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ORIGINAL ARTICLE

One Month Major Adverse Cardiac Events in Postmenopausal Females with Acute Coronary Syndromes; Conservative versus Invasive Management.

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ABSTRACT

Background: Myocardial infarction (MI) and cardiovascular disease were long believed to be exclusively male conditions. Thankfully, there is growing recognition in both the medical literature and the public that heart disease is the leading cause of mortality for women and that cardiovascular illness is gender insensitive. This study aimed to compare MACE among post-menopausal females admitted to CCU with acute coronary syndromes. **Methods:** The current study included 144 female patients with mean age 59.32 years. Mean BMI was 26.85 kg/m2, and positive family history was 78.5%. As regards comorbidity, 41.7%, 48.6%, and 41.7% had comorbid diabetes, hypertension, and dyslipidemia. STEMI was 55.6% of patients in which 10 cases received thrombolytic therapy and 70 cases admitted to PCI. NSTEMI and unstable angina patients were 44.4% in which 20 cases were admitted for PCI and 44 cases received medical treatment.

Results: we enrolled 144 post-menopausal patients presented with acute coronary syndromes and in comparison between the conservative and invasive methods of treatment in each group of STEMI and NSTEMI and following-up the patients for one month for MACE, the MACE was higher in group of invasive arm than conservative arm with 37.8% versus 18.5 % respectively, Heart failure was 7.4% versus 21.1%, Serious arrhythmia was 14.8% versus 26.7%, Reinfarction was 6.7% versus 3.7%,Mortality was 6% versus 0%.

Conclusion: According to the findings of our research, it is possible to conclude, "Compared to the non-invasive approach, the invasive option is associated with worse outcomes in patients with NSTEMI. The non-invasive strategy is associated with better outcomes than the invasive option.

Keywords: Myocardial infarction; Acute coronary syndrome; Major cardiac events; Postmenopausal females

Introduction

At 49% of all fatalities in women compared to 40% in males, cardiovascular disease is currently the top cause of death for women in Europe. Due to estrogen's protective effect on atherosclerosis, women are less vulnerable to early cardiovascular death, especially from ischemic heart disease, which accounts for most of the increased cardiovascular mortality among women [1].

Endogenous estrogen is believed to protect women against cardiovascular disease, especially coronary artery disease, because it has a variety of effects on the circulatory system [2].

By increasing lipoproteins with a higher density and decreasing those with a lower density, estrogen improves the cholesterol profile. It also lowers blood pressure by relaxing smooth muscle cells and may help the body eliminate cellular free radicals, which could otherwise trigger inflammatory reactions and heart disease. Women who arrive with cardiovascular disease, especially ACS, later in life may be partially explained by the loss of the protective estrogen action

following menopause. The symptoms that men and women with ACS present with may differ [3].

Delay in diagnosing ACS is common when symptoms are not recognized. Women are less likely than men to be sent for fibrinolysis or percutaneous intervention even after a diagnosis, and coronary angiography, which puts the myocardium at further risk and delays many patients' definitive treatment. In addition, women undergo less intense medical care both during and following an ACS incident. The combined consequences of these sex-related characteristics are long-lasting, and women consistently have worse post-ACS results than males [4, 5].

In reference to the European Society of Cardiology defines acute coronary syndrome as follows: there is a wide range in the way acute coronary syndromes (ACS) manifest clinically. Cardiogenic shock (CS), hemodynamic instability, or electrical arrest as a result of persistent ischemia, mechanical problems including those with severe mitral regurgitation and those who do not experience any pain when they first appear are among the conditions that fall under this category.

Acute coronary syndrome mortality is higher in women than in males, according to multiple studies. This difference in mortality has been ascribed to factors such as older age at presentation, more unusual symptoms that result in delayed diagnosis, and lower rates of early coronary intervention [6].

