

Gated SPECT Myocardial Perfusion Imaging at status-post Thrombolysis with Streptokinase

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ABSTRACT

Background: Adequate reperfusion by thrombolysis (TL) with streptokinase (STK) after an ST elevation myocardial infarction (STEMI) is associated with better patient outcome. This study described the attributes of patients who at status-post TL underwent gated SPECT myocardial perfusion imaging (GSMPI).

Patients and methods: This cross sectional retrospective study was conducted in 2017 on a group of patients who were referred to Nuclear Cardiology Division of National Institute of Nuclear Medicine and Allied Sciences (NINMAS) from February 2005 to October 2016 for GSMPI. Archive was reviewed to include those who received STK with diagnoses of an acute MI, then underwent coronary angiogram (CAG) and then underwent GSMPI. Findings from status-post TL CAG reports were compared with that from GSMPI.

Results: Among 1347 patients, 59 (4.4%) were eligible for analysis with mean age of 51.2 ± 9.5 years. GSMPI revealed normal perfusion in 16 (27%), abnormal perfusion in 43 patients with mean LV infarct size at rest of $48.6 \pm 17.2\%$ and ischemia in 13 patients with mean ischemic LV of $12.1 \pm 9.6\%$. Mean LVEF in normally perfused LV and in those with perfusion defects were $50.0 \pm 18.7\%$ and $39.5 \pm 14.9\%$ respectively ($p = 0.04$). CAG was normal in one among 43 patients with abnormal myocardial perfusion. CAG was abnormal in 75% (12 of 16) of patients with normal perfusion. Six (10% of 59) among that 12 with abnormal CAG and normal perfusion had further coronary revascularization (CR).

Conclusions: In this series, 27% (16/59) patients who had received STK had normal perfusion and at least in 10% (6/59) the normal perfusion despite an abnormal CAG and without further CR may indicate adequacy of TL using STK.

Key words: Myocardial perfusion imaging, SPECT, Thrombolysis, Streptokinase, Myocardial Infarction.

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INTRODUCTION

ST segment elevation myocardial infarction (STEMI) is commonly associated with an acute and complete

obstruction of epicardial arteries by fibrin-rich thrombi(1). Therapeutic coronary thrombolysis (TL) with streptokinase (STK) is indicated in patients with STEMI within 12 hours of the onset of symptoms (2). Administration of STK can achieve reperfusion by lysis of infarct artery thrombi through its capability of converting circulating and clot-bound plasminogen to plasmin resulting in systemic fibrinogenolysis (3). Adequate reperfusion by TL using STK after an STEMI is reportedly associated with reduction of infarct size and improvement of left ventricular (LV) ejection fraction (EF) leading to improved survival (4) as well as a relative reduction in mortality by 18% (5).

GSMPI derived quantifications of myocardial salvage and cardiac positron emission tomography (cardiac PET) derived quantifications of myocardial viability are validated tool for assessment of adequacy of TL that can further aid selection of therapeutic strategy in patients at status-post TL (6–8) and at status post coronary revascularization (CR) (9). Outcome and adequacy of reperfusion by TL with STK in cases of STEMI has been reported from Bangladesh using CAG derived TIMI flow(10) and ECG derived ST segment resolution (11). This study was conducted with a primary objective to describe the attributes of eligible patients which in turn appraised the retrospectively played role of one-time point GSMPI in patients at status-post TL with STK and raised insight to context relevant geo-temporal scopes of nuclear imaging.

PATIENTS AND METHODS

Study population

This cross sectional retrospective study was conducted in 2017. Study population was a group of patients who

were referred to Nuclear Cardiology Division of NINMAS from February 2005 to October 2016 for GSMPI. Clinical record and image interpretation of all patients from the divisional archive were reviewed and those who received TL using STK with diagnosis of an acute STEMI, then underwent CAG and subsequently GSMPI were included in the study.

Data analyses

All relevant demographic and clinical data were entered in to analyses. Myocardial perfusion, categorized as normal perfusion or abnormal were cross-tabulated with the angiogram findings categorized also as normal or abnormal; to check proportion of normal myocardial perfusion despite a previous abnormal CAG which would indicate adequate restoration of perfusion at status-post TL. Categorical data were presented as frequencies and percentages. Continuous data were presented as means and standard deviations (SD) and value ranges. Means were compared using independent sample t-test; SPSS v.25 was used.

RESULTS

Patient characteristics

Although 1347 patients underwent GSMPI within the mentioned time span of 608 weeks, 59 patients (56 males and three female) were eligible for analysis. Thus, 4.4% of the patients who were referred to NINMAS for GSMPI were at status-post TL with STK due to acute STEMI with a CAG done after the TL and before the GSMPI. Mean age were 51.2 ± 9.5 years (34-72 years). Mean time difference from TL to CAG was 12.4 ± 17.9 weeks, from CAG to GSMPI was 10.3 ± 11.9 weeks and from TL to GSMPI was 20.8 ± 16.4 weeks (table-1).

