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Myocardial Perfusion Grade by Coronary Angiography can Predict Final Infarct Size and Left Ventricular Function in Patients with ST-elevation Myocardial Infarction Treated with a Pharmaco-invasive Strategy

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Abstract

BACKGROUND: Primary percutaneous coronary intervention (PCI) is the reperfusion strategy of choice in ST-elevation myocardial infarction (STEMI). Transfer for early angioplasty after thrombolytic therapy should be done without delay and has been directly related to improved patients' outcome compared with thrombolysis alone. TIMI myocardial perfusion (TMP) grade provides important prognostic information for epicardial flow.

AIM: We studied the relationship between TMP grade (at the end of the PCI procedure) and left ventricular ejection fraction (LVEF) and infarct size within 1 month in such patients.

METHODS: A total of forty patients with diagnosis of STEMI (mean age 57.32 ± 10.44, 33 men) were studied, all patients underwent primary PCI. Grading of myocardial perfusion was done immediately post-PCI. Infarction size, end-diastolic volume (EDV), end-systolic volume (ESV), and LVEF were all measured by myocardial perfusion imaging (Gated single-photon emission computed tomography) within 1 month of STEMI.

RESULTS: Final infarct size ranged from 0 to 59 cm (mean =19.18 ± 15.8 cm). EDV ranged from 52 to 228 ml (mean = 128.60 ± 51.01 ml). ESV ranged from 16 to 169 ml (mean =72.05 ± 42.09 ml) and EF ranged from 21% to 72% (mean = 46.0 ± 12.80%). Viable but ischemic myocardial area ranged from 0 to 18 cm (mean =3.38 ± 4.45 cm). There was a significant "negative" correlation between the myocardial perfusion grade and the final infarct size. Furthermore, myocardial perfusion grade was significantly inversely related to EDV and ESV, but directly related to EF. Patients who received thrombolytic therapy had significant lesser perfusion grade than who underwent PCI directly.

CONCLUSION: Assessment of the myocardial perfusion grade during PCI is a good prognostic marker about the final infarct size, ESV, EDV, and EF in patients with STEMI treated with a pharmaco-invasive strategy (thrombolytic followed by PCI).

Background

Primary percutaneous coronary intervention (PCI) is considered superior to any other reperfusion strategies in the core treatment of ST-elevation myocardial infarction (STEMI). However, in rural areas where PCI service is unavailable and transfer times of more than 90–120 min to PCI, initial thrombolysis is considered the treatment of choice [1]. Post-thrombolytic therapy – transfer for early angioplasty has been shown to improve outcome compared with initial thrombolysis alone [2] and has shown the same outcome and safety results to those of primary PCI in areas with long transfer delay [3], [4].

Thrombolysis in myocardial infarction (TIMI) flow in the epicardial artery is defined as successful reperfusion in STEMI [5]. Although, complete restoration of epicardial flow does not always mean neither flow restoration on the myocardial level nor microvascular reperfusion. Moreover, normal tissue perfusion may be obtained in only (25–55%) of patients [6], [7].

However, TIMI myocardial perfusion (TMP) grade can delineate excellent data about epicardial flow, it is also capable to provide prognostic data beyond that [6], [7]. Full reperfusion at the myocardial level is as important as restoration of TIMI 3 flow. TMP is an independent predictor of both myocardial function recovery and long-term survival. TIMI flow grade classification has been used to assess coronary blood flow especially in STEMI, it has been a valuable method to compare angiographic outcomes following reperfusion, and the association of the TIMI flow grades (TFGs) with clinical morbidity and mortality [8], [9], [10].

Myocardial perfusion imaging has both diagnostic and prognostic uses, because it permits cardiac risk stratification of patients. The presence of normal perfusion images with or without angiographically documented coronary artery disease is usually associated with a good prognosis, with a better survival rate [11], [12]. In addition to the mere presence of a reversible ischemic defect on a perfusion scan, the greater the number and the more severe segments with reversible defects, the stronger the unfavorable patient outcome [13]. Therefore, myocardial perfusion imaging has an important prognostic value which is directly linked to the severity and extent of the perfusion abnormalities.

Patients and Methods

Patient's selection

We studied 40 patients who were admitted to Egyptian National Heart Institute CCU with the diagnosis of STEMI whose symptoms onset is <12 h and underwent either thrombolytic therapy then rescue successful PCI/facilitated PCI, or successful primary PCI from the start, in the first 24 h from hospital admission.

