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Six-month Outcome after Early Invasive Versus Delayed Ischaemia Driven Percutaneous Coronary Intervention in Non-ST Elevated Myocardial Infarction

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Abstract

Background: Optimal timing of PCI and comparative outcome between early invasive strategy and ischaemia guided delayed invasive strategy is still in debate in reducing long-term cardiovascular complications in NSTEMI. Objective: The aim of the study was to assess the impact of an early invasive strategy or ischaemia guided delayed invasive strategy on six months clinical outcomes in NSTEMI patients undergoing PCI, from a Bangladesh health service perspective. Materials and Method: It was an observational cross-sectional comparative study conducted in cardiology department of BSMMU from November 2019 to February 2021. Study procedure: This study enrolled 389 adult patients of NSTEMI who underwent PCI which met inclusion and exclusion criteria. Study subjects were divided into two groups: early and delayed groups. This study considered an early invasive strategy as - revascularization within 72h for patients presented with NSTEMI with high-risk features defined by a GRACE score > 140 and for those at lower risk with GRACE score <140; delayed ischaemia driven strategy as - revascularization after 72h, reserved for refractory, recurrent or severe exercise-induced ischaemia. Coronary angiogram (CAG) and PCI were performed by respective consultant according to current practice guidelines. After index PCI, patients were followed up at 06 months for MACEs (Myocardial re-infarction, target vessel revascularization, stroke, hospitalization due to ischaemic causes and cardiac death) and findings of 2 groups were compared.

Results: At 6 months after index PCI, patients in the early group despite having worse initial presentation and higher GRACE score had better outcome in comparison with the delayed group who had a statistically significant higher incidence of cardiac death, MI, and target vessel revascularization (p=0.002, p=0.004 and p=0.031). However, incidence of stroke, major bleeding and hospitalization due to ischemia were not significantly different between the groups (p>0.05). Conclusion: Adoption of an early invasive strategy in NSTEMI patients undergoing PCI may be beneficial in reducing the risk of MACEs and associated with improved clinical outcome after PCI at 6 months follow-up.

Keywords: Non-ST elevated myocardial infarction (NSTEMI), Percutaneous coronary intervention (PCI), Major adverse cardiovascular events (MACEs).

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Introduction

Several randomized trials and meta-analyses have shown a benefit of an early invasive strategy followed by revascularization over a conservative or selective invasive approach with respect to death and myocardial infarction (MI) in non-ST-elevation acute coronary syndromes (NSTE-ACS).[1-3] Although numerous trials have investigated the outcome of an early versus a delayed invasive treatment strategy in patients with non-ST elevation acute coronary syndrome (NSTE-ACS), controversy remains about the optimal timing of angiography and revascularization in this patient group. Coronary artery disease (CAD) is an increasingly important medical and public health concern, and is the leading cause of mortality in Bangladesh. Like other South Asians, Bangladeshis are unduly prone to develop CAD, which is often follows a rapidly progressive course and angiographically more severe disease.[4] Early intervention has the potential to prevent ischemic events during the waiting time from event to revascularization.[5] Conversely, a delayed intervention may avoid procedure- related complications by allowing plaque to stabilize during the

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waiting period, as the patient undergoes medical therapy.[6,7] The benefit of early revascularization reported by clinical trials is largely driven by lower incidence of refractory ischemia[8] or new MI,[5,9] rather than survival. Although a routine invasive policy is currently recommended by guidelines,[10,11] the optimal timing of such intervention is not well established.

Current updated Guidelines on myocardial revascularization of Non-ST elevated myocardial infarction (NSTEMI) recommend, the use of an early invasive strategy within 12–24 h for patients with high-risk features defined by a GRACE score >140 and invasive strategy or ischemia-guided strategy within 72 h for those at lower risk with GRACE score <140.[12,13] An ischemia-guided approach is recommended for patients with a low-risk score (TIMI 0 or 1, GRACE <140), other patients will benefit from an invasive strategy.

New angioplasty techniques, such as drug- eluting stents, most likely have a critical role in improving the results of PCI in NSTEMI patients. The use of stents has improved the short and long term outcomes of PCI in NSTEMI patients in terms of Major Adverse Cardiovascular Events (MACEs) include cardiac death, myocardial re- infarction, stroke, stent thrombosis, target vessel revascularization for ischemia. With these uncertainties, we designed the study to determine the optimal timing of PCI in patients with non-ST-elevation MI (NSTEMI). Therefore, this study was designed to observe the difference in outcome between early invasive and delayed ischaemia driven successful PCI with drug-eluting stenting in NSTE- ACS patients in relation to major adverse cardiovascular events (MACEs) during 6 months follow up.