While 36 patients underwent pharmacological stress, 15 underwent treadmill exercise and rest only imaging was performed on eight. GSMPI revealed normal perfusion in 16 (27%) and abnormal perfusion in 43 patients who had mean total LV infarct size of $48.6 \pm 17.2\%$ at rest. The LAD territory in addition to being the most frequently affected one by fixed perfusion defect had been observed to have larger mean infarct proportion in comparison to any other territory. Combined stress and

rest perfusion scans could reveal reversible perfusion defects in 13 patients with mean total ischemic LV proportion of $12.1 \pm 9.6\%$. The RCA territory was the most frequently affected one by reversible perfusion defect as well as had the larger mean ischemic myocardial proportion in comparison to the other two territories.

Independent sample t-test was done to check distribution of quantitative variables between the categories of CAG as well as that of GSMPI; both categorized as normal and abnormal. Among the categories of CAG, the means of no variable were found to be significantly different ($p > 0.05$). On the contrary, among the categories of GSMPI, there was significant difference of mean exercise time during exercise-treadmill test, LV diameters and LVEF on echocardiography as well as LV volumes and LVEF on GSMPI both at stress and rest ($p < 0.05$), as shown in Table-2.

Comparison of CAG results with that of GSMPI

The CAG results were reported as normal in 11 patients, single vessel disease in 20 patients, double vessels disease in 12 patients and triple vessels disease in 16 patients. Among the normal labeled CAG, non-critical lesions were however present in six patients while the other five among the 59 (8.5%) had entirely normal epicardial coronary arteries. One out of this five patients with normal CAG had an abnormal myocardial perfusion which was likely due to microvascular dysfunction. Among the 16 patients (27% of 59) who had normal myocardial perfusion, 12 (75% of 16) had an abnormal CAG, a mismatch that indicated therapeutic adequacy of STK for TL during AMI. This data is presented in Table-3.

However, six among the 12 (50% of 12 and 10% of 59) with normal perfusion despite an abnormal CAG had undergone further CR with percutaneous transluminal angioplasty in addition to TL and before the GSMPI. Thus, it can be permitted to assume that in this series, TL was adequate in at least rest of the six (50% of 12 and 10% of 59) patients considering that they had abnormal CAG and had not undergone any further CR other than TL.