Patient preparation

Diagnosis of acute myocardial infarction was made on typical chest pain and/or new ischemic electrocardiographic (ECG) changes with elevation of cardiac enzymes. Cardiac biomarkers (CK, CK–MB, troponin, and lactate dehydrogenase) were estimated on admission, post-PCI every 6 h in the first 24 h and then once daily till clinically not needed. The culprit artery was identified using coronary angiography or according to ECG criteria. Cardiomyopathic patients, moderate, or severe valvular heart disease, and those younger than 18 years were excluded from the study.

PCI

Myocardial perfusion was graded according to the TIMI myocardial perfusion grade (TMPG) into:

- Grade 0: Dye fails to enter the microvasculature; there is no blush or opacification of the myocardium in the culprit lesion's distribution
- Grade I: Dye enters slowly the microvasculature but fails to exit; there is blush of the myocardium in the culprit lesion's distribution that does not clear from the microvasculature, and dye staining is usually present on the next injection (around 30 s between each injection)
- Grade II: Dye enters and exits slowly from the microvasculature; there is blush or of the myocardium in the culprit lesion's distribution that is persistent at the end of the washout phase (i.e., Dye staining is usually persistent after three cardiac cycles and does not decrease in intensity during washout)
- Grade III: Dye enters and exits normally from the microvasculature; there is blush of the myocardium in the culprit lesion's distribution which clears normally (i.e., Dye is mildly/ moderately persistent after three cardiac cycles of the washout phase and diminishes in intensity during the washout phase).

Myocardial perfusion imaging

We aimed to assess the infarct size after 1 month of STEMI, patients in the study underwent Myocardial Perfusion Imaging using Gated single-photon emission computed tomography (SPECT) imaging which was done at rest 1 h following the injection of 25 mCi of Tc99m sestamibi. AT peak exercise, each patient at the study was injected with 25 mCi of Tc99 sestamibi and exercise was continued for 1 min. Gating post-stress tomographic imaging was performed 30 min after stress. The treadmill exercise using Bruce protocol and the metabolic equivalents were calculated.

The tracer uptake was then analyzed on computerized maps. Activity which is >2.5 Standard deviations below the corresponding normal mean values was considered abnormal. The number of abnormal pixels divided by the total number of left ventricle pixels times 100 and then the result was automatically reported by the computer as a perfusion defect. Having MIBI uptake below 50% of the maximum was defined as a non-viable myocardium.

Resting myocardial segmental perfusion was scored on a score scale of 0–4; where 0 is considered to be normal, while 1 is equivocal, 2 is considered moderate, 3 is expressed as severe reduction of segment perfusion (radioisotope uptake), and 4 means totally absent perfusion with absence of radioisotope uptake.

The infarct size reference range was expressed as: Defect <10% means small infarction, while 10–15% infarct size means moderate size infarction, while more than 15% means large infarction.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS computer software package version 20.0. Qualitative data were described using both numbers and percentage. We have tested the distribution normality using Kolmogorov–Smirnov test. Quantitative data were described in the form of a range (from minimum to maximum), mean, standard deviation, and median.

Data were analyzed using Chi-square test, Fisher's Exact, or Monte Carlo correction – F-test ANOVA, Mann–Whitney test, Kruskal–Wallis test, and

Spearman coefficient with significance level reaching up to 5%.

Results

a. Demographic data: Our studied patients' age range was 32–85 years old (57.32), 33 of them are males while remaining seven are females (Table 1)

Table 1: Distribution of the studied cases according demographic data (n=40)

Demographic Data	n	%
Gender		
Male	33	82.5
Female	7	17.5
Age		
<50	8	20.0
50–60	18	45.0
>60	14	35.0
Min.–Max.	32.0–85.0	
Mean ± SD.	57.32 ± 10.44	
Median	57.50	

b. History and risk factors; hypertension was noted in 45% of them, diabetes mellitus in 50% of them with smoking history in 50% of them as well. Previous cardiovascular event was found in 15 patients

c. According to ECG and STEMI distribution; anterior infarction left anterior descending (LAD) was found in 55% of them, inferior infarction 42.5% of them, lateral infarction in 5%, and posterior infarction in 5% of them. (Figure 1).

