IMPACT OF MYOCARDIAL BLUSH ON LEFT VENTRICULAR REMODELING IN PATIENTS TREATED SUCCESSFULLY WITH PRIMARY OR RESCUE CORONARY INTERVENTION

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ABSTRACT

Background: Myocardial blush grade **(MBG)** in patients treated successful primary or rescue percutaneous coronary intervention **(PCI)** for anterior ST elevation myocardial infarction **(STEMI)** is a good indicator of microvascular reperfusion that may impact left ventricular **(LV)** remodeling.

Methods: this study included 60 consecutive patients suffered from anterior STEMI whom primary or rescue PCI were done , we evaluate MBG after primary or rescue PCI immediately . For each patient transthoracic echocardiography was done at 24 hours and repeat after 6 months after PCI for evaluation of LV function and volumes.

Results: patients with myocardial reperfusion MBG (II-III) after primary or rescue PCI was associated with a highly significantly lower rate of remodeling than the absence of myocardial reperfusion MBG (0-1) (12.1% vs. 75 %, P <0.001). also, after 6 months, patients with MBG (II-III) had significantly smaller LV end-diastolic volume (99 ± 23 vs. 113 ± 27 ml) compared with patients with MBG (0-1). LV remodeling was defined as an increase in end-diastolic volume **(LVED)** by more than 20%.

Conclusions: Microvascular reperfusion impairment , that assessed by MBG (0-1) in patients with STEMI treated successfully with primary or rescue PCI may be associated with LV dilatation and remodeling.

Keywords: myocardial blush, remodeling ,acute myocardial infarction, primary ,rescue, percutaneous coronary intervention, microvascular reperfusion.

Abbreviations: LV = left ventricular,MB = myocardial blush, PCI = percutaneous coronary intervention ,STEMI = ST elevation myocardial infarction

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INTRODUCTION

The advantage of primary or rescue coronary intervention (PCI) in patients with anterior STEMI have been referred to early reperfusion and restoration of thrombolysis in myocardial infarction grade 3 flow in the infarct-related artery [1]. However, recent studies were shown a high degree of LV dilation and remodeling that occurs in patients with STEMI even after successful primary or rescue PCI [2]. Some studied show that restoration and reperfusion of blood flow in the infarct-related artery may be associated with inadequate myocardial perfusion. [3]. The success of STEMI treatment is not justified only by the reperfusion of the infarct-related artery, but myocardial reperfusion is more important. Inspite of TIMI grade 3 flow, the infarct area may undergo less reperfusion at the level of myocardial tissue because of injury to the microvasculature by obstruction with neutrophil and debris, a phenomenon also known as the "no-reflow" phenomenon[4]. So, the angiographic myocardial blush score by contrast at the time of PCI based on the density of the dye and their washout in the infracted myocardium, is shown a simple method that correlates with myocardial tissue perfusion immediately after reperfusion of the infarct-related artery [5].

AIM OF THE WORK

The aim of this study is to assess the influence of Myocardial Blush Grade on Left Ventricular (LV) dilatation and remodeling in patients with ST elevation myocardial infarction (STEMI) whom undergoing successful primary or rescue PCI in patients.

PATIENTS AND METHODS

The study conducted in Cardiology department, faculty of medicine, Zagazig University and Damietta cardiac center from February 2014 to April 2015. it included 60 subjects; 53 males, 7 females ,aged 52.88 ± 8.89 years, with first anterior STEMI, All patients underwent general examination for vital signs (Bp, pulse, RR), and Local cardiac examination (S3 gallop, murmurs), also evaluated for presence of risk factors of IHD (Smoking, Hypertension, Diabetes mellitus, Dyslipidaemia), associated co morbidities ,

