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Impact of Diabetes Mellitus on Myocardial Reperfusion and Left Ventricular Remodelling in Patients with Acute Myocardial Infarction Treated with Primary Coronary Intervention

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Abstract

Background: Diabetes Mellitus (DM) in patients after acute Myocardial Infarction (MI) has been shown to be a strong predictor of short-and long-term mortality. It has also been recognized that DM is associated with an increased rate of post-infarction heart failure.

Aim of the Study: To evaluate the impact of diabetes mellitus on myocardial reperfusion after primary PCI in patients with acute myocardial infarction utilizing, resolution of ST- segment elevation and Myocardial Blush Grade (MBG) and to evaluate the impact of diabetes mellitus on left ventricular remodelling using 2-D speckle tracking.

Methods: The study population consisted of 100 patients with anterior STEMI (50 diabetics and 50 non-diabetic) all patients underwent 1ry PCI. Conventional 2D echocardiography to asses LVEF, EDV and ESV and speckle tracking echocardiography to asses LV global longitudinal strain and global circumferential strain was done within 72 hr of admission and after 3 months later and patients with LV remodelling, i.e. an increase >20% in LV End-Diastolic Volume (LVEDV), were identified.

Results: No significant difference was found regarding baseline clinical, angiographic and echocardiographic characteristics except in MBG3 (18% vs. 54 % p=0.001), MBG1 (32% vs. 8 % p=0.003), complete ST segment resolution (18% vs. 48 % p=0.001) and Absent ST segment resolution (28% vs. 10% p=0.022) between diabetics and non-diabetics respectively. Despite a similar incidence of LV remodelling in DM and non-DM groups (22% vs. 16%, p=0.444), The 19 patients with LV remodelling had significantly more impaired LVEDV (99.84±19.24vs. 125.11±19.96, p=0.001), and LV global longitudinal strain (GLS) (-11.47±1.34%vs. -10.61±2.15%, p=0.021). Change in end diastolic volume showed the strongest correlation with the GLS (P= 0.042, r = 0.473) and apical circumferential strain (P=0.028, r=0.014). Furthermore, apical circumferential strain demonstrated the highest diagnostic accuracy: area under the Receiver Operating Characteristic (ROC) curve, with sensitivity 84.2% and specificity 88.9%, using a cut-off value >-11.7% and GLS with sensitivity 89.5% and specificity 65.4%, using a cut-off value >-12.5 % for prediction of LV remodelling.

Conclusion: Despite worse microvascular reperfusion and ST segment resolution in STEMI patients with diabetes, the incidence of LV remodelling was similar compared to non-DM patients and LV apical CS and GLS is a predictive parameter of future adverse remodelling.

Keywords: Diabetes mellitus; Myocardial infarction; Myocardial reperfusion; Primary coronary intervention

Background

Cardiovascular Disease (CVD) is the leading cause of morbidity and mortality among people with diabetes mellitus, who have a risk of cardiovascular mortality two to four times greater than that of people without diabetes [1].

The assessment of microvascular perfusion and integrity is integral for risk stratification in patients with AMI, especially after primary PCI, in whom TIMI-3 is restored in more than 90% of patients. In this regard, prior studies have demonstrated the prognostic utility of both STR and MBG in this setting. The electrocardiographic STR has been shown to be related to cell membrane integrity and myocyte function. Conversely, the angiographic measure of MB reflects anatomic microvascular patency [2].

However, only a little, and contradictory, data concerning the effect of DM on post-infarctional LV remodelling is available, particularly after primary coronary intervention. The relationship between LV remodelling and impaired microvascular reperfusion has been observed in several studies [3,4].

Aim of the Study: To evaluate the impact of diabetes mellitus on myocardial reperfusion after primary PCI in patients with acute myocardial infarction utilizing, resolution of ST- segment elevation and Myocardial Blush Grade (MBG) and to evaluate the impact of diabetes mellitus on left ventricular remodelling using 2-D speckle tracking.

