

ORIGINAL ARTICLE

Assessment of the Patient with Low-Risk Non-ST Segment Elevated Myocardial Infarction Undergoing Invasive Coronary Angiogram Based on Up-Front Non-Invasive Imaging

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Abstract:

Background: Routine ICA to detect significant CAD is risky, costly, and likely unnecessary in cases of type-2 MI or non-ischemic injury. This study evaluates noninvasive imaging as a safer, cost-effective alternative to guide ICA decisions.

Methods: This descriptive cross-sectional study was conducted at the echo and Cath laboratory as well as CT imaging laboratory of BSMMU. Two groups were created from the noninvasive imaging procedures. Anatomic imaging: CT angiography, Physiologic imaging which is subdivided SPECT-MPI and DSE. Sensitivity, specificity and predictive values of these anatomic and physiologic imaging was calculated. When initial CTA or MPI or DSE suggested myocardial ischemia/infarction/obstructive CAD, follow-up ICA was recommended and calculated.

Results: We have consecutively included 94 patients. In this study revealed that up-front CT detecting obstructive CAD of patient undergoing ICA sensitivity of 94%, specificity of 87%, PPV 89% and NPV 91%. Up-front SPECT MPI had a 92% sensitivity, 75% specificity, and 83% accuracy rate in identifying coronary artery disease in patients going through ICA. Up-front DSE detecting CAD of patient navigating ICA sensitivity of 84%, specificity of 81% and accuracy of 83%.

Conclusion: In order to accurately diagnosis and management of CAD along with reducing unnecessary invasive procedure, this study found that patients with low-risk ACS had undergone a non-invasive imaging approach before navigate through coronary angiogram.

Key words: Low-risk ST elevated myocardial infarction, Coronary CT angiogram (CTA), Single photon emission tomography myocardial perfusion imaging (SPECT MPI), dobutamine stress echocardiography (DSE), Invasive coronary angiogram (ICA), Coronary artery disease (CAD)

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Key messages: To assess the invasive strategy in patient with low risk non-STEMI based on up-front non-invasive imaging.

To compare the up-front anatomic imaging (CT angiogram) with physiologic imaging (DSE or MPI) in patient with low risk non ST-elevated myocardial infarction navigating ICA.

Introduction:

Coronary computed tomography (CTA) has evolved as a logistically simple, accurate and low-risk noninvasive test to diagnose or rule-out coronary artery disease (CAD).¹⁵ Myocardial perfusion imaging (MPI) has been shown to be useful for risk assessment for a patient experiencing retro-sternal pain that could indicate acute coronary

syndrome (ACS) and may enhance assessment of ischemia, while a normal study is associated with excellent end results.¹⁷ In patients without STEMI diagnosis is more challenging. Most patients in the emergency department (55-60%) have no alarming ECG abnormalities and no history of CAD.¹⁰ Typically such patients are addressed & are further risk stratified usually by TIMI score⁴ and with those intermediate to low risk going through a period of observation with serial enzymes with or without some form of stress testing, stress echocardiography or resting nuclear heart scan.³ A recent meta-analysis of CTA in elective patients showed a pool sensitivity of 90%, specificity of 97%, a NPV of 99% and a PPV of 76% for the identification of notable stenosis in contrast to ICA.¹⁶ CTA has the unique ability to non-invasively detect both significant artery stenosis and coronary atherosclerotic plaque.¹⁴ The use of rest MPI with either 99m TC-sestamibi or 99m TC-tetrofosmin in patient experiencing severe retrosternal pain for detecting ACS has been well validated.¹³ A meta-analysis has demonstrated that stress echocardiography with exercise and dobutamine has a sensitivity of 83% & 81%, respectively and a specificity of 84% & 84% respectively.¹² CTA can be performed safely in patient with non-STEMI without major side effects or harm from delaying ICA and the diagnostic performance of CTA to rule in or rule out in notable coronary artery disease (>50% coronary artery stenosis) in patients with non-STEMI was a NPV of 90.9%, sensitivity of 96.5%, PPV of 87.9% & a specificity of 72.4%.²¹

