

## COMPARISON OF INVASIVE VERSUS MEDICAL STRATEGY OF PATIENTS WITH NON-ST ELEVATION MYOCARDIAL INFARCTION WITH INTERMEDIATE THROMBOLYSIS IN MYOCARDIAL INFARCTION SCORE

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**Abstract:** *Non-ST-elevation myocardial infarction (NSTEMI) and unstable angina pectoris are frequent causes of hospital admission in the elderly. However, clinical trials targeting this population are scarce, making these patients less likely to receive treatment according to guidelines. This study was designed to compare the outcome of invasive versus a medical strategy of patients with non-ST elevation myocardial infarction with intermediate Thrombolysis in Myocardial Infarction score. This study was conducted at the Department of Cardiology, Rehmatul lil Alameen Institute of Cardiology, Lahore, from 21-5-2019 to 21-11-2019. A total of 220 (110 patients in each group) patients fulfilling inclusion criteria from emergencies were recruited. Then patients were randomly divided into two groups by using the lottery method. In group A, patients were managed through an invasive strategy. In group B, patients underwent medication only. Patients in the invasive strategy underwent percutaneous coronary intervention, or coronary artery bypass graft patients in the medical strategy group were given standard medical management per hospital protocol. Then patients were followed up there for 3 days. After 3 days, patients were discharged and were followed up in OPD for 30 days. It was noted if the patient presented again in an emergency with recurrent myocardial infarction (MI) or if death occurred within 30 days. This study compared an invasive and medical strategy in NSTEMI patients regarding recurrent MI and mortality within 30 days. According to the findings of this study, no significant difference was seen in recurrent MI (Group-A: 13.6% & Group-B: 12.7%, p-value=0.84) in both groups, but mortality (Group-A: 10.9% & Group-B: 3.6%, p-value=0.037) was significantly higher in patients who underwent invasive strategy. Considering the results of this study, it can be concluded that NSTEMI patients treated with conservative treatment had a low mortality rate and fewer chances of recurrent MI.*

**Keywords:** Outcome, Invasive, Medical Strategy, Non-ST Elevation, Myocardial Infarction, Thrombolysis, Score

### Introduction

Non-ST-elevation myocardial infarction (NSTEMI) accounted for more than two-thirds of all acute coronary syndrome (ACS) cases in the United States in 2009. Furthermore, cardiovascular disease, including NSTEMI, remains the leading cause of mortality worldwide (Li et al., 2014). Long-term outcomes have not improved in NSTEMI patients at the same rate seen in ST-segment elevation myocardial infarction patients, possibly reflecting NSTEMI patients' more complex clinical phenotype, including older age, the greater burden of comorbidities and the higher likelihood of a previous MI (Cohen, 2016). The management of NSTEMI is guided by risk stratification, with an early invasive strategy favored in high-risk patients, especially for patients with positive cardiac necrosis biomarkers

(Amsterdam et al., 2014; Hung et al., 2018). People with NSTEMI are managed with medical therapy, invasive angiography, and revascularization. Specifically, two approaches have evolved: either a routine 'invasive' strategy whereby all patients undergo coronary angiography shortly after admission and, if indicated, coronary revascularization; or a selective 'invasive' (also referred to as 'conservative') strategy in which medical therapy alone is used initially, with a selection of patients for angiography based upon evidence of persistent myocardial ischemia. Uncertainty exists regarding which strategy provides the best outcomes for these patients (Fanning et al., 2016). Previous studies have demonstrated improved outcomes with an early invasive strategy in patients with NSTEMI. However, there are limited data outcomes compared

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to medical versus invasive strategies for NSTEMI (Kolte et al., 2013). It has been reported in a trial that with an invasive strategy, recurrent MI developed in 8% of cases in 1% who received medical strategy, while death occurred in 5% with invasive strategy while 1% with medical strategy after NSTEMI (Boden, 2003). While another trial showed that with an invasive strategy, recurrent MI developed in 17% of cases; in 30% who received the medical strategy, death occurred in 25% with an invasive strategy, while 27% with the medical strategy after NSTEMI (Tegn et al., 2016). The rationale of this study is to compare the outcome of invasive versus a medical strategy of patients with NSTEMI with intermediate Thrombolysis in Myocardial Infarction score. It has been noticed from the literature that with an invasive strategy, there are more chances of complications after NSTEMI than medical strategy. But controversial evidence has been found in the literature, which creates an ambiguity whether the conservative or medical strategy is appropriate for NSTEMI patients with intermediate TIMI or invasive strategy. So, this study would help us to confirm the beneficial role of more appropriate methods to manage NSTEMI patients with intermediate TIMI score.