Patients and Methods

This study is a Single centre, cross sectional, comparative study, conducted at coronary care unit of National Heart Institute - Cairo - Egypt, during the period from June 2016 to October 2017. One hundred patients (50 diabetic patients and 50 non-diabetic patients) with first attack anterior STEMI treated by primary Percutaneous Coronary Intervention (PCI) were enrolled in the study.

Exclusion Criteria

Acute STEMI other than anterior STEMI, Patients with two vessel or three vessel disease, Patients with previous CABG or STEMI, Patient received pharmacological reperfusion therapy, Patient with pervious PCI and Patient presented with cardiogenic shock.

All patients were subjected to the following:

Full history taking, complete general, local examination, Blood samples were taken upon admission for measurement of glucose concentrations and ECG

Echocardiography

Conventional Transthoracic echocardiographic and speckle tracking studies had been performed during the first 72 hrs of hospitalization and three months later. All patients were examined in left lateral position using (PHILIPS EPIQ 7C release 1.2.1)

Conventional Transthoracic Echocardiography

Ordinary basic transthoracic echocardiography study had been done including the following: From the parasternal long axis view; the following was obtained; left ventricular dimensions, aortic root dimension and also left atrial dimension. The left ventricular ejection fraction by modified Simpson's was calculated, the E/A ratio were calculated, the deceleration time of the mitral E wave was also measured by pulsed Doppler over mitral valve and from the apical views; ejection fraction was calculated using modified Simpson's rule. LV remodelling was defined as an increase of at least 20% of Left Ventricular End-Diastolic Volume (LVEDV) from the first post infarction imaging [5].

2-D Speckle Tracking Echocardiography Study

The following views were taken for later analysis; apical 4 chamber view, apical 2 chamber view, apical 3 chamber view, parasternal long axis view and parasternal short axis view at basal, mid and apical levels. In blinded post-processing, longitudinal deformation and circumferential deformation had been assessed by speckle tracking, to measure the Peak Systolic Longitudinal Strain (PSLS) for the 17 segment LV model from the apical views and The Peak Systolic Circumferential Strain (PSCS) for 16 segments protocol were calculated from the short axis views, with high frame rates (> 60 frames/s) using commercial imaging analysis software (PHILIPS EPIQ 7C release 1.2.1)

End-systole was defined as aortic valve closure in the apical long axis view by continuous Doppler wave recording. Automated delineation of endocardial borders was obtained through marking the mitral annulus level at the apex on each digital loop. The area of interest was manually adjusted if automated delineation was not optimal. Segments with poor image acquisition or artefacts were excluded due to inability to measure longitudinal strain (LS) [6].

A bull's eye diagram can then be created from the data obtained from all myocardial segments with interplanar values interpolated. The diagnostic information of each trace in contained in a parametric colour, labelling qualitative and quantitative indices of myocardial wall motion [7].

Reperfusion Strategy

All the patients were subjected to reperfusion by PCI. all patients received; Aspirin 300 mg, (nitro-glycerine infusion, oxygen supplementation) when needed and Anti-coagulation with unfractionated heparin was routinely given (80-100 unit/kg) and Patients received Clopidogrel (loaded with 600 mg at the opinion discretion, followed by 75 mg per day) in addition to conventional

treatment {Beta- blocker, nitrates, ACEI, & statin}. Right femoral artery puncture using Seldinger's technique was done. TIMI flow grade was evaluated from the baseline angiogram and after the completion of coronary angioplasty. Myocardial Blush Grade (MBG) was assessed and Blush was graded according to dye density score: 0 - no myocardial blush or no persistent blush, 1 - minimal blush, 2 - moderate blush but less that obtained during angiography of contralateral or ipsilateral non-infarct-related artery, and 3 - normal myocardial blush.

Statistical Analysis

Statistical presentation and analysis of the present study was conducted, using the mean, standard Deviation, Analysis of variance tests, unpaired student t-test, Linear Correlation Coefficient [r], Logistic Regression, ROC-curve, Paired t-test and chi-square tests by (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). P-value of < 0.05 was considered statistically significant.