Methods

Study design and Patients

This observational cross-sectional study was conducted at the Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, Dhaka. The center has consistently been ranked as the one of the top hospitals in Bangladesh. Total duration was from November, 2019 to February, 2021. We studied 389 adult patients (age ≥18 years) of NSTEMI. Patients were excluded if they had chronic coronary syndrome, unstable angina congenital heart disease, significant valvular heart disease, cardiomyopathies, severe renal dysfunction, history of percutaneous coronary intervention and coronary artery bypass grafting. The protocol was approved by the local ethics committee and Institutional Review Board (IRB). Written informed consent was obtained from each patient after careful explanation.

Study procedure

Adult patients of NSTEMI who underwent invasive coronary angiography with percutaneous coronary intervention (PCI) were included in this study as per inclusion and exclusion criteria. Detailed history, physical examination and relevant laboratory tests including ECG and echocardiogram were done. Patients were divided into two groups: in one group - Patients undergoing early invasive strategy with PCI & in other group - Patients undergoing delayed ischaemia driven PCI. In this study we considered an early invasive strategy as - revascularization within 72h for patients presented with NSTEMI with high-risk features defined by a GRACE score > 140 and for those at lower risk with GRACE score <140; delayed ischaemia driven strategy as - revascularization after 72h, reserved for refractory, recurrent or severe exercise-induced ischaemia. Then patients underwent invasive evaluation by coronary angiography with PCI performed using drug Eluting Coronary Stent (DES) via either the trans-femoral or trans-radial approach by expert interventional cardiologist using standard protocols. Procedural anticoagulation was achieved with unfractionated heparin; glycoprotein IIb/IIIa inhibitors were used whenever needed. Patients were receiving 180 mg of Ticagrelor before the intervention. Thereafter, 75 mg of aspirin daily and 90 mg of Ticagrelor twice daily was prescribed. Other standard drugs (angiotensin converting enzyme inhibitors, beta blockers, statins and oral hypoglycemic agents) were unchanged during the study in order to minimize the effects of alterations on the variables.

Post PCI assessment by symptoms, H/O - occurrence of MACEs (hospitalization due to ischaemic causes, hospitalization due to myocardial re-infarction, hospitalization due to other cardiac causes, target vessel revascularization due to ischaemia, death due to cardiac causes, occurrence of Stroke, occurrence of major bleeding), detailed clinical examination and relevant laboratory investigation were done after 6-month and recorded in predesigned structured proforma of data collection sheet. After that variables were compared between these two groups of patients: to find out any statistically significant difference.

Statistical analysis

After collection of all information, these data were checked, verified for consistency and edited for finalized result. Continuous variables are expressed as mean value±standard deviation or as median. Categorical variables are expressed as absolute number and percentages which were presented as frequency tables and charts. Continuous data were analyzed and compared by Student's t-test and categorical data by Chi-square test. Binary logistic regression analysis was used to determine independent predictors of MACEs Differences were considered significant when P value less than 0.05. Statistical analyses were carried out by SPSS version 25.0 windows software.

Results

Of the 396 patients in the study, 227 patients were in 'early' group and 162 patients were in 'delayed' group. Owing to withdrawal of consent, 2 patients were excluded and 5 patients lost to follow up, leading to 389 patients for the final analysis. Baseline characteristics were well balanced between treatment groups (Table 1). Then findings after 6-months follow up were compared between two study groups. Complete 6-month follow-up was obtained for >98% of patients.

The mean age of the participants of early and delayed group were 52.61±10.91 and 52.26±8.92 years respectively. A male predominance (65.8% vs. 88.9%) was observed in either group. Majority of the patients in both groups were overweight and obese, and less than one fourth of study subjects had normal (18.0-22.9 kg/m2) BMI (BMI>23 is considered overweight in Asian). Most of the patients had multiple risk factors. Hypertension was the most prevalent risk factor in both groups 60.5%. Distribution of risk factors among the study subjects were Hypertension (60.5% vs 55.6%), DM (52.6% vs 44.4%), smoking (36.8% vs 51.9%), dyslipidemia (52.2% vs 44.9%), CKD (1.7% vs 7.8%) and family history of CAD (52.4% vs 43.9%) in early and delayed group respectively (Table I).

Table-I

Associations of the various demographic, clinical, biochemical and echocardiographic variables between early and delayed groups of study patients (N=389)