The best course of treatment is rigorous medical therapy, which is sometimes followed by revascularization and diagnostic coronary angiography. In five major randomized experiments (VANQWISH, FRISC II, [TACTICS– TIMI 18], TIMI IIIB, and [RITA-3]), "conservative" method (angiography and revascularization only in cases when no other treatment worked or there was evidence of severe residual ischemia) was compared to a standard early invasive approach (revascularization after early angiography, depending on angiographic results) [7].

The FRISC II, TACTICS–TIMI 18, and RITA-3 trials all demonstrated the benefits of an early invasive approach, particularly in high-risk patient categories such those who initially presented with elevated cardiac troponin levels [8]. Therefore, the current study sought to compare the two treatment modalities (conservative versus invasive) for postmenopausal women with ACS (STEMI, NSTMEI, US), during first month of management in Zagazig University.

Subjects and Methods

A Cohort study that was conducted in cardiology department Zagazig University Hospital and National heart institute in Giza, from March 2022 to January 2023 and included 144 consecutive cases admitted to CCUs with signs and symptoms of acute coronary syndromes.

Every patient provided written informed consent, and the Zagazig University Faculty of Medicine's Research Ethical Committee approved the study. The study was conducted in accordance with the World Medical Association's Ethical Code (Declaration of Helsinki) for Human Studies.

Inclusion Criteria were post-menopausal females, patients with acute coronary syndrome (STEMI, NSTEMI, Unstable angina). Exclusion criteria was for patients with other cardiac structural disease, patients with CKD, end stage liver cell failure.

Data on demographic variables and risk factors were obtained for all patients before and after treatment with either the conservative or invasive technique.

Demographic characteristics for the following 1- Age, 2- Diabetes mellitus with diagnostic criteria of AIC: ≥6.5%, Fasting plasma glucose: ≥ 126mg/dl Two-hour plasma glucose ≥ 200mg/dl during OOGTT and or random blood glucose: ≥ 200 mg/dl plus classic symptoms of diabetes. 3-Hypertension, 4-Dyslipidemia, 5-Long term medication, 6-Smoking, 7-Family History, 8-BMI.

Physical examination was obtained for: Pulse and blood pressure, cardiac examination, abdominal and chest examination, neurological examination.

As evidence of ACS, a resting 12 lead ECG was collected in each patient immediately upon presentation. Observing changes such as ST segment deviation, T wave modifications, pathological Q wave, new bundle branch

block, and other types of arrhythmias such as heart block.

Diagnosis of STEMI by Diagnostic ST elevation in absence of left ventricular hypertrophy or left bundle branch block (LBBB) new ST elevation at J point ≥ 2 mm (0.2 millivolts [mV]) in men or ≥ 1.5 mm (0.15 mV) in women in leads V2-V3 ≥ 1 mm (0.1 mV) in 2 other contiguous chest leads or limb leads New or presumably new LBBB considered a STEMI equivalent and full filling the definition of MI according to the fourth definition of MI with rising CTN troponin and or fall above the 99th percentile.

NSTEMI cases include transient ST-segment elevation, chronic or temporary ST-segment depression, and T wave abnormalities such as hyper acute T waves, T wave inversion, biphasic T waves, flat T waves, and false normalization of T waves. Alternatively, the ECG could be normal, with most individuals in this category thereafter exhibiting a typical rise and decrease in cardiac troponin levels (i.e., meeting MI criteria).

The cases of NSTEMI also justified according to their risk stratification in the following pattern:

A-Very high risk: 1- Hemodynamic instability or cardiogenic shock. 2-Recurrent or ongoing chest pain refractory to medical treatment. 3-Acute heart failure presumed secondary to ongoing myocardial ischemia. 4-Life-threatening arrhythmias or cardiac arrest after presentation. 5-Mechanical complications 6- Recurrent dynamic ECG changes suggestive of ischemia.

B- High risk: 1-Confirmed diagnosis of NSTEMI based on ESC algorithms. 2-GRACE risk score >140. 3-Transient ST-segment elevation. 4-Dynamic ST-segment or T wave changes.