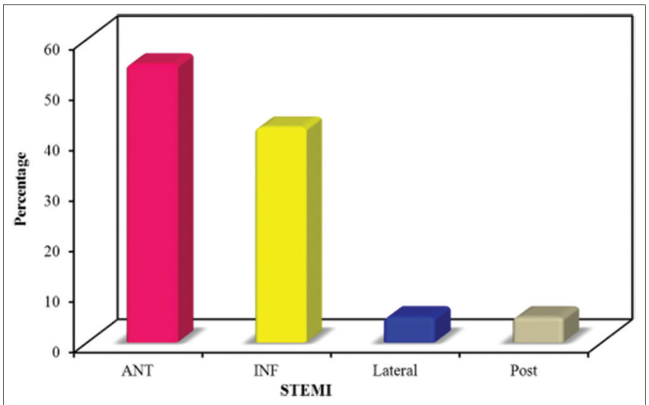

Figure 1: Distribution of the studied cases according to ST-elevation myocardial infarction (n = 40)

d. Hospital management

The mean time from pain to cath or thrombolytic was (2.85 ± 1.91) ranging from 1 h to 10 h.

Immediate angiography was performed in 29 patients (72.5%), while Rescue PCI group in 11 patients (27.5%). On studying the relationship between thrombolytic therapy to final infarct size, the patients who received thrombolytic therapy had significant lesser MPG than who underwent PCI directly (p = 0.004) (Figures 2 and 3).

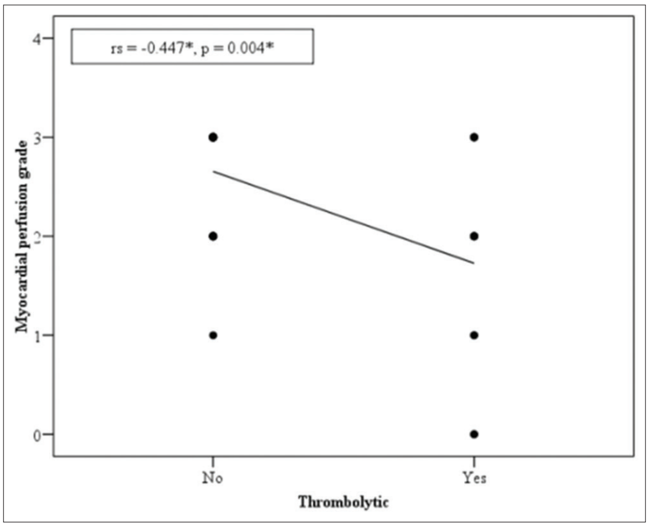

Figure 2: Correlation between thrombolytic and myocardial perfusion grade

e. Angiographic data

Myocardial perfusion grade ranging from 0 to 3, 5% of patients had MPG "0" while 7.5% had MPG "1" and 30% showed MPG "2" and the highest percentage of patients 57.5% had MPG "3." By CATH, 52.5% of patients the territory affected were LAD while 35% was RCA and the least was LCX with percentage of 17.5%. There were no significant differences in infarct related artery (LAD vs. LCX and RCA) between grades.

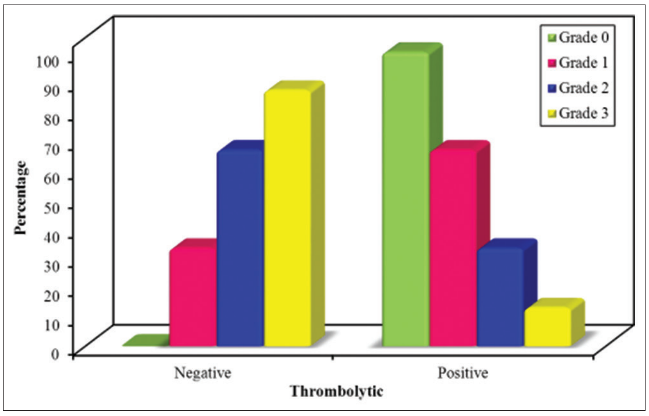

Figure 3: Relationship between myocardial perfusion grade with thrombolytic

f. Perfusion study

Final infarct size ranged from 0 to 59, with a mean of 19.18 ± 15.86cm. End diastolic volume (EDV) ranged from 52 to 228 ml with a mean of 128.60 ± 51.01 ml. End systolic volume (ESV) ranged from 16 to 169 ml with mean of 72.05 ± 42.09 and ejection fraction (EF) ranged from 21 % to 72% with a mean of 46.0 ± 12.80. Viable ischemic area ranged from 0 to 18 cm with 3.38 ± 4.45, Table 2.