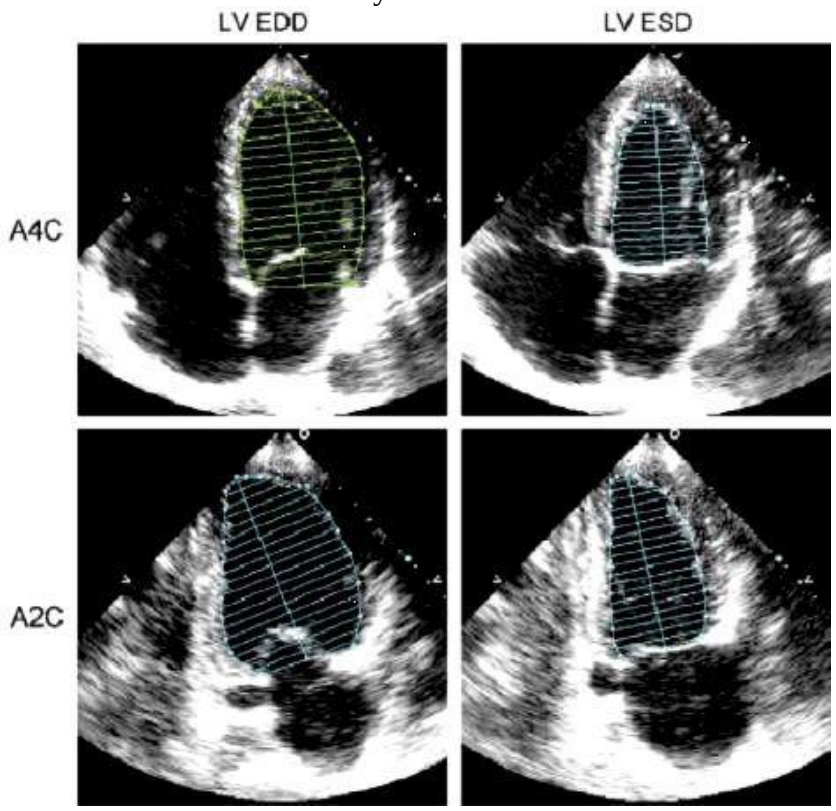
Routine laboratory investigations **a-** Cardiac biomarkers (total CK& CK-MB and Troponin). **b-** Kidney function tests (s. creatinine).**c-** Lipid profile including (Total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL)&triglycerides) **d-** Random blood sugar measured on admission * The inclusion criteria : **a)** patients with anterior wall STEMI (defined as typical chest pain more than 30 minutes and ECG changes (ST-segment elevation more than 2 mm in two contiguous electrocardiography leads) **b)** emergency PCI (primary PCI within 120 min. of onset of the symptom or rescue PCI) and **c)** successful recanalization and reperfusion of the infarct-related artery which assessed by TIMI grade 3 flow and visually assessed by residual stenosis in the infarct-related artery less than 20%. *The exclusion criteria were: **a)** valvular heart disease; and **b)** technically poor window for transthoracic two-dimensional echocardiography. The studied patients underwent 2-D echocardiography within 24 hours of the PCI and repeat after 6 months .

The study protocol was approved by the institutional ethics committee and all patients gave informed consent.

- **Surface ECG**

Standard 12 leads surface ECG was performed for all patients, immediately on admission and subsequently every 6 hours during first 24 hours, and once daily until discharge.

- **Echocardiography**



Echocardiographic examinations were performed with the VIVID 9 ultrasound system (GE, Horten, Norway) using 2.5–3.5 MHz transducers and SIMINS (G 60 S), Transthoracic two-dimensional echocardiography and the following data of the left ventricle will be determined: LVED volume , LVES volume and EF% will be calculated using Simpson's rule .LV remodeling defined as an increase in LVEDV more than 20% six months after reperfusion or recanalization.[6]

- **Coronary angiography and emergency PCI**

Patients received aspirin (300 mg loading then 150 mg daily), clopidogrel (600 mg loading then 150 mg /day maintenance dose). Un-fractionated heparin (UFH) (10000

units) bolus dose was injected after sheath insertion. The procedure was performed according to the standard technique of PCI. Femoral approach was the standard in all patients using 6-7 Fr sheath. Diagnostic coronary angiography was done to detect the culprit vessel. XB or JL guide catheters were used during PCI. Aspiration devices and glycoproteinsIIb/IIIa inhibitors were used in lesions with heavy thrombus burden and or impaired TIMI flow after PCI. The operator determined the size and length of the stent, the sheath was removed 6 hours later from the end of PCI and compression was done manually.

TIMI flow grade and MBG will be assessed on the angiograms taken shortly after PCI in the best view showing the infarct-related artery [7]. For MBG , we require ten seconds of cine filming to allow filling of the venous system that required to evaluate the washout phase of contrast dye.

Myocardial blush grade (MBG) is an angiographic measure of myocardial perfusion at the capillary level [8].