About 25% of patients with a clinical diagnosis of non-ST elevated myocardial infarction have obstruction in one major coronary artery, 30% in two coronary arteries, 20% in all three coronary arteries and 10% in left main coronary artery obstruction.⁵ According to Amsterdam EA et al. (2010), patients with chest pain who are “at low risk” for acute coronary syndrome (ACS) are those who: (1) are hemodynamically stable; (2) do not exhibit any alarming features during history or examination; and (3) do not exhibit immediate objective evidence of myocardial ischemia on initial electrocardiograms and cardiac biomarker

CAD is one of the most important causes of mortality and morbidity in the world. The gold standard for diagnosing CAD is ICA. The presence of an eye estimation of luminal narrowing is frequently the basis for the choice to revascularize region of the myocardium. Due to risk and invasiveness of coronary angiogram make a trustworthy non-invasive imaging approach that can more accurately

determine which vessel needs treatment. About half of the angiogram that show obstructive CAD are followed by an interventional procedure, whereas between 40% and 50% of coronary angiogram conducted annually in the US do not show occlusive coronary arteries. Therefore, a trustworthy non-invasive approach may be quite desirable in order to save health care costs and reduce needless intrusive testing. A non-invasive and safe substitute for cardiac catheterization is CTA.²²

MPI identifies and quantifies the degree of jeopardized myocardium during stress tests. MPI provides information on the extent and location of myocardial ischemia. A summed stress score (SSS) ≤ 3 is accepted as a normal result, while a score of 4-8 as a mild defect, 9-12 as a moderate defect and >12 as a severe defect. A summed rest score (SRS) <4 is normal, while a score of 4-8 as mild defect, a score of 9-13 as a moderate & a score of >13 as severe defect. A Summed difference score (SDS) can be calculated by subtracting the SRS from the SSS (SDS = SSS-SRS). A SDS of 1-3 represented mild ischemia, 4-7 moderate ischemia and >7 severe ischemia (Alexanderson E et al. 2016). Moderate to severe ischemia is defined as $\geq 10\%$ LV ischemia which seemed to be better outcome with revascularization than medical therapy.¹¹

DSE is a novel non-invasive imaging technique that assess cardiac function under stress brought on by dobutamine infusion with two-dimensional echocardiography. This test evaluate patients with history of CAD, whether confirmed or suspected. A 17-segment model is used to analyze segmental wall motion abnormality, and if more than two myocardial segments exhibit a new regional wall motion abnormality deemed suggestive of inducible myocardial ischaemia (Scherman L et al. 2022).

Methods

Study design and Sampling Methodology: In the department of Cardiology at Bangabandhu Sheikh Mujib Medical University (BSMMU), this descriptive cross-sectional study was carried out from January 2023 to April 2024.

This study included patients aged a minimum of 18 years clinically diagnosed with low risk non STEMI. Sample size, calculated using the formula $Z^2P(1-p)/e^2$, based on a 4.5% prevalence of ischemic heart disease in Bangladesh (Banerjee et al. 2017). With a 95% confidence interval ($Z=1.96$) and a 5% margin of error.

The calculated sample size was 66, and with a 30% non-response rate, the final target was 94 patients.

Data Collection Procedure

Patients who fulfilled the eligibility criteria were included. Patients aged a minimum of 18 years with clinically diagnosed low risk non STEMI were visited or hospitalized at the BSMMU in the department of cardiology after giving their informed consent were selected. Those with severe ischemia requiring immediate strategy (ongoing chest pain, dynamic ST-T changes) were excluded. A structured data sheet was used and a thorough clinical examination and entire history were documented. This study was carried out in echocardiography and cardiac catheterization laboratory in the department of cardiology and CT imaging laboratory in the department of radiology and imaging department at BSMMU.

Data collection & processing was organized with the involved personnel- including echo, cath lab and CT imaging technician.

Patients were divided into two groups for non-invasive imaging a) CT angiogram b) DSE or MPI. ICA was done when non-invasive imaging suggested myocardial ischemia/infarction/obstructive coronary artery disease.

Coronary CT angiogram: Image acquisition was performed a 64-detector CT scanner using a ECG-gated protocol. Tube voltage based on body mass index (BMI). Patients were pretreated with oral metoprolol and sublingual nitroglycerine was administered prior to contrast injection. Intravenous contrast media (Visipaque, GE Healthcare, London, UK) infused with biphasic injection protocol followed by a saline chaser. For each patient, CT image quality (diagnostic/non-diagnostic CT scans), presence and severity of CAD ($>50\%$ and $>70\%$ diameter stenosis) was evaluated.