On finding the relationship between myocardial perfusion grade and final infarct size, there was significant indirect correlation between the myocardial perfusion grade and the final infarct size, the higher the MP grade the lesser the infarct size with (p = 0.001). Furthermore, myocardial perfusion grade was significantly inversely related to EDV and ESV,

Table 2: Descriptive of the studied cases according to final infarct size

Demographic Data	Min.–Max.	Mean ± SD.	Median
Infarct size	0.0–59.0	19.18 ± 15.86	17.0
End Diastolic Volume	52.0–228.0	128.60 ± 51.01	111.50
End Systolic Volume	16.0–169.0	72.05 ± 42.09	59.0
Ejection fraction %	21.0–72.0	46.0 ± 12.80	45.50
SD%	0.0–18.0	3.38 ± 4.45	1.0

the higher the grade the lesser the EDV and ESV, with p = 0.019, 0.001, respectively. EF was strongly and significantly related to the MPG, the higher the grade the higher the EF with (p = 0.002). Patients with TMP Grade 3 post-PCI had significantly lower EDV, and ESV, higher left ventricular EF (LVEF) with p = 0.019, 0.001, and 0.002, respectively, and these patients also had significantly smaller infarct sizes with (p = 0.001) (Figures 4-8).

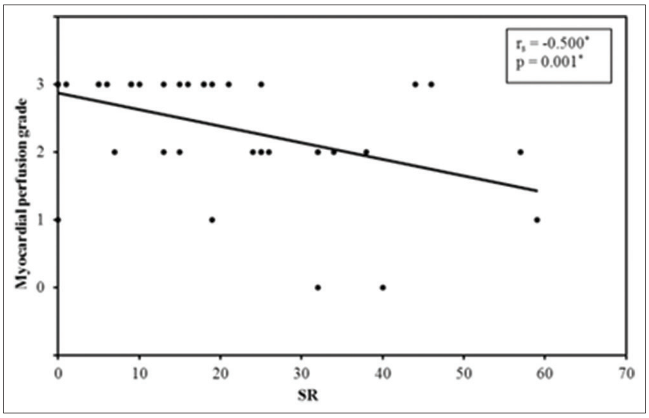

Figure 4: Correlation between myocardial perfusion grade and SR

Discussion

The final infarct size is highly related to several complications such as life-threatening arrhythmias or recurrent hospitalization as a result of heart failure. There are two main approaches widely available for the measurement of infarct size: Magnetic resonance imaging (MRI) and myocardial perfusion imaging technetium TC99m sestamibi SPECT.

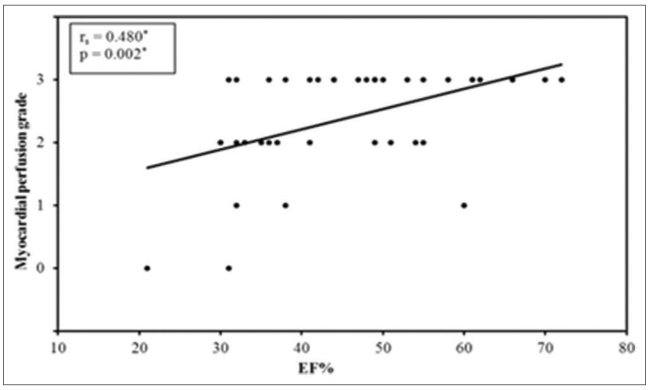

Figure 5: Correlation between myocardial perfusion grade and ejection fraction

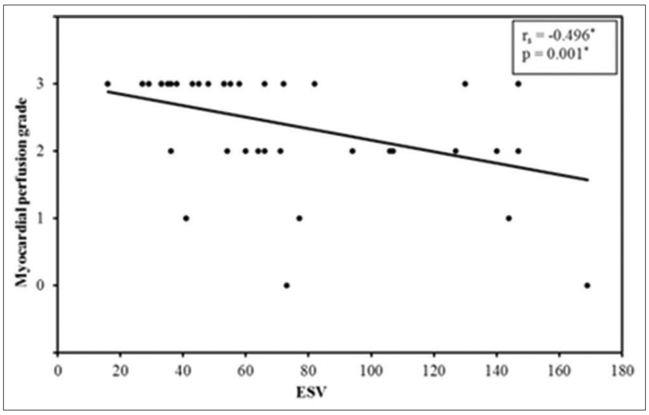

Figure 6: Correlation between myocardial perfusion grade and end systolic volume

This study aimed at assessment of the association between TIMI myocardial perfusion (TMP) at the end of the PCI procedure and LVEF in addition to infarct size within 1 month in such patients.