- **Statistical Analysis**

Data checked, entered and analyzed by SPSS version 20. Data were expressed as mean ± SD for quantitative values, numbers and percentage for categorical variables. ANOVA (f test), paired-t test, Chi-square (x^2) and Pearson's' correlation r were used when appropriate. We considered results statistically significant when p value ≤ 0.05.

RESULTS

The baseline demographic, clinical parameters of studied groups are shown in **Table (1).** There were no significant differences between four groups regarding; age, sex, , dyslipedemia, DM, hypertension, smoking and family history (P-value>0.05).

Table (1): Baseline characteristic and MBG:

		Grade 0 (12)	Grade I (14)	Grade II (20)	Grade III (14)		P-value
Age	**Mean ±SD**	56.3±7.1	57.3±3.8	55±7.9	55±7.2	F=0.4	0.751
FMC	**Mean ±SD**	195±71.7	178.5±72.1	147.8±66	121.4±39.1	F=3.5	0.02
Sex	**Male**	11(91.7%)	11 (78.6%)	20 (100%)	11(78.6%)	χ2=5.3	0.147
	Female	1(8.3%)	3 (21.4%)	0 (0%)	3 (21.4%)		
Hypretension		9(75%)	7(50%)	14(70%)	10(71.4%)	χ2= 2.4	0.499
DM		7(58.3%)	7(50%)	13(65%)	10(71.4%)	χ2= 1.5	0.677
Smoking		11(91.7%)	9(64.3%)	19(95%)	10(71.4%)	χ2= 7	0.072
Dyslipedemia		5(41.7%)	6(42.9%)	10(50%)	8(57.1%)	χ2= 0.8	0.84
Family history		10(83.3%)	8(57.1%)	12(60%)	9(64.3%)	χ2= 2.4	0.498

**** <u>Time to first medical contact and MBG</u>:**

There were a significant difference between four groups regarding first medical contact(FMC),(P-value<0.05) there was significant difference between different MBG with inverse correlation between time to FMC and MBG **figure (1).**

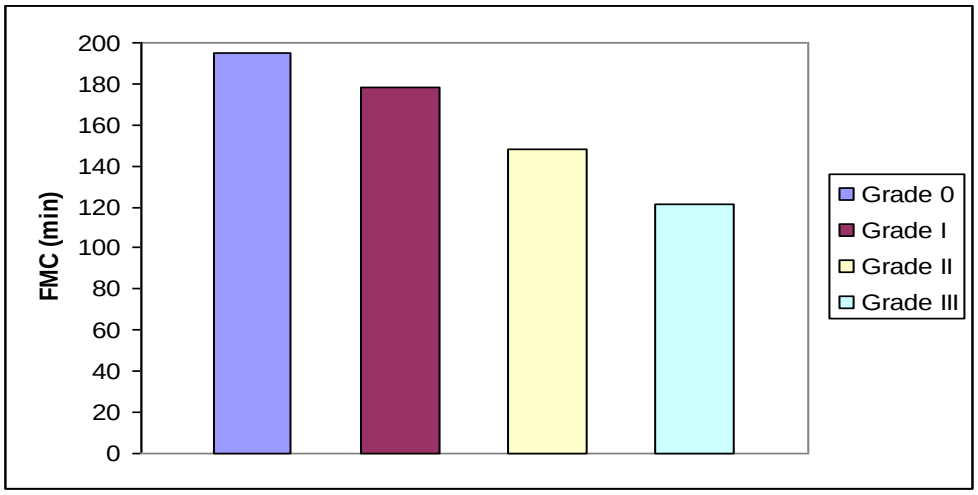


Figure (1): Time to first medical contact and MBG

****Emergency PCI data and MBG:**

There was no significant difference between four groups regarding type of PCI (P-value=0.469) .rescue PCI was done for 25 cases, 15 of them have good myocardial blush, MBGII and MBG III, Also, there was no significant difference between four groups regarding aspiration (P-value=0.32). There was no significant difference between four groups regarding usage of GPllb/llla inhibitors (P-value=0.423), multivessel PCI were done to 9 patients with significant difference as all patients had MBG II and MBG III **Table (2)**.