Results

This study was conducted prospective on 100 (50 diabetics and 50 non-diabetic) patients with acute STEMI subjected to primary PCI. The general characteristics of the patient population are set out in Table 1. There was no significant difference between two groups.

	Diabetic		Non Diabetic		Total		Tests	
	N	%	N	%	N	%	X^2/t	P-value
Sex								
Male	33	66.0	38	76.0	71	71.0	1.214	0.271
Female	17	34.0	12	24.0	29	29.0		
Age								
Mean±SD	54.60±7.77		55.56±9.87				0.541	0.590
Cardiovascular risk factors								
Hypertension	36	72.0	27	54.0	63	63.0	3.475	0.062
Dyslipidemia	32	64.0	25	50.0	57	57.0	1.999	0.157
Family history	14	28.0	9	18.0	23	23.0	1.412	0.235
Smoking	26	52.0	34	68.0	60	60.0	2.667	0.102

Table 1: Comparative analysis between diabetic group and non-diabetic group in relation to demographic characteristics of study.

Myocardial Reperfusion

Impaired myocardial reperfusion shown more in diabetic patient with MBG3 (18% vs. 54 % p = 0.001) and MBG1 (32% vs. 8 % p = 0.003) between diabetics and non-diabetics respectively (Figure 1). ST segment resolution after the procedure was observed significantly more often in the non-DM group than in the DM group especially in complete ST segment resolution (18% vs. 48 % p = 0.001) and Absent ST segment resolution (28% vs. 10% p = 0.022) (Figure 2).

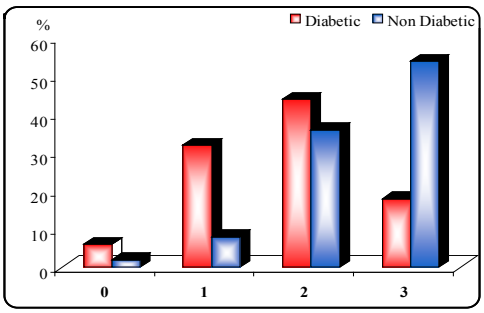

Figure 1: Comparative analysis between diabetic and non-diabetic groups in relation to myocardial blush grade of study.

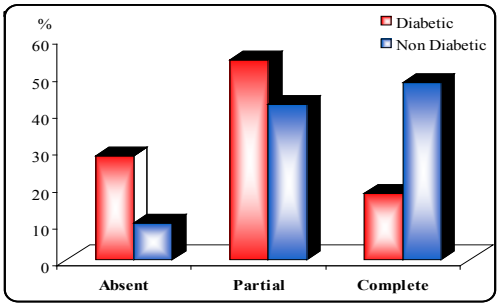

Figure 2: Comparative analysis between diabetic and non-diabetic groups in relation to ECG resolution of study.

Echocardiographic Assessment

There was no statistically significant difference between diabetic and non-diabetic patients at basic and three months later in conventional echo and speckle tracking data (Table 2). LV remodelling, defined as EDV progression over 20% of baseline EDV, was observed in 11 (22%) patients with DM and in 8(16%) patients of the non-DM group (22% vs. 16% p = 0.444) (Figure 3).

	Diabetic				**Non Diabetic**			
	Basic	3 mon.	**Paired t-test**		Basic	3 mon.	**Paired t-test**	
	Mean±SD	Mean±SD	t	P-value	Mean±SD	Mean±SD	t	P-value
EF%	47.7±4.92	51.06±6.61	2.883	0.005*	48.32±4.83	53.08±6.61	4.111	0.003*
LVEDV	100.04±20.28	104.76±21.04	1.142	0.256	96.74±17.77	100.44±21.72	0.134	0.894
LVESV	47.96±15.39	52.3±10.78	1.633	0.106	44.52±15.57	50.16±12.74	1.982	0.052
E/A ratio	0.78±0.31	0.92±0.43	1.867	0.065	0.80±0.22	0.87±0.25	0.128	0.898
DCT E	190.8±25.25	185.96±34.14	1.036	0.305	196.66±19.73	190.74±22.61	1.854	0.070

Table 2: Comparative analysis between diabetic and non-diabetic groups in relation to echocardiographic parameters basic and 3 months post myocardial infarction.