## Methodology

This Randomized Controlled Trial was conducted at the Department of Cardiology, Rehmatul lil Alameen Institute of Cardiology, Lahore, from 21-05-2019 to 21-11-2019. The sample size of 220 was calculated by using the WHO calculator. Non-probability, consecutive sampling was used to collect the information. Patients of age 40-70 years of either gender presenting with NSTEMI with intermediate TIMI score were included in the study. In contrast, patients with diabetic (BSR>180gm/dl) and other valvular heart diseases (on medical record), hypertensive (BP≥140/90mmHg), renal failure (serum creatinine>1.2mg/dl) or on hemodialysis, liver disease (AST & ALT >40IU, bilirubin >5mg/dl), patients with recurrent MI (medical record), smoker (>5pack year) were excluded from the study.

Informed consent was taken. Demographic information (like name, age, sex, and duration of symptoms) was also obtained. Then patients were randomly divided into two groups by using the lottery method. In group A, patients were managed through an invasive strategy. In group B, patients underwent medication only. Patients in the invasive strategy underwent percutaneous coronary intervention or coronary artery bypass graft. Patients in the medical strategy group were given standard medical management per hospital protocol. Then patients were followed up there for 3 days. After 3 days, patients were discharged and were followed up in OPD for 30 days. It was noted if the patient presented again in an emergency with recurrent MI or if death occurred within 30 days. All this information was recorded on the predesigned proforma. Data was entered in SPSS version 21 and analyzed through it. Mean ± SD was calculated for age and duration of symptoms. Frequency and percentage were calculated for gender and outcome (recurrent MI and death). The chi-square test was applied to compare outcomes in both groups. P-value ≤0.05 was considered significant. Data was stratified for age, gender, BMI, and duration of symptoms. Post-stratification, the Chi-square test was applied to compare outcomes in both groups for each stratum. P-value ≤0.05 was considered significant.

## Results

The mean age of patients in Group-A and Group-B was 47.51±10.15 and 52.10±10.38 years. In Group-A 71(64.5%) patients were male and 39(35.5%) were female. While in Group-B 56(50.9%) patients were male and 54 (49.1%) were female. The mean duration of symptoms in Group-A and Group-B was 26/49±3.16 and 25.72±3.21. Group-A and Group B's mean body mass index was 26.49±3.16 and 25.72±3.21, respectively. The frequency of recurrent MI did not show any significant difference in both treatment groups. I.e. Group-A: 13.6% & Group-B: 12.7%, p- value=0.84. (Mortality rate was significantly higher in patients who underwent invasive strategy, i.e., Group-A: 10.9% & Group-B: 3.6%, p- value=0.037 (table 1).

**Table 1 Demographic variables of both groups**

Variables	Constructs	Group-A	Group-B	P-value
Age		49.51 ± 10.15	52.10 ±10.38	<b>0.09</b>
Duration of symptoms		26.49 ± 3.16	25.72 ± 3.21	<b>0.63</b>
Body Mass Index		26.49 ± 3.16	25.72 ± 3.21	<b>0.087</b>
Gender	Male	71(64.5%)	56(50.9%)	<b>0.36</b>
	Female	39(35.5%)	54(49.1%)	
Recurrent MI	Yes	15(13.6%)	14(12.7%)	<b>0.84</b>
	No	95(86.4%)	96(87.3%)	
Death (within 30 days)	Yes	12(10.9%)	4(3.6%)	<b>0.037</b>
	No	98(89.1%)	106(96.4%)	

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Significant differences were observed in the treatment groups for repeat myocardial infarction (MI) and

mortality in patients aged >60 years, with Group-A showing higher rates.