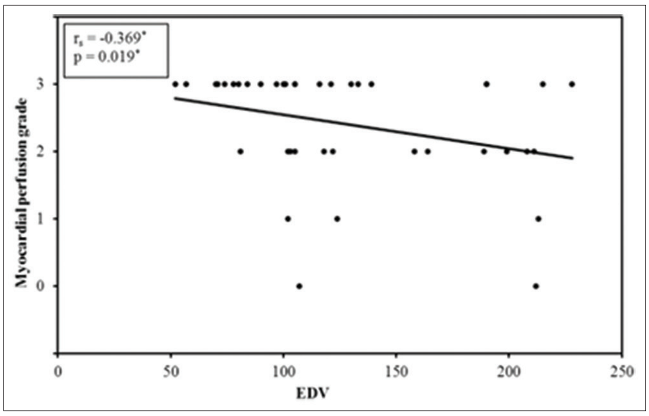

Figure 7: Correlation between myocardial perfusion grade and end diastolic volume

There was a significant correlation between the myocardial perfusion grade and the final infarct size; the higher the MP grade the lesser the infarct size with (p = 0.001(. This was in agreement with Pride *et al*. [14] and has studied 3491 STEMI patients treated with thrombolytic therapy, angiography was done 2–8 days with a median 3½ days after randomization. They

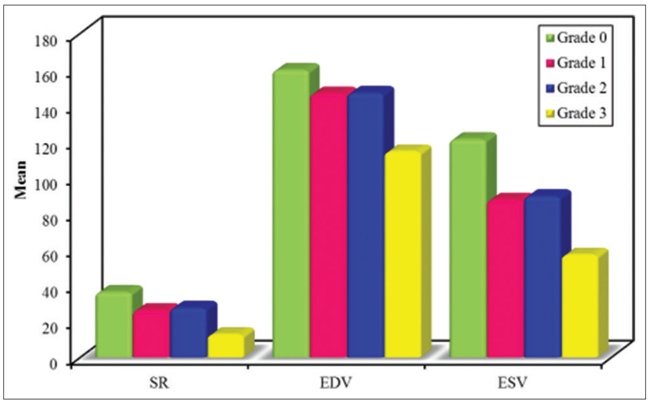

Figure 8: Relationship between myocardial perfusion grade with sr, end diastolic volume, and end systolic volume

calculated the sum of the TIMI Flow Grade and Myocardial Perfusion Grade before and after PCI. It concluded that patients with high score who were treated with PCI showed better outcome in both morbidity and mortality. In addition, Bethke *et al*. [15] studied (89) patients with STEMI treated with fibrinolytic and early PCI, at the end of PCI TMP was assessed. After 3 months, MRI was done to assess infarct size and EF. Results showed that MPG can predict final infarct size in patients treated with thrombolytic therapy and PCI. Moreover, Haager *et al*. [9] in a study conducted over 253 patients found that myocardial perfusion grade (0–1) was a good predictor for long-term mortality after PCI in acute myocardial infarction while corrected TIMI frame count (cTFC) was a less powerful predictor.

Gibson *et al*. [8] studied STEMI with TIMI flow Grade 2 or 3 flows in 49 centers with 2-year follow-up. The study concluded that both improved epicardial flow (TFG 2 or 3) and tissue level perfusion (TMPG 2 or 3) at 90 min after thrombolytic administration were associated with better 2 year survival. However, Wong *et al*. [16] enrolled primary PCI patients and used cardiac MRI to find that no correlation between TMP and LVEF after 3 months.

In our study, we found that myocardial perfusion grade was significantly inversely related to EDV and ESV; the higher the grade the lesser the EDV and ESV, with p = 0.019, 0.001, respectively, This was in agreement with De Luca *et al*. [17] study who studied 1548 STEMI patients that underwent PCI. Killip class was assessed at admission. Killip class was directly associated with myocardial perfusion, infarct size, EF, and higher mortality rate. Myocardial perfusion was an independent predictor in patients with advanced Killip's class at presentation of 1 year mortality (p = 0.005).