Variables	Early Group (n=227) mean±SD or No. %	Delayed Group (n=162) mean±SD or No. (%)	P Value
Age (year)	52.61±10.91	52.26±8.92	0.688ns
Sex			
Male	150(65.8)	144(88.9)	Â0.001s
Female	78(34.2)	18(11.1)	
BMI (kg/m2)	24.51±2.39	24.17±2.22	0.175ns
Risk factors			
Diabetes Mellitus	120(52.6)	72(44.4)	0.101ns
Hypertension	137(60.5)	90(55.6)	0.344ns
Smoking Status	126(55.7)	84(51.9)	0.475ns
Dyslipidemia	120(52.6)	79(48.7)	0.425ns
CKD	4(1.8)	5(3.0)	0.397ns
F/H of CAD	120(52.6)	72(44.4)	0.090ns
Clinical presentation			
Chest Pain	223(98.2)	160(98.8)	0.771ns
SOB	14(6.1)	4(2.2)	0.214ns
SBP (mmHg)	120.9±12.24	124.8±13.69	0.043s
Heart rate (bpm)	87.14±6.58	81.5±7.19	0.001s
Biochemical tests			
HbA1c (%)	8.9±1.0	7.1±1.3	0.029s
Lipid profiles (mg/dl)			
Total cholesterol	195.9±73.9	190.6±66.9	0.806ns
Triglyceride	210.0±61.0	195.5±62.3	0.470ns
HDL-C	44.5±12.3	46.9±9.8	0.460n
LDL-C	120.3±36.8	124.6±31.8	s0.677ns
S.Creatinine (mg/dl)	1.1±0.18	1.07±0.13	0.678ns
Ischaemic ECG changes	147(64.9)	30(18.5)	<0.001s
ST-segment depressionT-wave inversion	162(71.1)	18(11.1)	<0.001s
Echocardiography			
LVEF (%)	51.5±9.1	52.5±9.8	0.750ns
GRACE Score	143.14±19.4	127.3±14.7	<0.001s

BMI=Body Mass Index, CAD=Coronary Artery Disease, CKD=Chronic Kidney Disease, GRACE=Global Registry of Acute Coronary Events, HDL-C=High Density Lipoprotein-Cholesterol, LDL-C=Low Density Lipoprotein-Cholesterol, LVEF=Left Ventricular Ejection Fraction, SBP=Systolic Blood Pressure, SOB= shortness of breath, s=significant, ns=not significant.

Double vessel disease (DVD) was more common in delayed group (51.9%) than early group (50.0%) but the difference was statistically not significant (p=0.751). Single vessel disease (SVD) more common in delayed group (48.1%) and triple vessel disease (TVD) were more common in early group (13.2%). PCI to RCA, LAD and LCX were more common in early group (Table II).

During 6-months follow up, clinical outcomes were found better in early group than in delayed group in terms of symptoms (chest pain-10.5% vs 17.3%, SOB-6.1% vs 6.2%) and good functional capacity (90.3% vs 86.4%), poor functional capacity (9.7% vs 13.6%) (Table III).

The use of medication, including Dual antiplatelet therapy (DAPT) in the form of aspirin and thienopyridines (ticagrelor), angiotensin-converting enzyme-inhibitors, and statins, was high and similar in the two treatment groups.

Table-II

Angiographic characteristics of the study patients (N=389)

Vaiables	Early Group (n=227) No. (%)	Delayed Group (n=162) No. (%)	p-value
Extent of coronary disease			
SVD	84(36.8)	78(48.1)	0.027s
DVD	114(50.0)	84(51.9)	0.751ns
TVD	30(13.2)	0(0)	Â0.001s
Culprit lesionLM	6(2.6)	12(7.4)	0.027s
LAD	108(47.4)	66(40.7)	0.181ns
LCX	108(47.4)	36(22.2)	<0.001s
RCA	120(52.6)	60(37.0)	0.002s

SVD=Single vessel disease, DVD=Double vessel disease, TVD=Triple vessel disease, LAD=Left Anterior Descending, LCX=Left Circumflex, RCA=Right Coronary Artery, s=significant, ns=not significant.

Table-III

Six months clinical outcomes between two groups (N=389)

Vaiables		Early Group (n=227) No. (%)	Delayed Group (n=162) No. (%)	p-value
Symptoms	Chest pain	24(10.5)	28(17.3)	0.171ns
	SOB	14(6.1)	10(6.2)	0.993ns
Functional Capacity	Good	206(90.3)	140(86.4)	0.393ns
	Poor	22(9.7)	22(13.6)	

SOB= shortness of breath, s=significant, ns=not significant.

Table-IV

Six months clinical outcomes between two groups (N=389)

Major adverse cardiovascular Events (MACEs)	Early Group (n=227) No. (%)	Delayed Group (n=162) No. (%)	p-value
MI	6(2.6)	15(9.2)	0.004s
Target Vessel revascularization	8(3.5)	14(8.4)	0.031s
Cardiac Death	7(3.1)	17(10.5)	0.002s
Stroke	2(0.9)	4(2.5)	0.210ns
Major Bleeding	2(0.9)	2(1.2)	0.733ns
Hospitalization due to Ischaemia cause	6(2.6)	8(4.9)	0.230ns

s=significant, ns=not significant.