Non-high risk.

According to the fourth universal definition of MI: Patients with troponin levels below the 99th centile was diagnosed with UA. Patients with troponin levels over the 99th centile will be diagnosed with NSTEMIMI.

During the patient's hospitalization, a bedside screening ECHO utilizing a "Siemens machine with 2.5 MHz probe" was performed during and before discharging from hospital and for one month follow-up, with special emphasis paid to detecting estimation of left ventricular (LVEF) by M-mode method. Assessment Left ventricular end systolic dimension (LVESD) using M-mode method, left ventricular end diastolic dimension (LVEDD) using M-mode method. Assessment of evidence of diastolic dysfunction. Assessment of regional wall motion index.

Laboratory test included Cardiac enzymes if above the upper limit of 99th it will be positive and if below the 99th percentile will be negative, CKMB (IU) Hemoglobin level (g/dl), Serum creatinine (mg/dl).

METHODS

Patients of each group (STEMI, NSTEMI) are divided into two categories arms according to the received type of management, either conservative or invasive strategies.

Conservative treatment (Pharmacological therapy): Strategy of treatment conducted according to European society of Cardiology for management of acute coronary syndrome presenting cases. After confirming the diagnosis using clinical examination, ECG, Lab tests Cases were divided into: (A) STEMI (B)-NSTEMI (C)-Unstable angina.

In STEMI, NSTEMI and Unstable Angina presenting cases the following medical treatment is given:

A-Anti-platelet B- Anti-coagulant C-Fibrinolysis (Pharmaco-invasive) using Streptokinase in cases of STEMI group only if PCI is not applicable within 120 minutes, and not more than 12 hours from beginning of symptoms. D-Beta-blockers E-Lipid-lowering therapy. F- Mineralocorticoid/aldosterone receptor antagonists G-Nitrates H-Angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers I-Intravenous opioids in patients present with severe chest pain.

Invasive strategy*:* PCI is the priority strategy for acute presenting cases for STEMI, High risk NSTEMI however, Thrombolytic (Pharmaco-invasive) is alternative measure of treatment for cases of STEMI if PCI delay over 120 minutes. In STEMI cases with Indication for invasive strategy PCI is the preferred reperfusion strategy in patients presented within 2 hours, provided it can be performed expeditiously and not preferred

after 48 hours if the patient is hemodynamically stable except for ongoing severe ischemic symptoms and signs.

Indication for invasive strategy for STEMI cases: PCI is the preferred reperfusion strategy in patients with STEMI within 2h up to 24 hours and not preferred for patients present with more than 48 hours and symptoms relieved of symptom onset, provided it can be performed expeditiously. And not preferred after 48 hours after STEMI if the patient is hemodynamically stable except for symptoms of severe ischemic symptoms and signs**.**

Indication for invasive strategy for NSTEMI cases: Early invasive strategy within less than 2 hours is recommended in patients presenting with NSTEMI presentation and with very high-risk stratification including:

1- Cardiogenic shock. 2- Hemodynamic instability. 3- Recurrent/Refractory chest pain despite medical treatment. 4- Life threating arrhythmias. 5- Mechanical Complication of MI. 6- Acute heart failure clearly related to NSTEMI. 7- ST-segment depression>1mm/6leads plus 1mm elevation in AVR and/or V1. OR within 24 hours for high-risk stratification for the following:

1- Established diagnosis of NSTEMI diagnosis. 2- Dynamic new or presumably new contagious ST/T-segment. 3- Resuscitated cardiac arrest without ST-segment elevation or cardiac arrest.4- Grace risk score >140

Coronary Angiography and its role:

Using the dye-filled guiding catheter as a reference, digital coronary angiograms were evaluated offline with an automated edge identification system (Philips Integrin 5000, Netherlands).