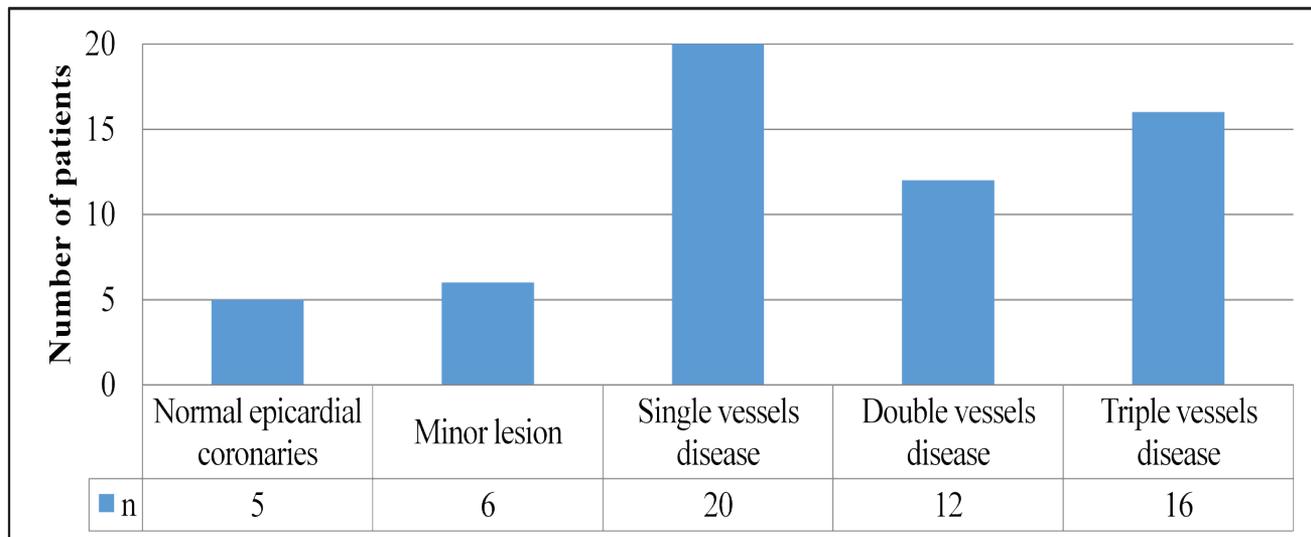


Figure 1: Distribution of coronary angiogram results among the study patients

Table 1: Demographic and clinical characteristics

Trait	Mean ± SD	Range
Age (year)	51.2 ± 9.5	34-72
Interval (weeks)		
TL to CAG	12.4±17.9	0-56
CAG to GSMPI	10.3 ± 11.9	2-55
TL to GSMPI	20.8 ± 16.4	1-59
Mean total LV infarct size (n=43)	48.6 ± 17.2%	8-72
Mean total LV ischemia (n = 13)	12.1± 9.6%	2-32
Fixed perfusion defect size		
% of LAD territory (n=38)	68.3 ± 23.1	3-100
% of LCX territory (n=22)	35.1±15.6	6-64
% of RCA territory (n=25)	32.9±22.5	6-96
Reversible perfusion defect size		
% of LAD territory (n=7)	7.3 ± 8.6	4-22
% of LCX territory (n=8)	12.5 ±13.6	4-43
% of RCA territory (n=12)	31.9 ± 21.9	6-88

Table 2: Results from independent sample T-test of significantly different quantitative variables among GSMPI categories

Traits (unit)	GS MPI perfusion categories		
	Normal	Abnormal	
Exercise time on ETT (min)	9.7±0.7	7.1±2.5	0.02
Echo LVEF (%)	47.8±15.2	40.5±8.9	0.002
Echo EDD (mm)	51.6±15.9	55.1±7.3	0.008
Echo ESD (mm)	44.2±14.3	43.0±8.2	0.02
GS MPI LVEF (%) at stress	59.0±18.0	41.8±15.6	0.008
GS MPI EDV (ml) at stress	76.8±23.4	164.2±64.3	0.005
GS MPI ESV (ml) at stress	28.8±14.5	101.7±60.1	0.01
GS MPI LVEF (%) at rest	50.0±18.7	39.5±14.9	0.04
GS MPI EDV (ml) at rest	90.5±32.7	156.6±50.3	0.001
GS MPI ESV (ml) at rest	41.3±24.2	99.1±50.7	0.003

ETT Exercise treadmill test, Echo Echocardiogram, LVEF Left ventricular ejection fraction, EDD End diastolic diameter, ESD End systolic diameter, EDV End diastolic volume, ESV End systolic volume, GSMPI Gated SPECT MPI

Table 3: Cross tabulation of CAG results against GSMPI findings in study patients

		CAG		
		Normal	Abnormal	Total
SPECT perfusion	Normal	4 (CR 0)	12 (CR 6)	16
	Abnormal	1 (CR 0)	42 (CR 11)	43
	Total	5	54	59

Table 4: Key findings from reported studies with single-time point myocardial perfusion imaging after thrombolysis

Author	Year	Country	n	Time of SPECT since thrombolysis	Results
Jain et al	1990	USA	46	4.7-5.5 days	Pharmacological stress SPECT identifies more patients with ischemia than symptom limited exercise treadmill test
Grip et al	1993	Sweden	57	4 hours	Smaller perfusion defect size in late thrombolysis (≥ 12 hours) with anti-coagulant maintenance in comparison to no treatment.
Sezer et al	2009	Turkey		6 months	Significant reduction of infarct size in streptokinase + PCI in comparison to PCI alone

Table 5: Key findings from reported studies with two-time point myocardial perfusion imaging after thrombolysis

Author	Year	Country	n	Time point since tracer injection from onset of symptoms/thrombolysis		Change in perfusion defect size
				SPECT 1 (within)	SPECT 2 (at/after)	
Bassand et al	1990	France	231	4 hours	Day 21	Reduction of 33% for anterior wall and 16% for the inferior wall with a concomitant rise of LVEF of ~6%
Bostrom et al	1992	Sweden	16	4 hours	Day 2-4	Reduction >10%, if thrombolysis < 3 hours while < 10% if thrombolysed after > 3 hours
Bouvier et al	1998	Sweden	71	3-5 days	6 months	While 32% patients had unchanged or increased perfusion defect size on late scan, the remainder had up to 20% reduction.
Keng et al	2000	Singapore	18	4 hours	Day 5-7	Reduction of 12% with indifference of result compared to angioplasty

DISCUSSION

Streptokinase and ST segment elevation MI

This study is the first one to describe GSMPI attributes of patients at status-post TL using STK due to STEMI from Bangladesh. STK, one of the first thrombolytic agents was discovered in 1933, used for therapeutic thrombolysis in acute MI in 1958, used in intracoronary infusion in 1979 (12) and was validated by GISSI trial as a thrombolytic treatment modality for AMI in 1986 (5). TL using STK is indicated in STEMI but not in NSTEMI due to difference in composition of the pathogenic thrombus and the extent of coronary artery occlusion by it (1,13).

