	0.059
LVIDd	0.004	0.005	0.693	0.489	0.052	0.048

DM: diabetes mellitus, CAD: coronary artery disease, HsTnT: high-sensitive Troponin T, Hs CRP: high-sensitivity C-reactive protein, GLS: global Longitudinal Strain, LVIDs: left ventricular internal dimension end-systolic, LVID d: left ventricular internal dimension end-diastolic, LVEF: left ventricular ejection fraction, LAVI: left atrial volume index, ***:** *: statistically significant as P value <0.05

Table 7: Comparisons of baseline characteristics, baseline echocardiographic parameters between groups

		Normal group (n=178)	New-onset atrial fibrillation (n=22)	P value
Age (years)		64.63 ± 9.79	65.23 ± 8.57	0.785
Sex	**Male**	133 (74.7%)	14 (63.6%)	0.307
	Female	45 (25.3%)	8 (36.4%)	
BMI (Kg/m^2)		27.8 ± 3.1	28.9 ± 3.6	0.148
BB		55 (30.9%)	7 (31.8%)	1.0
CCB		44 (24.7%)	8 (36.4%)	0.302
Killip class	**I**	106 (59.6%)	10 (45.5%)	0.448
	II	31 (17.4%)	5 (22.7%)	
	III	41 (23.0%)	7 (31.8%)	
DM		52 (29.4%)	8 (36.4%)	0.623
HTN		86 (48.3%)	17 (77.2%)	**0.012***
Smoking		92 (51.7%)	13 (59.1%)	0.652
History of CAD		56 (31.5%)	5 (22.7%)	0.471
ACS type	**STEMI**	101 (56.7%)	12 (54.5%)	1.0
	NSTEMI	77 (43.3%)	10 (45.5%)	
SBP (mmHg)		140.7 ± 12.5	138.64 ± 12.1	0.459
DBP (mmHg)		83.3 ±8.3	82.3 ± 9.2	0.583
HR (beats/min)		75.4 ± 10.2	74.23 ± 8.6	0.612
Hb (g/dL)		12.5 ± 1.7	12.9 ± 1.6	0.219
PLT (*10^{3}cells/µL)		249.8 ± 60.1	225.2 ± 52.7	0.069
Creatinine (mg/dL)		1.1 ± 0.2	1.1 ± 0.12	0.967
TSH (mIU/L)		1.2 ± 0.1	1.2 ± 0.10	0.418
Potassium (mmol/L)		4.1 ± 0.3	4.2 ± 0.4	0.246
Calcium (mg/dL)		4.1 ± 0.3	4.2 ± 0.40	0.139
Troponin (ng/mL)		14.9 ± 2.4	14.8 ± 3.0	0.884
Peak HsTnT (ng/L)		9904.3 ± 3142.5	9597.0 ± 2994.4	0.664
Hs CRP (mg/L)		31.4 ± 9.8	31.9 ± 7.8	0.808
HbA1c (%)		6.2 ± 0.86	6.3 ± 0.8	0.711
Cholesterol (mg/dL)		230.2 ± 18.3	234.1 ± 17.7	0.349
LDL (mg/dL)		121.6 ± 10.263	127.5 ± 10.2	**0.012***
HDL (mg/dL)		42.8 ± 7.4	42.8 ± 6.3	0.990
TG (mg/dL)		141.9 ± 9.6	139.7 ± 9.8	0.296
LAD lesion		70 (39.3%)	12 (54.5%)	0.254
LCX lesion		71 (39.9%)	13 (59.0%)	0.135
RCA lesion		51 (28.7%)	6 (27.3%)	1.0
MVD		18 (10.1%)	3 (13.6%)	0.889
No. of stent	**One**	65 (36.5%)	10 (45.4%)	0.697
	Two	81 (45.5%)	9 (40.9%)	
	More than 2	32 (18.0%)	3 (13.7%)	
Final TIMI	**0-1**	14 (7.9%)	3 (13.6%)	0.409
	2-3	164 (92.1%)	19 (86.4%)	
ECG data				
P-max (ms)		112.9 ± 11.2	110.6 ± 10.8	0.355
P-min (ms)		72.9 ± 10.8	72.9 ± 10.06	0.996
PWD (ms)		40.3 ± 10.5	45.5 ± 9.4	**0.027***
PR interval (ms)		170.2 ± 22.6	173.1 ± 20.3	0.577