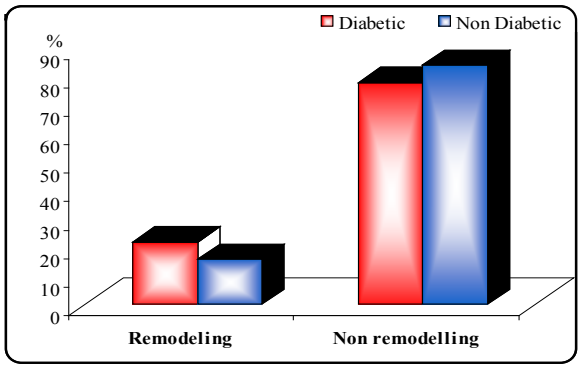

Figure 3: Comparative analysis between diabetic and non-diabetic groups regarding LV remodeling within three months of study.

From the previous study during follow up, we found 19 patients have remodelling and 81 patient's have-not remodelling. So another subdivision into two groups remodelling and non-remodelling were done. In LV remodelling group shown a significant different between LVEDV at basic and after 3 months follow (99.84±19.24 ml vs. 125.11±19.96 ml with p <0.001) and GLS at basic and after 3 months follow (-11.47±1.34 % vs. -10.61±2.15% with p =0.021) (Tables 3 and 4).

	Remodelling				**Non remodelling**			
	Basic	3 months	**Paired t-test**		Basic	3 mon.	**Paired t-test**	
	Mean±SD	Mean±SD	t	P-value	Mean±SD	Mean±SD	t	P-value
EF%	46.11±3.77	45.00±4.96	1.069	0.299	47.85±5.21	54.25±4.67	8.233	<0.001**
LVEDV	99.84±19.24	125.11±19.96	8.204	<0.001**	92.21±17.31	97.47±17.38	1.930	0.055
LVESV	49.68±15.46	59.00±14.69	3.933	0.002*	44.13±11.80	40.90±9.84	1.892	0.060
E/A ratio	0.77±0.15	1.10±0.55	2.770	0.013*	0.84±0.23	0.84±0.26	0.096	0.923
DCT E	184.68±21.65	175.11±36.87	2.014	0.046*	191.53±23.79	189.72±25.27	0.582	0.562

Table 3: Comparative analysis between Remodeling and non-Remodeling groups in relation to echocardiographic parameters basic and 3 months post myocardial infarction.

	Remodelling				**Non remodelling**			
	Basic	3 mon.	**Paired t-test**		Basic	3 mon.	**Paired t-test**	
	Mean±SD	Mean±SD	t	P-value	Mean±SD	Mean±SD	t	P-value
saxM C. strain	-12.49±7.78	-13.64±4.54	0.575	0.572	-14.75±4.90	-17.00±7.41	2.406	0.018*
saxA C. strain	-10.61±5.88	-11.02±3.42	0.386	0.704	-13.35±5.26	-15.59±3.62	3.157	0.002*
saxB C. strain	-10.77±6.96	-11.68±3.23	0.530	0.603	-16.89±4.94	-17.25±3.77	0.521	0.602
AP3L strain	-11.62±2.08	-10.86±5.07	0.679	0.506	-13.03±3.61	-14.73±5.12	2.442	0.016*
AP4L strain	-12.18±2.71	-11.54±2.56	0.736	0.471	-13.96±3.87	-15.97±3.25	3.580	0.003*
AP2L strain	-11.03±2.47	-10.67±3.01	0.460	0.651	-14.12±3.19	-15.61±3.53	2.819	0.005*
GLS	-11.47±1.34	-10.61±2.15	2.529	0.021*	-11.99±6.47	-13.84±2.74	2.370	0.019*
GCS	-11.36±5.98	-12.14±2.26	0.579	0.570	-13.06±5.78	-15.57±7.21	2.445	0.016*

Table 4: Comparative analysis between Remodelling and non-Remodelling in relation to speckle tracking parameters basic and 3 months post myocardial infarction.