Berk *et al*. [18] studied 45 dilated cardiomyopathy patients using SPECT and 2D ECHO. Patients underwent resting myocardial gated SPECT, Gated SPECT data, Data were obtained about left ventricular end diastolic and ESV and LVEF were expressed. He concluded that 2D echocardiography and SPECT are good correlates for the results of left ventricular end systolic and EDV and EF.

Similarly, Schaefer *et al*. [19] conducted a study on 70 patients with coronary artery disease they were examined using (99m) Tc-MIBI SPECT 1 h after tracer injection at rest. Using Simpson's rule ESV, EDV were calculated, and as a reference cardiac MRI (CMRI) was done. Data gained by SPECT were the same as data gained by cardiac MRI.

In our study, we have found that EF was strongly and significantly related to the MPG, the higher the grade the higher the EF (p = 0.002). This was in agreement with, Gai *et al*. [20] who studied 34 patients who underwent both coronary angiography and SPECT, and the comparison was made between chronic total occlusion versus stenosis, MPG Grades 1 and 2 versus MPG Grade 3, they compared successful PCI versus failed PCI. MPG was correlated to EF. There was a significant improvement for the total blush and EF after PCI. Van't Hof *et al*. [21] carried a study over 6 years on 777 patients who underwent primary PCI and studied the value of angiographic evidence of myocardial blush grade in relation to the long-term mortality and extent of ST-segment elevation resolution, left ventricular function, and enzymatic infarct size. The myocardial blush was significantly related to the resolution of the early ST-segment on the 12-lead ECG.

Appelbaum *et al*. [22] also studied 21 STEMI patients after successful primary PCI. Post-PCI, contrast-enhanced CMR was done within 7 days of presentation and follow-up CMR at 3 months. TMPG, infarct size, LVEF (EF), TFG, and corrected cTFC were assessed. They concluded that STEMI patients undergoing primary PCI, post-PCI TMPG correlated with CMR measures of infarct size. Consequently, the use of both measurements in the assessment of microvascular integrity and infarct size post-STEMI may aid in the evaluation of further therapeutic strategies.

Regarding the relationship between thrombolytic therapy to MPG, MPG totally was significantly directly related to direct PCI without prior thrombolytic (p = 0.012). Svensson *et al*. [23] also concluded that early invasive therapy result in superior epicardial flow in the infarct related artery. Epicardial flow in the infarct-related artery was better after invasive therapy and in addition to better clinical outcome after PCI compared with after fibrinolysis.

De Boer *et al*. [13] who studied 300 STEMI patients and concluded that primary PCI resulted in smaller infarct size than intravenous thrombolytics.

Sutton *et al*. [24] enrolled 307 STEMI patients with failed fibrinolysis. They underwent emergency coronary angiography with or without rescue PCI. Rescue PCI did not show improved survival rate after 30 days duration, but improved event-free life, due to a reduction in need for subsequent revascularization. Rescue PCI was associated with more cerebrovascular complications and need for transfusions and did not result in preservation of left ventricular systolic function at 30 days assessment.

On the other hand, Rahuman *et al*. [25], from the cardiology PCI Clinic of the National Hospital of Sri Lanka (NHSL), included all acute SEMI patients from March 2013 to April 2015 who were presenting with <24 h door-to-balloon time for primary PCI and <72 h door-to-balloon time, 90 min after failed thrombolysis for rescue PCI, and their in-hospital results were analyzed, comparing rescue and primary PCI patients. They concluded that major adverse cardiac events in hospital are similar in both primary and rescue intervention groups, supporting the rescue as an option for patients with no immediate access to PCI facilities.

Similarly, Collet *et al*. [26] study on 5253 patients concluded that rescue PCI after failed fibrinolysis had reduced mortality and the rate of death or reinfarction (10.8% vs. 16.8%) compared with a conservative approach.

Conclusion

Assessment of the myocardial perfusion grade during PCI can predict the final infarct size, EF, ESV, EDV, and in patients with STEMI treated with pharmaco-invasive strategy (thrombolytics followed by PCI). Direct PCI without prior thrombolytic is the best treatment strategy in STEMI.

Disclosure/Declaration

This manuscript reports on experiments on human subjects.

The procedure followed in accordance with the “Declaration of Helsinki” and the ethical standards of Cairo University committee on human experimentation.

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