	Normal group (n=178)	New-onset atrial fibrillation (n=22)	P value
Conventional echocardiography			
LVIDs (mm)	55.4 ± 4.6	57.5 ± 6.9	0.059
LVIDd (mm)	38.0 ± 4.4	39.9 ± 6.1	0.161
$LAVI_{max}$	43.1 ± 5.5	47.0 ± 7.8	**0.024***
$LAVI_{min}$	26.7 ± 7.1	28.9 ± 5.3	0.160
LAVI-pre	36.0 ± 8.3	38.3 ± 7.4	0.226
E/A ratio	0.96 ± 0.32	1.1± 0.32	0.054
LVEF (%)	54.9 ± 7.5	52.7 ± 7.4	0.206
Mitral regurgitation	63 (35.4%)	16 (72.7%)	**0.001***
Tissue Doppler imaging			
E/E' ratio	14.0± 3.34	15.2 ± 5.7	0.348
Lateral mitral P-A' interval (ms)	45.9 ± 2.6	49.4 ± 4.1	**0.001***
Septal mitral P-As interval (ms)	38.9 ± 2.1	40.1 ± 2.5	**0.022***
Tricuspid P-A' interval (ms)	36.9 ± 1.4	37.5 ± 1.1	**0.043***
LA Dyssynchrony (ms)	6.9 ± 2.8	9.3 ± 3.6	**0.006***
Inter-atrial Dyssynchrony (ms)	8.93± 4.72	12.36± 5.04	**0.001***

BMI: body mass index, DM: diabetes mellitus, CAD: coronary artery disease, ACS: acute coronary syndrome, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, Hb: Hemoglobin, PLT: platelet count, TSH: thyroid stimulating hormone, HsTnT: high-sensitive Troponin T, Hs CRP: high-sensitivity C-reactive protein, ECG: electrocardiogram, PWD:P Wave Dispersion, LVIDs: left ventricular internal dimension end-systolic, LVIDd: left ventricular internal dimension end-diastolic, LVEF: left ventricular ejection fraction, LAVI: left atrial volume index, GLS: global Longitudinal Strain, Data presents as mean ± SD or frequency. Data presents as mean ± SD, *: statistically significant as P value <0.05.

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Discussion

Regarding the ACS type, STEMI was found in 113 (56.5%) patients and NSTE-ACS was found in 87 (43.5%). In Ticagrelor group, STEMI was found in 58 (58%) patients and NSTE-ACS was found in 42 (42%) patients. In Clopidogrel group, STEMI was found in 55 (55%) patients and NSTE-ACS was found in 45 (45%) patients. Our results are in the same line with a study reported that rate of patients diagnosed with STEMI in the ticagrelor group was found to be higher than in the clopidogrel group (72.2% versus 45.2%, P < 0.001) [4].

Regarding lab investigations and lipid profile in our findings, our results disagree with those documented by a study found that 24th hour troponin levels were significantly higher in the ticagrelor group [14.15 (3.28–54.95) vs 9.61 (1.27–35.5); P-value = 0.003]. This variation may be due to different sample size as they include 831 patients: 410 in the Ticagrelor group and 421 in Clopidogrel group [4].

In terms of ECG data, P-max, P-min, PWD, PR interval, P wave axis, were insignificantly different between the studied groups (P-value > 0.05). Regarding conventional echocardiography, LVIDs, LVIDd, LAVI max, LAVI min, LAVI-pre, E/A ratio and LVEF were insignificantly different between the studied groups. Consistently, a study documented that P wave axis, LVIDs, LVIDd, LAVI max, LAVI min, LAVI-pre, E/A ratio and LVEF were insignificantly different between the studied groups [4].

In the current work, the incidence of AF was insignificantly different between the studied groups. In harmony with our findings, a study reported that there was no significant relationship between antiplatelet use and AF predictors (P > 0.05) [4].

According to our findings, inter-atrial Dyssynchrony can significantly predict the incidence of AF with AUC 0.704 (95% CI: 0.694 - 0.817) and P value <0.001, at cut off value >7.9, with 81.82% sensitivity, 44.94% specificity, 15.5 PPV and 95.2 NPV. LAVI max can significantly predict the incidence of AF with AUC 0.656 (95% CI: 0.585-0.721) and P value = 0.039, at cut off value >41.26, with 68.18 % sensitivity, 44.38 % specificity, 13.2 PPV and 91.9 NPV.