Cases admitted to PCI in acute settings was the standard base of treatment for all cases according to European society of cardiology for cases presented with STEMI and very high-risk group NSTEMI.

Strategy for following-up the patients:

During hospital-in stay: Symptoms of ischemia, Vital signs of the patient (Blood pressure, heart rate, Respiratory rate, temperature). Laboratory tests (CBC, Serum creatinine, CKMB). Serial ECG. Echocardiograph before discharge or even suspect cardiac mechanical complications. Also, the medical treatment in CCU and follow up complications.

After discharge: by routine visit outpatient clinic after 4 weeks after discharge for the following: Smoking cessation. LDL goal <55mg/dl, TG < 150 mg/dl. Glycated A1C <7%. Blood pressure target below 130/85. Clinical cardiac symptoms. Weight control.

STATISTICAL ANALYSIS

The statistical package for social sciences (SPSS 27.0, IBM/SPSS Inc., and Chicago, IL) was used to examine the results statistically. Two different kinds of statistical analysis were carried out: Data normalcy as a test of normalcy, the Kolmogorov-Smirnov test was employed; if the significance level is higher than 0.05, then normality is presumed. Characteristic statistics for parametric numerical data, the mean ± standard deviation (SD) was utilized, but for non-parametric numerical data, the median and range were employed. For non-numerical data, frequency and percentage were employed. Statistical inference or analysis. The statistical significance of the difference between the means of the two research groups was evaluated using the Student T Test. The statistical significance of the difference in a non-parametric variable between the two research groups was evaluated using the Mann Whitney Test (U test). For continuous data, a one-way ANOVA test was employed to determine whether there was a significant difference between more than two groups with normal distributions. The homogeneity of variances and the assumption of normality in each group were confirmed using the Shapiro-Wilk test and Levine's test, respectively. To investigate the association between two or more qualitative variables, the Chi-Square test was employed. The significance level at which the null hypothesis (the hypothesis of no difference) was rejected was indicated by the P-values associated with test statistics. This level was set at 0.05, meaning that P-values ≥ 0.05 are statistically non-significant, P-values < 0.05 are significant, and P-values < 0.01 are highly significant.

RESULTS

Table 1; showed that there was statistically insignificant difference between patients treated with various methods regarding either age or body mass index (non-significantly higher in patients underwent invasive technique). There is a statistically significant difference between patients who received various forms of care regarding heart rate (significantly higher in patients underwent invasive technique). The difference between patients who received different care strategies is not statistically significant regarding risk factors including smoking, family history, comorbid diabetes, hypertension, or dyslipidemia. There is a statistically significant difference between patients who were managed using different strategies regarding hemoglobin level (Statistically higher in patients underwent conservative technique), serum creatinine and CK-MB (statistically lower in patients underwent conservative technique) and positive troponin test (63% of patients underwent conservative technique versus 98.9% of patients underwent invasive technique had positive troponin). There is a statistically significant difference between patients who were managed using different strategies regarding ejection fraction (statistically higher in patients underwent conservative technique). There is no statistically significant difference between patients who received various therapy approaches regarding either LVEDD, LVESD or wall motion index.

Table 2; showed that there was statistically significant difference between patients underwent different management techniques regarding incidence of heart failure (in 7.4% versus 21.1% within conservative and invasive techniques respectively), and MACE (in 18.5% versus 37.8% within conservative and invasive techniques respectively). There is no statistically significant difference between patients who received various therapy approaches regarding incidence of serious arrhythmia or mortality. No one of the studied patients developed cerebrovascular stroke. Eighty patients had STEMI; of them 10 underwent conservative techniques while remaining 70 ones underwent PCI. Sixty-four patients had NSTEMI; of them, 44 patients underwent conservative therapy while twenty patients underwent PCI.