Myocardial perfusion imaging (MPI): Pharmacological stress was done with dobutamine following standard Mayo clinic protocol. At peak heart rate, 99m technetium-sestamibi (99Tc-MIBI) was infused intravenously, and the infusion was maintained for an additional minute. Scanning was started after 60-90 minutes of rest. Post-stress SPECT acquisition with gating was done. Rest study using the same acquisition method was done later on next day. A 17-segment model that was allocated into the regions of the left anterior descending coronary artery (LAD), left circumflex coronary artery (LCX), and right coronary artery (RCA) was used to analysis. These were classified as either ischemia or normal.

Segments of rest/stress MPI scans were assessed, and the percentage of ischemic myocardium was used to calculate the summed stress score (SSS), summed rest score (SRS),

and summed difference score (SDS). Segmental scores were assembled for each patient & vascular territory.

The summed stress score (SSS), which represents the magnitude and severity of the myocardial abnormality, including ischemia and infarction, is the sum of the total scores at stress.

Both the Summed Difference Score ($SDS > 4$) and the Summed Stress Score ($SSS > 8$) were assessed.

DSE: Baseline two dimensional transthoracic echocardiogram was used to collect image data prior to the procedure. Machine setting (Depth and gain) were optimized as required, and a DSE was performed with continuous ECG and oximetry monitoring and dobutamine administered intravenously via a cannula into an antecubital vein. Sphygmomanometric blood pressure recordings were made during each stage of the protocol. The DSE protocol comprised four stages, i.e. 'baseline', 'low dose' ($10 \mu\text{g/kg/min}$), 'peak dose' ($40 \mu\text{g/kg/min}$), and 'recovery' (typically 3 minutes after the cessation of the dobutamine infusion). Each stage consisted of acquisition of parasternal long- and short-axis views, as well as apical 4 chamber & 2 chamber views. A new regional wall motion abnormality in at least two contiguous left ventricular segments was one of the diagnostic endpoints. Segmental wall motion was analysed according to a 17-segment model, and was considered indicative of inducible ischaemia if >2 myocardial segments demonstrated a new regional wall motion abnormality (Scherman L et al. 2022). The development of new or worsening wall motion abnormality including declining wall motion after improvement at low-dose dobutamine was reflected myocardial ischemia.⁶

Statistical analysis:

All data was being processed by using SPSS program version 26. Data was expressed in frequencies and percentage for qualitative values and mean $\pm$ SD for quantitative values. Between groups association analysis was done by chi-square test for nonparametric variables and unpaired t-test for numerical values was used to compare between different types of non-invasive imaging. Validity test (sensitivity, specificity, PPV and NPV) were done by using 2X 2 table method as shown below.

P values ≤ 0.05 will be considered as statistically significant.

Results:

Ninety-four patients with low-risk acute coronary syndrome were assessed at BSMMU and subsequently navigated coronary angiography with up-front non-invasive imaging. The following tables and graphs display the results.

Table-I

Performance of patients with ACS with up-front CTA undergoing ICA (n=34)

ICA	CTA		Total test	Chi-square
	Positive	Negative		
ICA >50%	17 (TP)	2 (FP)	19	<0.0001
ICA <50%	1 (FN)	14 (TN)	15	
Total	18	16	34	
Diagnostic validity test				
Diagnostic metric		Values	95%CI	
Sensitivity		94.44%	72.76% to 99.89%	
Specificity		87.50%	61.62% to 98.44%	
Positive Predictive Value		89.47%	69.82% to 96.89%	
Negative Predictive Value		93.33%	67.37% to 98.95%	
Accuracy		91.18%	76.32% to 98.14%	

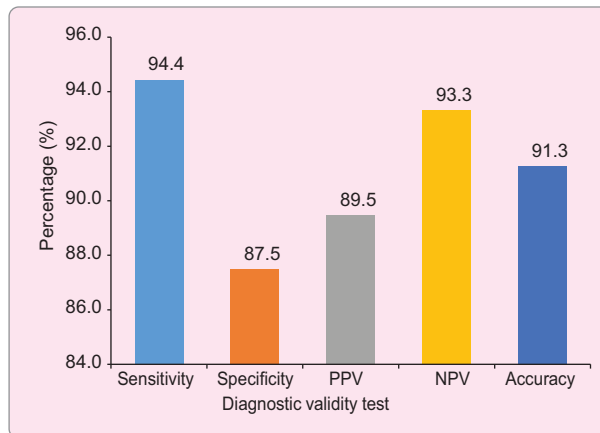


Figure-1: Bar diagram showing the sensitivity, specificity, positive and negative predictive values of patient with ACS with up-front CTA undergoing ICA