Linear Correlation coefficient was used and there was Positive correlation was found between change in end diastolic volume and CKMB with (P value = 0.005, r = 0.620), duration of chest pain (P value = 0.554, r = 0.014), saxA C. strain as (P value = 0.028, r = 0.014), GLS as (P value = 0.042, r = 0.473) and A negative correlation was found between change in end diastolic volume and EF% as (P value = 0.017, r = -0.540), MBG as (P value = 0.007, r = -0.593) (Figure 4).

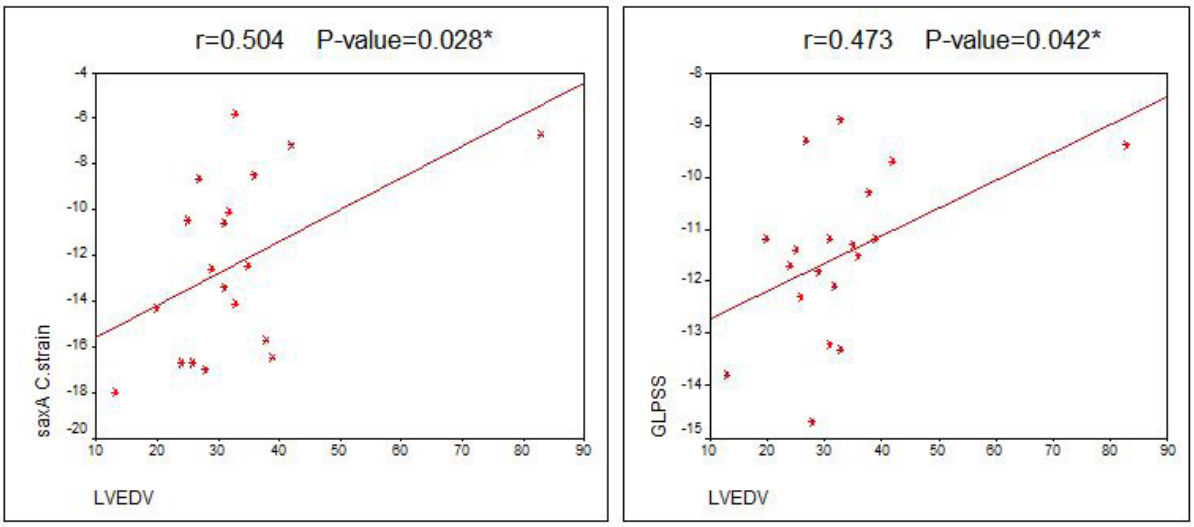

Figure 4: Positive correlation between LVEDV and sax Apical C. strain and GLS.

Logistic regression analyses revealed that the most statistically significant factors affecting remodelling were absent of ECG ST segment resolution, Smoking, CPK, CKMB, MBG, saxA C. strain and GLS, While other factors not affecting remodelling were DM, HTN, dyslipidaemia, EF, E/A ratio and GCS (Table 5).

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.
	B	Std. Error	Beta		
(Constant)	1.272	0.137		9.290	<0.001**
DM	0.136	0.087	0.174	1.568	0.121
HTN	0.036	0.074	0.044	0.482	0.631
Dyslipidemia	0.065	0.073	0.082	0.897	0.372
ECG resolution	0.001	0.007	0.007	2.276	0.027*
Smoking	0.156	0.069	0.195	2.397	0.025*
CPK	0.000	0.000	0.291	2.299	0.024*
CKMB	0.005	0.002	0.296	2.431	0.017*
D chest pain	0.056	0.023	0.354	2.431	0.017*
MBG	0.097	0.043	0.213	2.249	0.027*
EF%	0.013	0.008	0.167	1.617	0.109
E/A ratio	0.083	0.153	0.046	0.542	0.590
saxA C. strain	0.256	0.050	0.461	5.148	<0.001**
GLS	0.007	0.008	0.097	2.124	0.037*
GCS	0.010	0.007	0.147	0.074	0.941
Dependent Variable: Remodelling.					