**Table 2: Comparison of Recurrent MI (within 30 days) stratified for age, Gender, BMI, and duration of symptoms:**

Variables	Constructs		Group-A	Group-B	p-value
Age	28-45	Yes	8(16%)	4(10.5%)	<b>0.459</b>
		No	42(84%)	34(89.5%)	
	46-60	Yes	4(7.7%)	5(10.9%)	<b>0.587</b>
		No	48(92.3%)	41(89.1%)	
	>60	Yes	8(100%)	5(19.2%)	<b>0.000</b>
		No	0(0%)	21(80.8%)	
Gender	Male	Yes	14(19.7%)	8(14.3%)	<b>0.422</b>
		No	57(80.3%)	48(85.7%)	
	Female	Yes	6(15.4%)	6(11.1%)	<b>0.544</b>
		No	33(84.6%)	48(88.9%)	
BMI	Normal	Yes	8(22.9%)	6(14.3%)	<b>0.322</b>
		No	27(77.1%)	36(85.7%)	
	Overweight	Yes	8(19.5%)	5(11.6%)	<b>0.318</b>
		No	33(80.5%)	38(88.4%)	
	Obese	Yes	4(11.8%)	3(12%)	<b>0.978</b>
		No	30(88.2%)	22(88%)	
Duration of symptoms	1-3	Yes	11(25%)	5(10.9%)	<b>0.080</b>
		No	33(75%)	41(89.1%)	
	4-7	Yes	5(12.5%)	5(13.5%)	<b>0.895</b>
		No	35(87.5%)	32(86.5%)	
	8-10	Yes	4(15.4%)	4(14.8%)	<b>0.954</b>
		No	22(84.6%)	23(85.2%)	

**Table 3: Comparison of death (within 30 days) stratified for age, Gender, BMI, and duration of symptoms.**

Variables	Constructs		Group-A	Group-B	p-value
Age	28-45	Yes	5(10%)	2(5.3%)	<b>0.416</b>
		No	45(90%)	36(94.7%)	
	46-60	Yes	3(5.8%)	1(2.2%)	<b>0.369</b>
		No	49(94.2%)	45(97.8%)	
	>60	Yes	4(50%)	1(3.8%)	<b>0.001</b>
		No	4(50%)	25(96.2%)	
Gender	Male	Yes	10(14.1%)	2(3.6%)	<b>0.044</b>
		No	61(85.9%)	54(96.4%)	
	Female	Yes	2(5.1%)	2(5.1%)	<b>0.738</b>
		No	37(94.9%)	52(96.3%)	
BMI	Normal	Yes	3(8.6%)	1(2.4%)	<b>0.223</b>
		No	32(91.4%)	41(97.6%)	
	Overweight	Yes	5(12.2%)	2(4.7%)	<b>0.211</b>
		No	36(87.8%)	41(95.3%)	
	Obese	Yes	4(11.8%)	1(4%)	<b>0.290</b>
		No	30(88.2%)	24(96%)	
Duration of symptoms	1-3	Yes	6(13.6%)	3(6.5%)	<b>0.261</b>
		No	38(86.4%)	43(93.5%)	
	4-7	Yes	2(5%)	0(0%)	<b>0.168</b>
		No	38(95%)	37(100%)	
	8-10	Yes	4(15.4%)	1(3.7%)	<b>0.146</b>
		No	22(84.6%)	26(96.3%)	

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Regarding gender, there were no significant differences in repeat MI between male and female patients (Male:  $p$ -value=0.422, Female:  $p$ -value=0.544, Table-9). However, for male patients, mortality was significantly higher in Group-A compared to Group-B (Group-A: 14.1% & Group-B: 3.6%,  $p$ -value=0.044). No significant difference in mortality rates was observed in female patients (Group-A: 5.1% & Group-B: 5.1%,  $p$ -value=0.738). Body mass index (BMI) did not significantly impact repeat MI and mortality in both treatment groups. Similarly, the duration of symptoms did not significantly impact repeat MI and mortality in either treatment group (table 2, 3). However, no significant differences in other age groups regarding repeat MI were found. The findings were as follows: Age (>60 years): Group-A: 100% & Group-B: 19.2%,  $p$ -value=0.000 for repeat MI, and Group-A: 50% & Group-B: 3.8%,  $p$ -value=0.001 for mortality.