I. STEMI group

Table: 3 There was no statistically significant difference between STEMI patients who received different management strategies regarding those who did not, based on age, BMI, heart rate, or risk factors. There is no statistically significant difference between STEMI patients who received different management strategies regarding those who did not, as measured by LVEDD, LVESD, EF, or wall motion index. There is a statistically significant difference in serum creatinine between patients with STEMI who received different management strategies (significantly higher in individuals who underwent invasive technique). There is no statistically significant difference between STEMI patients who had various management strategies regarding test data (hemoglobin troponin, or CK-MB). There is no statistically significant difference between STEMI patients treated with different approaches regarding ST segment elevation. Table 3; showed that there was statistically non-significant difference between patients with STEMI who underwent different management techniques regarding incidence of serious arrhythmia, heart failure, Reinfarction, MACE or mortality. No one of the studied patients developed cerebrovascular stroke.

II. NSTEMI group

Table: 4 There was statistically significant difference between patients with NSTEMI who underwent different management techniques regarding age, and heart rate (both are significantly higher in patients underwent invasive technique). There is no statistically significant difference between STEMI patients who received different management strategies compared to those who did not, based on BMI or risk factors. There is a statistically significant difference between patients with N0n-stemi who were managed using different approaches regarding both serum creatinine (significantly higher in patients underwent invasive technique) and hemoglobin (significantly lower in patients underwent invasive technique). There is no statistically significant difference between patients with NSTEMI who underwent

different therapeutic strategies regarding their laboratory data (troponin or CK-MB) analyzed. There is a statistically significant difference between patients with NSTEMI who were managed using different approaches regarding ECG abnormalities. ST segment depression prevailed in 4.5% within conservative technique versus 95% within invasive technique. T wave depression prevailed 65.9% within conservative technique versus 5% within invasive technique. There is a statistically significant difference between patients with NSTEMI who were managed using different approaches regarding LVESD (significantly lower in conservative technique) and EF (significantly higher in conservative technique). There is no statistically significant difference between STEMI patients who had different management strategies compared to those who had LVEDD or wall motion index.

Table 4; showed that there was a statistically significant difference between patients with NSTEMI who were managed differently regarding incidence of serious arrhythmia, heart failure, and MACE. Heart failure occurred in 6.8% versus 45% within patients who underwent conservative and invasive techniques. MACE occurred in 13.6% versus 55% within patients underwent conservative and invasive techniques. Serious arrhythmia occurred in 9.1% versus 50% within patients underwent conservative and invasive techniques. There is statistically non-significant difference between patients with NSTEMI who underwent different management techniques regarding mortality. No one of the studied patients developed cerebrovascular stroke.

III. Predictors of MACE

Table 5; showed that there was statistically significant difference between both groups regarding the incidence of MACE and hypertension (43% of patients with no MACE versus 61.4% of those with MACE had hypertension), and heart rate (significantly higher in patients with MACE). There is statistically non-significant difference between incidence of MACE and either age, BMI, or other risk factors. There is statistically significant difference between incidence of MACE regarding both hemoglobin (significantly lower in patients with MACE). There is statistically non-significant difference between incidence of MACE and studied laboratory data (creatinine, troponin, or CK-MB). There is a statistically significant difference between incidence of MACE and ECG abnormalities. ST segment depression prevailed in 10% within No MACE patients versus 25% in patients with MACE. T wave depression prevailed in 26% of No MACE patients versus 9.1% in patients with MACE. There is a statistically significant difference between incidence of MACE and, LVESD (significantly lower in patients with MACE) and EF (significantly higher in conservative technique). There is statistically non-significant difference between incidence of MACE and either LVEDD, or wall motion index. There is statistically non-significant difference between incidence of MACE and diagnosis. About 61%, 34.1% and 4.5% of patients with MACE had STEMI, NSTEMI or stable angina. There is a statistically significant difference between incidence of MACE and management technique. About 23%, and 77.3% of patients with MACE underwent conservative and invasive management techniques.