In agreement with our results a prospective, nonrandomized single-center study was performed to assess the relationship between atrial dyssynchrony after performing primary PCI for STEMI and development of in-hospital NOAF. A total of 440 STEMI patients underwent primary PCI and were monitored for NOAF during hospitalization. Immediately after primary PCI, P-wave dispersion was calculated, and conventional/tissue Doppler echocardiography was done. The authors stated by using ROC curve analysis that inter-atrial dyssynchrony showed the highest diagnostic performance (AUC 85%, 95% CI: 0.77–0.94, P < .001). A cutoff value at 23.8 ms showed a good validity for predicting NOAF with a sensitivity of 93.8% and a specificity of 68.1% [8].

In the present study, hypertension was significantly higher in New-onset atrial fibrillation (77.2% vs. 48.3%, P value =0.012) and LDL significantly higher in New-onset atrial fibrillation (127.5 ± 10.2 vs. 121.6 ±10.263, P value=0.012). Our results are compatible with a study reported that the group with NOAF showed significantly higher prevalence of hypertension (P = .049) [8].

In the present study, conventional echocardiography data were insignificantly different between both groups except LAVI max which was significantly higher in New-onset atrial fibrillation (P value=0.024). Our results agree with those documented by a study showed that indexed left atrial maximum volume ($LAVI_{max}$), left atrial dyssynchrony, and inter-atrial dyssynchrony were significantly higher in NOAF group (P < 0.001) [8]. In contrast to this

observation, other studies failed to demonstrate any predictive value of $LAVI_{max}$ in the acute phase after STEMI [9, 10]. This discrepancy probably stems from the fact that $LAVI_{max}$ is not likely to be affected by acute hemodynamic changes after STEMI but reflects the chronic effect of increased left ventricular filling pressure over time.

Conclusion

In the current study, there was no significant difference between patients with ACS who received ticagrelor or clopidogrel in development of new onset AF regarding ECG data, conventional echocardiography and tissue Doppler echocardiography as AF predictors. MI was significantly lower in Ticagrelor group compared to Clopidogrel group and bleeding was significantly higher in Ticagrelor group compared to Clopidogrel group. Left atrial dyssynchrony and inter-atrial Dyssynchrony can significantly predict the incidence of AF.

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Author contribution

Authors contributed equally in the study**.**

Conflicts of interest

No conflicts of interest

References

1. Bergmark BA, Mathenge N, Merlini PA, Lawrence-Wright MB, Giugliano RP. Acute coronary syndromes. Lancet. 2022;399:1347-58.
2. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39:119-77.
3. Fender AC, Dobrev D. Pleiotropic actions of ticagrelor versus clopidogrel - Do molecular differences translate into superior clinical efficacy after myocardial infarction? Int J Cardiol Heart Vasc. 2020;27:100508.
4. Algül E, Sunman H, Dural M, Guliyev İ, Aker M, Felekoğlu MA, et al. Comparison of atrial fibrillation predictors in patients with acute coronary syndrome using ticagrelor or clopidogrel. Turk J Med Sci. 2019;49:1358-65.
5. Reiss AB, Grossfeld D, Kasselman LJ, Renna HA, Vernice NA, Drewes W, et al. Adenosine and the Cardiovascular System. Am J Cardiovasc Drugs. 2019;19:449-64.
6. Gupta A, Lokhandwala Y, Rai N, Malviya A. Adenosine-A drug with myriad utility in the diagnosis and treatment of arrhythmias. J Arrhythm. 2021;37:103-12.
7. Low A, Leong K, Sharma A, Oqueli E. Ticagrelor-associated ventricular pauses: a case report and literature review. Eur Heart J Case Rep. 2019;3:yty156.
8. Ibrahim I, Taha Hassanin M, El Zaki MM. Tissue Doppler-derived atrial dyssynchrony predicts new-onset atrial fibrillation during hospitalization for ST-elevation myocardial infarction. Echocardiography. 2019;36:1799-805.
9. Lønborg JT, Engstrøm T, Møller JE, Ahtarovski KA, Kelbæk H, Holmvang L, et al. Left atrial volume and function in patients following ST elevation myocardial infarction and the association with clinical outcome: a cardiovascular magnetic resonance study. Eur Heart J Cardiovasc Imaging. 2013;14:118-27.
10. Modin D, Olsen FJ, Pedersen S, Jensen JS, Biering-Sørensen T. Measures of left atrial function predict incident atrial fibrillation in STEMI patients treated with primary percutaneous coronary intervention. Int J Cardiol. 2018;263:1-6.

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