## Discussion

The current clinical practice guidelines recommend an invasive strategy in non-ST elevation myocardial infarction (non-STEMI consisting of routine cardiac catheterization and revascularization during admission. This recommendation comes from three large, randomized trials (FRISC-2, RITA-3, and ICTUS) whose meta-analysis has demonstrated the benefits of invasive management (Amsterdam et al., 2014; Prejean et al., 2018). In this study, the invasive and medical strategy was compared in NSTEMI patients in terms of recurrent MI and mortality within 30 days. According to the findings of this study, no significant difference was seen in recurrent MI (Group-A: 13.6% & Group-B: 12.7%,  $p$ -value=0.84) in both groups, but mortality (Group-A: 10.9% & Group-B: 3.6%,  $p$ -value=0.037) was significantly higher in patients who underwent invasive strategy. Previous studies have demonstrated improved outcomes with an early invasive strategy in patients with NSTEMI. However, there is limited data outcome compared to the medical versus invasive strategy for NSTEMI (Kolte et al., 2013). Sonali R Gnanenthiran, in her meta-analysis, showed that routine invasive therapy reduces MI and recurrent revascularization and may reduce mortality at the expense of major bleeding in elderly patients with NSTEMI (Gnanenthiran et al., 2017). Boden WE have reported that with an invasive strategy, recurrent MI developed in 8% of cases in 1% who received medical strategy, death occurred in 5% with invasive strategy and 1% with medical strategy after NSTEMI. While another trial by Tegn N showed that with an invasive strategy, recurrent MI developed in 17% of cases in 30% who received the medical strategy, while death occurred in 25% with the invasive strategy while 27% with the medical strategy after NSTEMI.

8 Results of this study are consistent with the findings of Boden WE but not in line with the findings of Tegn N. The After Eighty study found a reduction in MI (17% vs. 30%,  $p$ =0.0003) and need for urgent revascularization (2% vs. 11%,  $p$ =0.0001) in the routine invasive therapy group compared with those medically managed, but no difference in mortality (25% vs. 27%,  $p$ =0.53) at 18-month follow-up (Tegn et al., 2016). In contrast, the Italian Elderly ACS study found no differences between routine invasive therapy and initial medical management (MI 7.1% vs. 10.7%,  $p$ =0.27; mortality 12.3% vs. 13.8%,  $p$ =0.65) at 1 year (Savonitto et al., 2012).

The routine provision of invasive therapy thus continues to be controversial. Both of these studies did not support the findings of this study while reporting controversial findings for long-term follow-up for both treatment strategies. Recently, the MOSCA randomized trial evaluated the efficacy of an invasive strategy in elderly patients with NSTEMI and comorbidities. Although this was a small trial, there were no differences between the invasive and conservative strategies. In an exploratory non-pre-specified analysis, the invasive strategy reduced the probability of death or ischemic events at 3 months. This benefit, nonetheless, vanished at a 2.5-years follow-up (Sanchis et al., 2016). Juan Sanchisa and his team compared the conservative and invasive strategies in NSTEMI patients. As per their findings, the invasive strategy, however, tended to improve 3-month outcomes in terms of mortality (HR= 0.348, 95% CI 0.122–0.991,  $p$ -value=0.048), and of mortality or ischemic events (re-infarction or post-discharge revascularization) (HR= 0.432, 95% CI 0.190–0.984,  $p$ -value= 0.046) (Sanchis et al., 2016). The "routine early invasive strategy" is typically defined as cardiac catheterization followed by PCI in patients without a clinical contraindication within the first 24 to 48 h of presentation. Proponents of this strategy believe it is appropriate for all patients presenting with ACS, including those with NSTEMI and those with biomarker negative. Clinicians who favor the more invasive approach to treatment tend to argue that any form of risk stratification results in less definitive management. The rationale behind this concept is that once coronary angiography is performed, the cardiologist can tailor therapy more appropriately.

## Conclusion

Considering the results of this study, it can be concluded that NSTEMI patients treated with conservative treatment had a low mortality rate and fewer chances of recurrent MI.

## Conflict of interest



The authors declared absence of conflict of interest.

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