Utility of MPI at status-post thrombolysis

This study compares myocardial perfusion from one-time point GSMPI in a small group of patients at status-post TL with the corresponding CAG to assume myocardial salvage. Though the historical evidences of myocardial salvage by streptokinase were stated using

planar imaging (14), GSMPI has validated capability of assessing area at risk and final infarct size(8). Studies reported with one-time point MPI revealed higher sensitivity of post TL pharmacological stress MPI over exercise treadmill test (15), found association of smaller infarct size with late TL in comparison to non-intervention in a delayed presentation (16), with TL in addition to primary PCI over PCI alone (17) and with targeted intracoronary TL over thrombus aspiration (18). Other groups of investigator have used two-point MPI to identify the myocardium at risk on early scan, then to check the final infarct size as a long term outcome on a delayed scan and finally to estimate the TL mediated myocardial salvage as the difference of sizes between perfusion deficit on those two consecutive scans (19).

A report of two-time point post TL MPI has observed small reinfarct size in anterior wall in comparison to inferior wall (20). On the contrary, this series of single-time point MPI observed larger sizes of infarct in

anterior walls while the inferior walls tended to have larger proportions ischemia. Other reports of two-time point post TL MPI have observed correlation of larger salvage with early thrombolysis (21), reduction of infarct size upto 20% in 68% of the study subjects (22) and a comparable outcome with that of angioplasty (23).

In the current series, GSMPI could find LV ischemia in 13 (22%) patients at status-post TL which should have guided their further clinical management. In our previous series 34.5% patients had ischemia in revascularized LV territory at status-post CR (9).

No-reflow phenomenon

In the entire series, one patient with normal epicardial coronaries had an abnormal myocardial perfusion, a mismatch, which was presumed to be a case of microvascular dysfunction. The 'no-reflow phenomenon' of STEMI or non-resumption of myocardial reperfusion despite recanalization of an occluded infarct related artery has been blamed as Achilles hill of CR using thrombolysis (TL) or primary percutaneous transluminal coronary angioplasty which results mostly from microvascular dysfunction or distal micro-thromboembolization (24), resulting in failure of thrombolysis reported as high as 56.8% with higher incidences of post procedure recurrent acute coronary syndrome and death after one year (25). The angiographic methods for quantification of this phenomenon include myocardial blush grade, Thrombolysis In Myocardial Infarction (TIMI) myocardial perfusion grade and the corrected TIMI frame count (26). Echocardiographic indices include regional contrast score index from myocardial contrast echocardiogram and EAS index from pulsed wave tissue Doppler imaging (27). Post thrombolysis myocardial perfusion SPECT was able to detect perfusion abnormalities in patients despite TIMI grade 3 flow (18). Dual tracer SPECT using perfusion/metabolism mismatch ratio was found to be useful for evaluating no-reflow phenomenon despite TIMI grade 3 after reperfusion therapy (28).

Limitation of the study

The study being retrospective and consisting of one-time point imaging data, was unable to report quantifications

of myocardial salvage by comparing serial imaging. Partial availability of quantitative cardiac enzyme during acute MI precluded indirect estimation of initial myocardial damage and therefore the other possible comparison of myocardial salvage. Scans included in this study were done within a variable interval from one to 59 weeks of the incident TL during an acute MI which in addition to being inhomogeneous are also incongruent with the maximum reported interval in the literature (Table-4 and Table-5). The current series did not assess effects of risk factors, CR and pharmacotherapy on perfusion defect size. Also, the assessments of myocardial salvage by SPECT derived LV quantitative parameters and accounts of further clinical management after detection of myocardial ischemia by GSMPI at status-post TL were beyond the scope of this study.

Recommendations

The unaddressed issues by this study justifies further exploration through a suitably-designed prospective study with utilization of GSMPI derived quantitative parameters and follow up data in patients at status-post TL from Bangladesh. The assessment of myocardium at risk using two-time point SPECT consistently requires round the clock availability of tracer and gamma camera which is an yet to be achieved reality in majority of the clinical settings (19). Thus, the estimates of perfusion-metabolism mismatch derived from combined GSMPI and cardiac FDG-PET can provide assessments of no-reflow phenomenon and myocardial salvage.

CONCLUSION

In this series of status-post TL patients, 27% had normal perfusion while TL was adequate in at least 10% of patients considering that they had an abnormal CAG and had not undergone any CR other than TL. LV ischemia was discovered in 22% patients. Further prospective study with inclusion of SPECT and cardiac PET parameters appears to be clinically meaningful.

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