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Original Research Article

Evaluation of coronary microcirculation by myocardial contrast echocardiography in patients of ST elevation myocardial infarction

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ABSTRACT

Background: No reflow phenomenon observed during catheter intervention has been associated with poor cardiovascular outcomes. Assessment of filling defect by myocardial contrast echocardiography (MCE) correlates with no reflow. Limited studies are available for the same. This study was designed to look for impact of type of therapy for revascularization (whether percutaneous coronary intervention or thrombolysis) and its evaluation by MCE and follow up echocardiography parameters.
Methods: Total 50 consecutive patients of ST-elevation myocardial infarction (STEMI) were taken study including recent STEMI (within 7 days). After all routine investigations patient underwent coronary angiography and percutaneous coronary intervention (PCI) procedure. Following completion of procedure, thrombolysis in myocardial infarction (TIMI) flow, TIMI frame count, and myocardial blush grade were calculated and noted. Post revascularization contrast echocardiography was done after patient stabilization. Findings were correlated with cath-lab parameters applying appropriate statistical tests. Follow up was planned after 30 days.
Results: 50 consecutive patients admitted with acute myocardial infarction (MI) or recent MI (0-7 day) who underwent primary PCI - 82% (n=41) or thrombolysed with various thrombolytic agents - 18% (n=9). Mean age of the study group was 55.02±12.65 years. There was significant association in between TIMI 3 flow and absence of filling defect in MCE (p=0.03), but no significant association found in between revascularization therapy (Either PCI or Thrombolysis) and filling defect in MCE (p=0.08).
Conclusions: Our study found good correlation between myocardial contrast score with angiographically measured TIMI flow and improved echocardiographic findings on follow up.

Keywords: MCE, Myocardial contrast echocardiography, No reflow, Contrast score index

INTRODUCTION

Currently primary percutaneous coronary intervention and thrombolysis are 2 major blood flow restoration therapy being provided in patient with acute myocardial infarction. Although in majority of patients it achieves goal of TIMI III blood flow, in many (up to 30 percent) it fails to achieve perfusion at microvascular level in the area at risk.[1,2]

This phenomenon of no reflow at microvascular level is associated with larger infarct area, poor contractility, increased ventricular dysfunction and heart failure which ultimately leads to increased mortality. Proposed reasons behind no reflow at microvascular level are microvascular disruption, altered chemical milieu, plugging of thromboembolic debris, endothelial and myocardial edema.[3-7]

Observed coronary no flow in cath-lab could be studies noninvasively by means of contrast echocardiography.[8,9] This study was planned to evaluate the impact of reperfusion therapy (percutaneous coronary intervention - PCI or thrombolysis) for acute coronary syndrome on coronary microcirculation evaluation by myocardial contrast echocardiography (MCS).

METHODS

This study was conducted in Krishna Institute of Medical Sciences, Telangana, India from July 2015 to June 2016 for a period of one year. Study was approved by institutional ethical committee. We studied 50 consecutive cases with recent ST-elevation myocardial infarction (STEMI) (within 1 week) undergoing primary or elective percutaneous coronary intervention or thrombolysis. After taking detailed history and thorough physical examination, patient underwent primary PCI if indicated as per the American College of Cardiology (ACC) guidelines.

Patients who received thrombolytic therapy outside hospital recently (within one week) and presented to our hospital for further management and angiogram were also included. Angiogram was done followed by percutaneous transluminal coronary angioplasty (PTCA) and stenting according to clinician's decision. The infarct-related vessel was analyzed before and after primary coronary angioplasty to assess the residual stenosis. In case of multi vessel disease only infarct related vessel was treated and patients who had significant disease in vessels other than infarct related artery were not considered for study. Angiography was done at rate of 15 frames per second.

Following completion of procedure thrombolysis in myocardial infarction (TIMI) flow, TIMI frame count, and myocardial blush grade were calculated and noted. All patients received standard pharmacotherapy as per the guidelines.

Echocardiogram was done pre and post revascularization but only post revascularization parameters were recorded for further evaluation. Echo was done with Philips iE33 machine with S5 probe. Left ventricular end diastolic (LVED) and left ventricular end systolic (LVES) volumes were calculated along with ejection fraction by Biplane Simpson method. Regional wall motion abnormality was recorded in all 17 segments of left ventricle in apical four chamber, apical two chamber and three chamber view. The following numerical score is assigned to each wall segment on the basis of its contractile function as assessed visually: 1=normal (>40% thickening with systole); 2=hypokinesis (10% to 40% thickening); 3=severe hypokinesis to akinesis (<10% thickening); 4=dyskinesis; and 5=aneurysm.[10]

The wall motion score index (WMSI) is calculated by dividing the sum of these numbers by the number of segments visualized.[10] After 24 hour to 96 hour post procedure patient underwent MCE after clinical stabilization. DEFINITY® Lantheus medical imaging (Perflutren lipid microsphere) is used as contrast agent as continuous infusion after reconstitution of 1.3 milliliters of definity contrast with 50 milliliters of 0.9% saline and given at rate of 50-70 ml/hour and rate adjusted for adequate left ventricular opacification.