Table-II

Performance of patients with ACS with up-front SPECT-MPI undergoing ICA (n=30)

ICA	MPI		Total	Chi-square
	SSS >8 and SDS>4	SSS <8 and SDS<4		
ICA >50%	13(TP)	4(FP)	test 17	0.001
ICA <50%	1(FN)	12 (TN)	13	
Total	14	16	30	
Diagnostic validity test				
Diagnostic metric		Values	95%CI	
Sensitivity		92.87%	66.13% to 99.81%	
Specificity		75.00%	47.62% to 92.73%	
Positive Predictive Value		76.47%	57.87% to 88.49%	
Negative Predictive Value		92.30%	63.99% to 98.78%	
Accuracy		83.33%	65.27% to 94.35%	

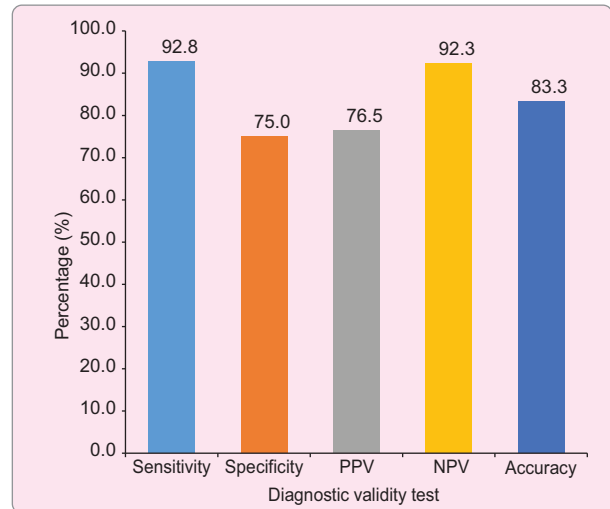


Figure-2: Bar diagram showing the sensitivity, specificity, positive and negative predictive values of patient with ACS with up-front SPECT MPI undergoing ICA

Table-III

Performance of patients with ACS with up-front DSE undergoing ICA (n=30)

ICA	DSE- Inducible ischemia		Total	Chi-square test
	DSE>2 segments	DSE <2 segments		
ICA >50%	16(TP)	2(FP)	18	0.001
ICA <50%	3(FN)	9 (TN)	12	
Total	19	11	30	
Diagnostic validity test				
Diagnostic metric		Values	95%CI	
Sensitivity		84.211%	60.422% to 96.617%	
Specificity		81.818%	48.224% to 97.717%	
Positive Predictive Value		88.889%	69.228% to 96.604%	
Negative Predictive Value		75.000%	50.586% to 89.787%	
Accuracy		83.333%	65.279% to 94.358%	

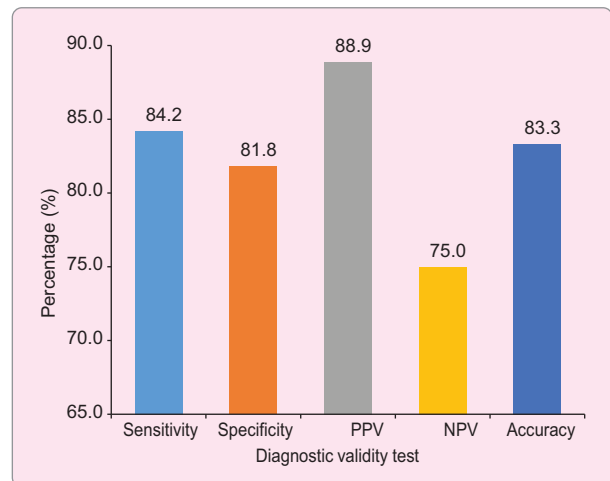


Figure-3: Bar diagram showing the sensitivity, specificity, positive and negative predictive values of patient with ACS with up-front DSE undergoing ICA in detecting obstructed CAD

Discussion

This observational study was conducted from June 2023 from April 2024, in the department of cardiology & CT imaging lab at BSMMU.