Table (2): Emergency PCI data and MBG

Variable		Grade 0 (12)		Grade I (14)		Grade II (20)		Grade III (14)		χ^2	P-value
		No	%	No	%	No	%	No	%		
Type of PCI	1ry	8	66.7	8	57.1	12	60	7	50	0.774	0.855
	Rescue	4	33.3	6	42.9	8	40	7	50		
Aspiration		4	33.3	9	64.3	8	40	9	64.3	3.5	0.32
Use of GPllb/llla inhibitors		2	16.7	3	21.4	6	30	1	7.1	2.8	0.423
Multivessel PCI		0	0	0	0	3	15	6	42.9	13.1	0.004

Emergency PCI data and remodeling:**

13 (61.9%) of patients who undergo primary PCI had remodeling versus 8(38.1%) of patients who undergo rescue PCI (P-value=0.286). 10 (47.6%) of patients who undergo thrombus aspiration had remodeling versus 20(51.3%) of patients who didn't have remodeling (P-value=0.787). 3 (14.3%) of patients who used Glycoprotein IIb/IIIa inhibitors had remodeling versus 9 (23.1%) of patients who didn't have remodeling (P-value=0.417) **Table (3).**

Table (3): Emergency PCI data and remodeling.

Variable		Remodeling (21)		No Remodeling (39)		χ2	P-value
		No	%	No	%		
Type of PCI	Primary	13	61.9	22	56.4	1.13	0.287
	Rescue	8	38.1	17	43.5		
Aspiration		10	47.6	20	51.3	0.073	0.787
Use of GPllb/llla inhibitors		3	14.3	9	23.1	0.659	0.417
Myocardial Blush		1	4.8	31	79.5	30.624	0.000

****Echocardiographic data and MBG:**

-End diastolic volume (EDV). At 24 hours post PCI, there was significant difference between four groups regarding EDV (p-value 0.028). After 6 months, there was significant difference between four groups regarding EDV (p-value 0.001)**.**

-End systolic volume (ESV). At 24 hours post PCI, there was significant difference between four groups regarding ESV (p-value 0.048). After 6 months, there was significant difference between four groups regarding ESV (p-value 0.000)**.**

-Ejection fraction (EF). At 24 hours post PCI, there was significant difference between four groups regarding EF (p-value 0.001). After 6 months, there was significant difference between four groups regarding EF (p-value 0.0001)

-Rmodeling defined as >20% increase in EDV , 100% of patients with grade 0 MBG versus 50% of grade I versus 5% of grade II versus 7.1% of grade III MBG had ventricular remodeling at 6 months (P- value <0.001).**Table (4)**

Table (4): Echocardiographic data and MBG

Variable	Grade 0 (12)	Grade I (14)	Grade II (20)	Grade III (14)	F	P-value
EDV within 24h (ml)	115.1±26.7	110.4±21.7	114.9±20.8	93.1±18.7	3.3	0.028
EDV after 6 months (ml)	143.4±23.6	120.9±32.9	107.6±26.3	91.9±21.3	8.9	0.0001
ESV within 24h (ml)	60.4±17.5	55.9±15.6	46.6±16.6	44.1±18.6	2.8	0.048
ESV after 6 months (ml)	87.8±17.3	70.8±29.1	45.8±23.9	39.7±15.5	13.3	0.0001
EF% within 24h	47.4±7.7	47.4±8.1	55.3±9.6	58.3±7.1	6.2	0.001
EF% after 6 months	38.9±4.3	44.2±10.2	51.2±9.7	57.8±9.7	11.1	0.0001
Remodeling	12(100%)	7(50%)	1(5%)	1(7.1%)	χ^2 = 36.4	<0.001

EDV:enddiastolic volume, ESV: endsystolic volume, EF: ejection fraction

Univariate regression analysis

	Coefficients	Standard Error	t Stat	P-value	Lower 95.0%	Upper 95.0%
AGE	-0.00033	0.00612	-0.05365	0.957453	-0.01266	0.011999
Gender	0.219699	0.234781	0.935763	0.35439	-0.25317	0.692571
HTN	-0.01879	0.121191	-0.15508	0.87745	-0.26289	0.225296
DM	-0.03843	0.100246	-0.38336	0.70326	-0.24033	0.163475
Dyslipidemic	0.193809	0.101597	1.907626	0.062834	-0.01082	0.398436
Smoking	0.324755	0.185104	1.754445	0.086162	-0.04806	0.697574
FamilyHx	0.186623	0.10924	1.708383	0.094456	-0.0334	0.406643
time to FMC	0.000732	0.000368	1.986952	0.053036	-0.25987	0.001473
troponin i	0.021504	0.00772	2.785669	0.007791	0.005956	0.037052
peak CK	-0.00011	0.00021	-0.50585	0.615433	-0.00053	0.000317
peak CK MB	0.000608	0.00074	0.821632	0.415619	-0.00088	0.002099
stent diameter	0.051241	0.176182	0.29084	0.77251	-0.30361	0.406089
stent length	0.010513	0.011777	0.892708	0.376763	-0.01321	0.034233
MBG	-0.1462	0.069158	-2.11404	0.040086	-0.28549	-0.00691