Images were recorded in two chamber four chamber and three chamber view using Philips iE 33 echocardiography machine with S5 probe with emission frequency of 1.7 MHz, receiving frequency of 3.4 MHz. MCE done with 0.1 mechanical index of and focus kept at level of mitral annulus and image adjusted for optimal visualization of endocardial myocardial border. After definity contrast appeared in left ventricular cavity high mechanical index (1.9) ultrasound energy delivered with flash sequence for up to 5 cardiac cycles for destruction of micro bubbles and immediately after that images were recorded for up 15 cardiac cycles. A 4-point semi quantitative scoring system was used to assess transmural contrast intensity at 15 cardiac cycles following micro bubble destruction in all 17 segments: 0=drop out area, 1=normal contrast intensity, 2=mild reduction, 3=moderate to severe reduction, and 4=absent contrast.

Contrast score index (CSI) was thus calculated by dividing the sum of the perfusion score of all analyzed segments by the number of segments analyzed.[10] The echo drops out areas were not included in calculation. Semi quantitative assessment of MCE was performed using QLab software (Philips medical systems). A region of interest was drawn transmurally within each segment, avoiding the high-intensity epicardial and endocardial borders.

As a routine protocol in our hospital patients are asked for follow up after one month of revascularization. During follow up visit echocardiogram was done with measurement of left ventricular end diastolic, end systolic volumes, ejection fraction, regional wall motion abnormality, regional wall motion score index. All the data is expressed in mean±standard deviation. Distribution is expressed as a percentage of total number in population in actual numbers. All the statistical analysis was done using statistical package for social sciences (SPSS) version 17.0 IBM Computers, New York. Relation between variables was analyzed using Pearson's correlation, where correlation (r) value greater than 0.300 and p value of <0.05 were considered significant correlation.

RESULTS

We have studied 50 consecutive patients admitted with acute MI or recent MI (0-7 day) who underwent primary PCI - 82% (n=41) or thrombolysed with various thrombolytic agents - 18% (n=9). Mean age of the study group was 55.02±12.65 years (Table 1).

In 16% of patients CSI was 1 and in 64% of patients it was found to be between 1-1.49 while 14% patients had CSI between 1.5-1.99 and remaining 6% patients had CSI >2.

Table 1: Baseline characteristics.

Variables	Frequency (%)
Age (years)	55.02±12.65
Men	40 (80)
Diabetic	22 (44)
Hypertensive	2 7(54)
Dyslipidemia	9 (18)
Smoker	15 (30)
Family history of CAD	24 (48)
Mean TIMI risk score	4.34±2.08
Previous history of CAD	17 (34)
Previous CABG	0
Previous PTCA	0
Primary PCI	41 (82)
Post thrombolysis	9 (18)
Window period	12.0±10.4 hours
Mean systolic blood pressure	85.9±36.64 mm Hg
Mean diastolic blood pressure	72±18.78 mm Hg
Mean heart rate	85.9±25.09 beats per minute
Raised JVP	12 (24)
Third heart sound	19 (38)
Killip score	1.78±0.91
Creatinine	1.54±0.82 mg/ dl
Leucocyte count	12398±4642.68 cells/dl
Single vessel disease	16 (32)
Multi vessel disease	34 (68)
Infarct related artery lad	21 (42)
Infarct related artery LCx	7 (14)
Infarct related artery RCA	22 (44)
Mean ST segment elevation at presentation	4.14±2.93
ST resolution > 50%	58%
ST resolution > 70%	34%
Post reperfusion TIMI flow grade III	30 (60)
Post reperfusion TIMI flow grade II	16 (32)
Drug eluding stent	27 (54)
Bare metal stent	23 (46)
Mean stent length	28.5±9.8 mm
Pre dilatation with balloon	25 (50)
Post stent balloon dilatation	18 (36)
Thrombus aspiration	31 (62)
GP IIb/ IIIa Inhibitor	33 (66)

In 24 (48%) patients there was filling defect in contrast echocardiography with contrast score of segment of segment 3 or 4 representing severe limitation in blood supply or no microcirculation at all following reperfusion. While in remaining 26 (52%) patients the coronary microcirculation was intact.