Table 5: Regression analysis for factor affecting remodelling.

Apical circumferential strain demonstrated the highest diagnostic accuracy

Area under the Receiver Operating Characteristic (ROC) curve, with sensitivity 84.2% and specificity 88.9%, using a cut off value >-11.7% and GLS with sensitivity 89.5% and specificity 65.4%, using a cut off value >-12.5% for prediction of LV remodelling (Figures 5 and 6).

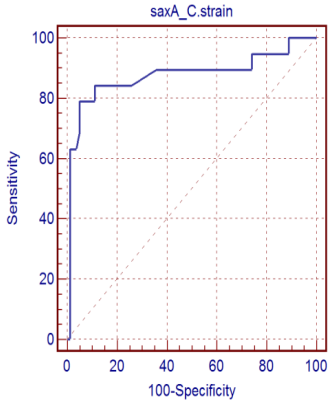

Figure 5: Accuracy (area under ROC curve) of short axis apical circumferential strain.

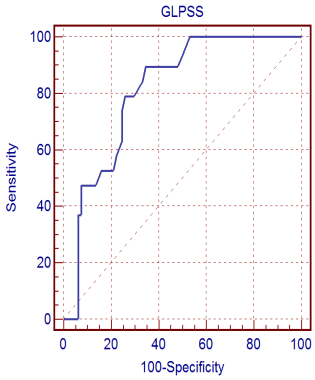

Figure 6: Accuracy (area under ROC curve) of GLS.

Discussion

This study was intended to assess myocardial reperfusion after primary PCI in acute STEMI diabetic patients versus non-diabetic patients using resolution of ST segment elevation after PCI, myocardial blush grading and left ventricular remodelling.

There was no significant difference between diabetic& non-diabetic regarding Demographic data (age and sex), there were 71 males (33 diabetic & 38 non-diabetic) and 29 females (17 diabetic & 12 non-diabetic) with a mean age of diabetic patients 54.60±.77years and non-diabetic 55.56±9.87 (Table 1).

Our results revealed that diabetic patients had impaired myocardial reperfusion either by MBG and ST segment resolution after primary PCI in comparison to non-diabetic patients (Figures 1 and 2). This was in agreement with Andrade et al. [8], Verouden et al. [9], Timmer et al. [10] who compared myocardial reperfusion after successful primary PCI in patients with ST-elevation myocardial infarction with versus without diabetes mellitus. Myocardial reperfusion was assessed by ST-segment resolution and Myocardial Blush Grades (MBG) in a total of 386 studied patients were studied. Patients with diabetes mellitus more frequently had reduced MBG (20% vs 10%, p = 0.02) and incomplete ST-segment resolution (55% vs 35%, p = 0.02) compared with non-diabetic patients, Marso et al. [11] who compared myocardial reperfusion and infarct sizes between diabetic and non-diabetic patients undergoing primary PCI for acute ST-segment elevation myocardial infarction in the EMERALD trial. They concluded that diabetic patients had impaired myocardial reperfusion after primary PCI as measured by myocardial blush grade 0/1 (34% vs 16%, p = 0.002) and lower rates of complete 30-minute STR (45% vs 65%, p = 0.005).

Contrary to our results regarding to MBG, data reported by Brener et al. [12] who found that there were no differences in MBG between patients with and without DM. This was due to wider study population as he studied 3,265 patients.