DISCUSSION

Ischemic heart disease (IHD) is the main cause of mortality in developed countries and its prevalence is increasing in developing countries [9]. Current therapy of acute myocardial infarction (AMI) is represented by early reperfusion of the myocardium., in some patients, successful restoring of the coronary artery after primary coronary intervention (PCI) is not associated with adequate perfusion of the ischemic myocardium [10]. **Srinivasan et al**, reported that a significant percentage of patients with ST-elevation myocardial infarction were had impairment of microvascular blood flow inspite of successful reperfusion and patency of the infarct-related artery. Microvascular impairment has been associated with a larger infarct size, heart failure , and death. It still unclear whether this association were due to direct mechanistic significance or whether the microvascular impairment is an epiphenomenon and a manifestation of more ischemic insult to the ischemic myocardium ,Although several mechanisms have been proposed for the microvascular impairment ,distal microembolization during mechanical reperfusion is likely to be an important factor [11] Myocardial blush grade (MBG) now is routinely used to assess the degree of myocardial reperfusion.[12]. **Marthe et al,** reported that MBG should be documented , with TIMI flow grade, at primary PCI in patients with STEMI in standard PCI reports in routine clinical practice[13]

The present study shows that the presence of myocardial reperfusion (MBG II-III) after emergency PCI was associated with a significantly lower rate of LV dilatation and remodeling than the absence of myocardial reperfusion (MB 0-1) .

In the present study, age of studied patients ranged from 29 to 70 years with a mean of 52 years and there was no significant variance between different MB grades. Males represented 88%. This was in agreement with **Korosoglou et al,** [14] who reported non significant difference between MBG 0, I, II and III as regard age or sex distribution. In addition **Marra et al,** [10] reported that no

significant difference between groups as regard age and sex distribution and MBG and these results are in accordance with those of the present work.

In the present study there was no significant difference between different MBG in risk factors of IHD. Similar results are reported by **Korosoglou et al,** [14] who reported that, there was no significant difference between different grades as regard hypertension, diabetes, elevated lipid levels and history of tobacco use. Similar results are reported by **Hamdan et al.** [15]. In addition, **Porto et al.** [16] reported that, there were no significant differences between the groups in the prevalence of risk factors, administration of drugs, or co morbidities, and these results are in agreement with that of the present study.

In the present study, we find that time from symptom onset to first medical contact (FMC) ranged from 50 to 300 minutes with a mean of 182 minutes and there was significant difference between different MBG with inverse correlation between time to FMC and MBG. These results are in accordance with those reported by **Hafiz et al,** who reported that Shorter pre-hospital delays in ST-elevation myocardial infarction (STEMI) are associated with improved outcomes. Moreover, **Koul et al**, showed that delays in FMC-to-PCI in excess of 1 hour were a significantly associated with an increase in severe left ventricular dysfunction at discharge and reported an overall significant association between increasing symptom-to-PCI delays and 1-year mortality [18]so, A goal of FMC-to-PCI of less than 1 hour might save patient lives

In the present study there was no signigicant difference as regard thrombus aspiration (TA) and MBG this was concordant with **Nilsen et al,** [19] who reported that in STEMI patients undergoing pPCI, the use of manual TA was associated with improved ST-segment resolution (STR) at discharge, but not with any difference in final TIMI flow and MBG.

Lagerqvist et al reported that aspiration of the thrombus in patients with STEMI before PCI did not decrease the rate of death from any cause , or stent thrombosis, or rehospitalization for myocardial infarction at 1 year according to the one-year follow-up results from the " TASTE Clinical Trials". [20]

In the contrary, **Vlaar et al** in the TAPAS trial demonstrated that routine use of manual aspiration with the Export catheter compared with PCI alone during PPCI reduced the incidence of the primary outcome of impaired microvascular perfusion MBG 0 or 1 [21]**.** After the publication of this trial, both the ESC and ACC/AHA guidelines included a class IIa recommendation for the use of routine thrombectomy during PPCI.