Mean contrast score in patients with filling defect was 1.53±0.30 while that in patients without filling defect was 1.16±0.15 ($p<0.0001$). There was significant difference in LVED, LVESV and regional wall motion score index (RWMSI) in these two groups but difference in ejection fraction was not significant. There was significant association in between TIMI 3 flow and absence of filling defect in MCE ($p=0.03$), but no significant association found in between revascularization therapy (either PCI or thrombolysis) and filling defect in MCE ($p=0.08$) (Table 2).

During follow up visit echocardiogram was done and LVESV, LVEDV and EF were calculated at mean follow up period of 39.54±17.21 days. MCE was not repeated at

follow up visit and patients were analyzed according to MCS at the time of post reperfusion to see the impact of microcirculatory flow in long term. At follow up LVEDV was 130.24±40.55 while LVESV was 63.86±36.59 and EF was 53.64±12.72 while regional wall motion score index was 1.33±0.41. At follow up period LVEDV decreased in patients without filling defect while that increased further in filling defect group. RWMSI improved in both the groups, while EF increased in no filling defect group while that further decreased in filling defect group (Table 3).

Table 2: Echocardiography including MCE post therapy (on admission).

Variable	Patients with filling defect in MCE	Patients without filling defect in MCE	P value
Number	24 (48%)	26 (52%)	NS
CSI	1.53±0.30	1.16±0.15	<0.001
LV EDV (ml)	144.66±43.06	114.53±31.74	0.006
LV ESV(ml)	74.91±41.75	48.5±19.9	<0.005
EF (%)	50.78±15.65	57.84±9.84	NS (0.06)
RWMSI	1.68±0.45	1.35±0.28	0.003
TIMI 3 flow	09	21	0.03

Table 3: Echocardiography on follow up.

Variable	Patients with filling defect in MCE	Patients without filling defect in MCE	P value
Number	24 (48%)	26 (52%)	NS
CSI (post reperfusion)	1.53±0.30	1.16±0.15	<0.001
Follow up LV EDV (ml)	153.12±42.08	109.11±25.08	<0.0001
Follow up LV ESV(ml)	83.75±40.87	45.5±18.9	<0.0001
Follow up EF (%)	47.72±14.23	59.10±8.13	0.0045
Follow up RWMSI	1.40±0.47	1.17±0.26	0.004

DISCUSSION

The mean age of the study population was 55 years, which is in concordance with few other recent studies published previously.[11-14] As expected, men comprised approximately 80% of the study population. While 44% of the patients were diagnosed diabetics, 54% of the study populations were hypertensive. Family history of coronary artery disease and previous history of coronary artery disease was reported by 46% and 34% of the patients respectively. 30% of the patients where current or reformed smokers, whereas 18% of the patients are dyslipidemic.

Most of the baseline characteristics of the study population are in accordance with previously published studies in the similar area. Kazberuk et al studied 43 patients of STEMI with MCE and angiographic parameters with mean age group of patients 60±11.[15]

We found significant correlation between MCE and post TIMI III score in the study population. Similar observations were reported previously by Yang et al in patients with ACS.[16] The same study further added that MCE is better measurement than TIMI for epicardial coronary tree flow.[17] Furthermore, for ACS patients screening before PCI, MCE technique could raise more necessary evidence for clinician in evaluating the status of myocardial perfusion by filtering the cases for correct treatment choice. The technique of MCE may therefore be a beneficial tool aiding before coronary angiography to predict TIMI risk and make a clinical decision.

Significant negative correlation between EF measured at follow up visit with contrast score index suggests that the regional wall motion abnormality due to stunned or hibernating myocardium improved over time. This finding is reinforced by our observations where, LVESV and LVEDV measured at follow up visit showed significant and strong positive correlation with contrast score index. Nevertheless more extensive research in this direction is required.

Furthermore we analyzed the absolute improvement in the ejection fraction, LVEDV, LVESV and RWMI between both the groups, we found patients without perfusion defect show trend towards improvement where, the average ejection fraction improved by 1.25%, LVEDV and LVESV reduced by 5.5 ml and 3 ml respectively at 40 days follow up in patients without filling defects. Likewise RWMI scores also showed inclination towards improvement in patients without filling defects. The average follow up period was 40 days which may be insufficient to elicit a significant change in the above stated variable.

CONCLUSION

Our study found good correlation between myocardial contrast score with angiographically measured TIMI flow and improved echocardiographic findings on follow up. MCE could be used as a tool to assess effectiveness of therapy in patients with STEMI.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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