The patients of the early group experienced a lower incidence of MI, target vessel revascularization (TVR) and cadiac death during follow up at 6-months post PCI. The incidence of MI, cardiac death, target vessel revascularization at 6-month after PCI was found statistically significant between early group than delayed group (p=0.004, p=0.002, p=0.031 respectively). No other adverse events were found significantly different between the two groups. Incidence of target vessel revascularization, cardiac death, stroke, major bleeding and hospitalization due to ischemia were higher in delayed group than early group (8.4% vs 3.5%, 10.5% vs 3.1%, 2.5% vs 0.9%, 1.2% vs 0.9%, and 4.9% vs 2.6%) and stroke, major bleeding and hospitalization due to ischemia (have p value of 0.210, 0.733 and 0.230 respectively) which were not statistically significant (Table 4). Binary logistic regression analysis for predictors of MACEs were presented in Table 5. After adjustment for potential confounders the risk of MACEs in delayed group of patients were 2.14 times (OR = 2.14; 95% CI, 1.17 - 3.68; p = Â0.001). The confounders included age, sex, BMI, hypertension, dyslipidemia, smoking, renal insufficiency, family history of CAD, DVD and TVD. The findings of the study data analyses are documented in Tables.

Discussion

In this single-center observational cross- sectional study, we investigated the outcome comparision between early and delayed invasive strategy in NSTEMI patients undergoing PCI with DES after 6-months follow up. In this analysis, NSTEMI patients undergoing early percutaneous intervention was associated with better clinical outcome.The patients of the early group experienced a lower incidence of MI, TVR and cadiac death during follow up at 6 months post PCI. Distribution of MACEs like stroke, major bleeding and hospitalization due to ischaemic causes were 0.9%, 0.9% and 2.6% in patients of early group and 2.5%, 1.2% and 4.9% in delayed group respectively, but which were not statistically significant. At 6 months following the drug eluting stent placement the incidence of MI in the early group was 2.6% as opposed to 9.2% in the delayed group which was statistically significant (p=0.004). Swahn et al. 2012, demonstrated prevalence of MI during follow up at 6 months post PCI was 7.8% in early group and 6.6% in delayed group respectively, HR 1.08(0.36-3.25).[14] Thiele H. et al. 2017, showed demonstrated incidence of MI during follow up at 6 months post PCI was 20% in early group and 16% in delayed group respectively, (p=0.070).15 The TACTICS TIMI-18 trial showed occurrence of death, nonfatal MI or rehospitalization for NSTE-ACS at six months was 19.4% with the conservative approach and 15.9% with the early invasive strategy (p = 0.025), with significant reductions in death or MI from 9.5% to 7.3% (p = 0.0498).[16]

The better prognosis with early vs. late PCI among NSTEMI patients in this study consistent with a few prior studies and it is worthwhile to compare the results of this study with those of landmark clinical trials: the TIMI- IIIB (the Thrombolysis In Myocardial Infarction) trials,[17] the VANQWISH (the Veterans Affairs Non–Q-Wave Infarction Strategies in Hospital) trials,[18] the FRISC II (the Fragmin and fast Revascularization during InStability in Coronary artery disease) trials,[19] and the TACTICS TIMI-[18] (the Treat Angina with Aggrastat and determine Cost of Therapy with an Invasive or Conservative Strategy) trials.[16] The TIMI-IIIB and the VANQWISH trials have been the primary basis for use of "ischemia-guided" therapy while the FRISC II and the TACTICS have, identified advantages of an "early invasive" approach. The TIMI-IIIB authors concluded that similar early and late outcomes were achieved with the two approaches with respect to death and MI. Given the similar outcomes with the two different strategies, patients could be managed individually depending upon the severity of their presentation, cardiac risk factors, left ventricular function, and response to medical therapy. The VANQWISH trial concluded that the early conservative approach was the preferred treatment strategy for patients with NSTEMI. Different enrollment criteria and baseline characteristics of the subjects may explain the discrepant results between this study and these major trials, this study included only patients undergoing PCI, whereas the majority of patients in those trials did not.

It was observed that, despite receiving standard treatment as well as advice for life style modification, dietary advice during discharge from hospital, incidence of MACEs were significantly higher at 6-months follow up in delayed group of patients in comparison to early group of patients.

Limitations

The sample was taken from a single center. Result of the study might be influenced by relatively smaller sample size. So, findings may not represent the impact of both the early invasive and delayed invasive strategy in all the Bangladeshi NSTEMI cohort undergoing PCI. The study sample was taken consecutively (non-randomly), sampling method was purposive, so there was risk of selection bias-which might have affected the outcome of the study.

Longer-term follow up will add further insight into the problem.

Conclusion

In conclusion, these data suggest that early invasive strategy in NSTEMI patients undergoing percutaneous coronary intervention (PCI) may be beneficial in reducing the risk of MACEs and improvement of the clinical outcome after PCI at 6 months follow-up.

Conflict of interest

Authors declare no conflicts of interest.

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