On doing multivariate regression, being hypertensive, increasing heart rate, conservative management, anterior, inferior ST segment elevation, and ST segment depression, non-significantly increased risk of MACE by 2.214, 1.035, 2.02, 2.524, 2.036, and 2.638 folds respectively. Increasing hemoglobin level, LVESD, and wave depression decreases the risk of MACE. Increased ejection fraction significantly decreases that risk as shown table 6.

Being hypertensive, increasing heart rate significantly increased risk of MACE by 2.738 and 1.06 folds respectively. Increasing hemoglobin level decreases risk of MACE as shown table 7.

Table 1: Baseline characteristics of studied groups of patients treated by conservative versus invasive methods of treatment.

	Conservative technique	Invasive technique	t	p
	Mean ± SD	Mean ± SD		
Age (year)	57.94 ± 7.04	60.14 ± 9.14	-1.619	0.108
BMI (kg/m^2)	26.67 ± 2.58	26.96 ± 2.63	-0.631	0.529
Heart rate (/minute)	84.85 ± 8.03	90 ± 12.1	-3.065	0.003*
LVEDD (cm)	4.82 ± 0.56	4.93 ± 0.5	-1.199	0.232
LVESD (cm)	3.46 ± 0.5	3.59 ± 0.5	-1.496	0.137
EF (%)	56.24 ± 5.82	51.23 ± 8.35	4.231	<0.001**
Wall motion index	1.45 ± 0.27	1.49 ± 0.29	-0.957	0.34
Hemoglobin (g/dl)	13.58 ± 1.08	12.76 ± 1.54	3.716	<0.001**
Serum creatinine mg/dl	1.09 ± 0.19	1.2 ± 0.35	-2.227	0.027*
	Median (IQR)	**Median (IQR)**	**Z**	**p**
CK-MB ng/ml	60(34.75 – 90.25)	90.5(67.75 – 114.25)	-3.874	<0.001**
	N=54 (%)	**N=90 (%)**	**χ^2**	**p**
Troponin (+ve)	34 (63%)	89 (98.9%)	34.97	<0.001**
Smoking	7 (13%)	9 (10%)	0.3	0.584
Family history	40 (74.1%)	73 (81.1%)	0.989	0.32
Diabetes	24 (44.4%)	36 (40%)	0.274	0.6
Hypertension	22 (40.7%)	48 (53.3%)	2.142	0.143
Dyslipidemia	24 (44.4%)	36 (40%)	0.274	0.6

χ^2Chi square test t independent sample t test Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant BMI body mass index IQR interquartile range.

Table 2: Comparison between management techniques; conservative versus invasive technique regarding MACE among all patients

	Conservative technique	Invasive technique	χ^2	p
	N=54(%)	N=90 (%)		
Cerebrovascular stroke	0 (0%)	0 (0%)	0	>0.999
Heart failure	4 (7.4%)	19 (21.1%)	4.722	0.03*
Serious arrhythmia	8 (14.8%)	24 (26.7%)	2.743	0.098
Reinfarction	2 (3.7%)	6 (6.7%)	Fisher	0.71
Mortality	0 (0%)	5 (5.6%)	Fisher	0.157
MACE	10 (18.5%)	34 (37.8%)	5.9	0.015*

χ^2Chi square test t independent sample t test Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant.

Table 3: Comparison between STEMI patients with different management techniques regarding baseline data.

	Conservative technique (Pharmaco-invasive)	Invasive technique	t	p
	Mean ± SD	Mean ± SD		
Age (year)	56.2 ± 11.76	58.59 ± 8.63	-0.78	0.43
BMI (kg/m^2)	25.9 ± 3.35	26.9 ± 2.6	-1.099	0.275
Heart rate (/minute)	90.0 ± 10.8	89.6 ± 11.61	0.242	0.809
LVEDD (cm)	4.8 ± 0.8	4.92 ± 0.49	-0.652	0.517
LVESD (cm)	3.55 ± 0.72	3.54 ± 0.49	0.072	0.942
EF (%)	53.5 ± 8.95	52.44 ± 8.13	0.38	0.705