Patients with acute coronary syndrome without history of high-risk patients (which mandates immediate or early invasive strategy) should be included for this study.

For non-invasive imaging, patients were divided into two groups: a) Anatomic imaging, which includes computerized tomography coronary angiography (CTA); and b) Physiologic imaging, which includes dobutamine stress echocardiography (DSE) and single photon emission tomography myocardial perfusion imaging (SPECT-MPI).

New diagnostic techniques that enable non-invasive visualization of coronary arteries have been developed as a result of the expense and danger of ICA. The sensitivity and specificity of multi-detector CT (MDCT) are 92% and 93%, respectively, with positive and negative predictive values of 79% and 97%.¹⁹

Up-front CT detection of obstructive CAD in patients having ICA had a sensitivity of 94%, specificity of 87%, positive predictive value of 89%, and negative predictive value of 91%, according to this study (Table I). There was statistical significant ($p < 0.001$).

The overall sensitivity, specificity, and accuracy of dobutamine stress MPI were 85%, 72% and 83% respectively.⁷

In this study (Table II) revealed that up-front SPECT MPI detecting coronary artery disease of patient undergoing ICA sensitivity of 92%, specificity of 75% and accuracy of 83%. This was statistically significant ($p = 0.001$).

For detection of coronary artery disease, dobutamine stress echocardiography (DSE) and technetium 99-m (Tc-99m) sestamibi single photon emission tomography had comparable sensitivity (87% and 80%, respectively), but DSE was more specific (91% vs. 73%) (Smart SC et al. 2000).

In this study (Table III) revealed that up-front DSE detecting coronary artery disease of patient undergoing ICA sensitivity of 84%, specificity of 81% and accuracy of 83%. This was statistically significant ($p = 0.001$).

DSE and MPI were both valuable non-invasive imaging techniques for assessing ischemic myocardium but MPI was generally considered more sensitive, while DSE was

more specific for detection of coronary artery disease. Objective images of blood flow was best provided by MPI which can be more easily interpreted than DSE but radiation exposure was a concern for MPI.

If the primary goal is to detect ischemic myocardium due to underlying coronary artery disease with higher sensitivity, MPI is generally preferred but if radiation exposure is a concern particularly in young patient, DSE is a safer option. While, CT angiogram due to its higher negative predictive value making a valuable non-invasive imaging techniques for exclude coronary artery disease.

This study has limitations. This was a non-randomized study with small sample size.

Not all samples could be included in the study due to lack of funding. DSE has limitations including operator dependence, subjective interpretation and detection of ischemia in extensive resting wall motion abnormalities. For both CTA and MPI, radiation exposure were a concern. ICA was evaluated by visual estimation

Conclusion:

Ischemic heart diseases remain the leading cause of death globally. This study revealed that patient with low risk ACS has undergone a non-invasive imaging approach prior to invasive procedure with an emphasis to improve diagnosis of coronary artery disease and delineate appropriate treatment of the culprit vessel. These methods has accurately select the patients for coronary angiogram, reducing unnecessary intervention and minimizing radiation exposure.

Author Contributions:

- Conception or design of the work; the acquisition, analysis, or interpretation of data for the work: MH, AKS, MFI, SM
- Drafting the work or reviewing it critically for important intellectual content: MH, AKS, MFI, SM, CMA
- Final approval of the version to be published: MH, CKS, MFI, SM
- Responsible for every facet of the task, making certain that inquiries concerning the integrity or correctness of any portion of the work are suitably looked into and addressed: SM, CMA, MFI, and MH

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Ethical approval

This descriptive cross-sectional study was carried out at the University Cardiac Center, Bangabandhu Sheikh Mujib Medical University with the approval of IRB at Dhaka

Data availability statement

We confirm that the data supporting the findings of this study will be shared upon reasonable request.

List of acronyms

ACS: Acute coronary Syndrome

BSMMU: Bangabandhu Sheikh Mujib Medical University

CTA: Computerized tomography coronary angiogram

CAG: Coronary Angiogram

CAD: Coronary Artery Disease

DSE: Dobutamine Stress Echocardiography

Non-STEMI: Non ST-segment Elevated Myocardial Infarction

NPV: Negative Predictive Value

PPV: Positive Predictive Value

SPECT MPI: Myocardial Perfusion Imaging using Single Photon Emission Computerized Tomography

SPSS: Social Science Statistical Package

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