Satoh et al. compare the efficacy of thrombus aspiration with and without usage of distal protection in patients with STEMI by using a filter devise system during primary PCI and conclude that thrombus aspiration with distal protection with a filter devise were more effective than thrombus aspiration alone in preserving the coronary perfusion , although it may not prevents LV remodeling .[22].

In the present study there was no significant difference between MBG and usage of glycoprotein (GP) IIb/IIIa inhibitors (P- value=0.4) . this was concordant with **Schulz, et al.** who reported that in patients with acute ST-segment elevation myocardial infarction (STEMI) underwent primary coronary interventions (PCI) the upstream usage of abciximab did not reduce the infarct size or improve clinical outcomes after 1 year of primary PCI. [23]

On the contrary, **Thiele et al.** reported that in primary PCI the intracoronary administration of abciximab is more superior to intravenous administration with reflect to infarct size, perfusion and extent of microvascular obstruction[24]. this discrepancy may be due to we use intravenous route only in our study not intracoronary.

A nother study by **Giuseppe et al,** [25] demonstrated the importance of early administration of GpIIb/IIIa inhibitors and it affected by the time from onset of the symptoms to GpIIb/IIIa inhibitors administration, they explained that in ST-segment elevation myocardial infarction a time-dependent composition of the coronary thrombus with more platelets in the first hours . they showed that in patients performed

primary angioplasty, time from onset of the symptoms to GpIIb/IIIa administration, severely impacts on distal embolization, myocardial perfusion (MBG) , and long-term survival. this discrepancies was due to upstream usage of GpIIb/IIIa inhibitors.

In the present study, complete revascularization occur in 9 patients with significant difference with MBG as all patients have MBG II-III. This was concordant with **Engstrøm et al,**[26] in **DANAMI3-PRIMULTI trial**, it concluded that complete revascularization resulted in a lower risk of the primary composite endpoint (all-cause death, nonfatal MI, and ischemia-driven revascularization (PCI or CABG) of non-IRA lesions compared with IRA PCI, but this was driven by a lower rate of repeat revascularization. No differences were seen between the groups with regard to nonfatal MI or mortality. On the contrary, **Goldstein et al,**[27]reported that PCI of non-infarct artery is not indicated and harmful unless multiple complex lesions are seen on angiography , these depend on clinical stability of the patient which defined as hypotension, low output , apparent shock,ventricular arrhythmias or symptomatic tachyarrhythmias, and recurrent ischemia.Also, **Hamdan et al**[15] and **Vlaar et al,** [21] found that PCI of a non-infarct artery (at the time of primary PCI) were associated with worse clinical result if done in stable patient.

In the present study there was significant increase of EDV at 6 months when compared to their values at 24 hours in MBG 0 and in MBG I , However, there was non-significant changes in EDV in patients with MBG II and III. In addition, changes in ESV and LVEF were in correlation with that of EDV. In the present study rescue PCI cases have better myocardial blush and no remodeling present in more 60 % of them but without significant difference and this reflect that rescue PCI is safe as well as primary PCI.

The predictors of remodeling were impaired myocardial blush and increase cardiac Troponine

These results reflects an inverse relationship between MBG grades and cardiac remodeling (with increased grade, remodeling decreased). These results are in agreement with that reported by **Hamdan et al,**[15] who reported that, at 6 months, patients with MBG II-III had significantly smaller LVED and LVES volumes, and significantly higher LV ejection fraction (EF) compared with patients with MBG 0-1. In addition, **van 't Hof et al**'[8] **and Hoffmann et al,** [28] reported significant increase of EF% in MBG II-III in comparison to MBG 0-I at the start of the study and at follow up, and these results reflects the good predictability power of MBG in cases before and after angioplasty.

CONCLUSIONS

Impaired MBG after emergency PCI is associated with increased risk of LV remodeling. It has the advantage of being simple method to assess myocardial microcirculation.

- **Limitations of our study were:** (1) Relatively small sample size (2) Short follow up period (3) Heterogenicity of emergency PCI (primary & rescue).

- **Acknowledgement**

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