There was no significant difference between two groups regarding Conventional 2D echo parameters (EF%, LVEDV, LVESV, E/A ratio and deceleration time) at basic and three months later and speckle tracking parameters (Table 2) in agreement with Araszkiewicz et al. [13], Amira et al. [14] who studied 30 patients with STEMI (9 diabetic, 21 non-diabetic) and found that there was no statistically significant difference between diabetic and non-diabetic patients as regarding LVEDV with p-value: 0.7, LVESV with p-value: 0.4, EF with p-value 0.6, or WMSI and Shah et al. [15] who found that in the VALIANT Echo study, including 594 patients, demonstrated no difference in changes in LV volumes and LVEF from baseline to 1-month and from 1-month to 20-month follow up between patients with and without diabetes. this was disagreement with Georgette et al. [16] who studied 433 and found that after STEMI, diabetic patients show more impaired LV GLS at both baseline and follow-up, despite having similar infarct size and LVEF at baseline and follow-up.

In our study after 3 months follow up, the estimated percentage of remodelling among all study population were 19% as follow 11 diabetic patients and 8 non-diabetic patients with no significant difference between diabetic and non-diabetic groups (Figure 3 in agreement with Araszkiewicz et al. [13].

So another subdivision into two groups remodelling and non-remodelling were done, according to echocardiographic data

significant difference between two groups were found in LVEDV with (P value <0.001), LVESV with (P value 0.002), E/A ratio with (P value 0.013), deceleration time with (P value 0.046) and GLS with (P value 0.021) (Tables 3 and 4).

In current study there was Positive correlation was found between change in end diastolic volume and CKMB with (P value = 0.005, r = 0.620), duration of chest pain (P value = 0.554, r = 0.014), saxA C. strain as (P value = 0.028, r = 0.014), GLS as (P value = 0.042, r = 0.473) and A negative correlation was found between change in end diastolic volume and EF% as (P value = 0.017, r = -0.540), MBG as (P value = 0.007, r = -0.593) (Figure 4).

This was in agreement with Hyun-Min et al. [17] who investigated 208 patients with STEMI patients and found that LV remodelling correlated with CK-MB, and Global Longitudinal Strain (GLS) and Farag and Al-Daydamony [18] who studied 232 STEMI patients treated with primary PCI and demonstrated that there was a significant negative correlation between LVEDV increase and MBG.

Logistic regression analyses revealed that ECG resolution, Smoking, CPK, CKMB, chest pain duration, MBG, saxA C. strain and GLS were independent predictors of LV remodelling (Table 5). This was in agreement with Galli and Lombardi [19] who showed high incidence of LV remodelling were in Patients who have a greater LVESV and a lower LVEF, high creatine kinase-MB and impaired microvasculature reperfusion, Bonios et al. [20] who studied 42 anterior STEMI patients treated with primary PCI and found that in patients with anterior AMI, LV apical circumferential strain in the early post-MI period constitutes a significant prognostic factor for LV remodelling at 3 months. Assessment of this parameter may identify patients at high risk for heart failure development and Rifqi et al. [21] who studied 40 STEMI patients treated with primary PCI and found that recovery of left ventricular function could be detected early post-revascularization of coronary artery disease by either ejection fraction or global longitudinal strain measurements; however, the latter is more accurate.

In our study cut off value of GLS as a predictor of remodelling was > -12.5 with a sensitivity 89% and specificity 65% and for apical circumferential strain was cut off value > -11.7 with a sensitivity 84% and specificity 89%. (Figures 5 and 6).

Conclusion

Despite worse microvascular reperfusion in STEMI patients with diabetes, the incidence of LV remodelling was similar compared to non-DM patients. During the early post-myocardial infarction period, LV apical CS and GLS constitutes some deformational parameters that can identify patients who are at risk of developing LV remodelling. There is a significant correlation between end diastolic volume and CKMB, duration of chest pain, EF%, MBG, saxA C. strain and GLS.

Limitations

It included a single medical centre (National Heart Institute), number of patients included in the study (100 patients) and our results cannot be directly extrapolated to other subgroup of patients, such as those treated with thrombolytic therapy.

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