	Conservative technique (Pharmaco-invasive)	Invasive technique	t	p
	Mean ± SD	Mean ± SD		
Wall motion index	1.43 ± 0.27	1.49 ± 0.29	-0.562	0.37
Hemoglobin (g/dl)	13.89 ± 1.04	12.99 ± 1.49	1.834	0.071
Serum creatinine	0.99 ± 0.11	1.12 ± 0.3	-2.677	0.031*
CK-MB mg/dl	87.5(53.75 – 125)	90(63.5 – 114.25)	-0.16	0.873
	N=10(%)	N=70 (%)	χ^2	p
Troponin (+ve)	9 (90%)	70 (100%)	Fisher	0.125
Smoking	3 (30%)	9 (12.9%)	Fisher	0.168
Family history	7 (70%)	57 (81.4%)	Fisher	0.41
Diabetes	6 (60%)	27 (38.6%)	1.658	0.198
Hypertension	4 (40%)	35 (50%)	Fisher	0.738
Dyslipidemia	2 (20%)	28 (40%)	Fisher	0.306
ST segment: **Anterior ST elevation** **Inferior ST elevation**	 4 (40%) 6 (60%)	 46 (65.7%) 24 (34.3%)	Fisher	0.164
	Conservative technique (Pharmaco-invasive) N=10(%)	Invasive technique N=70 (%)	χ^2	p
Cerebrovascular stroke	0 (0%)	0 (0%)	0	>0.999
Heart failure	1 (10%)	10 (14.3%)	Fisher	>0.999
Serious arrhythmia	4 (40%)	14 (20%)	Fisher	0.22
Reinfarction	1 (10%)	6 (8.6%)	Fisher	>0.999
Mortality	0 (0%)	3 (4.3%)	Fisher	>0.999
MACE	4 (40%)	23 (32.9%)	Fisher	0.726

χ^2Chi square test t independent sample t test Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant BMI body mass index IQR interquartile range.

Table 4: Comparison between NSTEMI patients with different management techniques regarding baseline data.

	Conservative technique (medical treatment)	Invasive technique	t	p
	Mean ± SD	Mean ± SD		
Age (year)	58.34 ± 5.6	65.0 ± 8.95	-3.957	<0.001**
BMI (kg/m^2)	26.85 ± 2.38	27.15 ± 2.8	-0.442	0.66
Heart rate (/minute)	83.68 ± 6.9	93.3 ± 13.45	-3.022	0.006*
LVEDD (cm)	4.83 ± 0.51	4.98 ± 0.52	-1.088	0.281
LVESD (cm)	3.44 ± 0.45	3.77 ± 0.48	-2.648	0.01*
EF (%)	56.86 ± 4.78	47.0 ± 7.88	5.181	<0.001**
Wall motion index	1.45 ± 0.27	1.52 ± 0.3	-0.903	0.37
Hemoglobin (g/dl)	13.51 ± 1.09	11.96 ± 1.46	4.73	<0.001**
Serum creatinine	1.12 ± 0.2	1.44 ± 0.41	-3.378	0.003*
	Median (IQR)	Median (IQR)	Z	p
CK-MB	57(32.5 – 90)	97(80.25 – 113.75)	-3.695	<0.001**
	N=44(%)	N=20 (%)	χ^2	p
Troponin (+ve)	25 (56.8%)	19 (95%)	9.333	0.002*
Smoking	4 (9.1%)	0 (0%)	Fisher	0.3
Family history	33 (75%)	16 (80%)	0.192	0.662

	Conservative technique (medical treatment)	Invasive technique	t	p
	Mean ± SD	Mean ± SD		
Diabetes	18 (40.9%)	9 (45%)	0.094	0.759
Hypertension	18 (40.9%)	13 (65%)	3.195	0.074
Dyslipidemia	22 (50%)	8 (40%)	0.552	0.457
ST segment: **ST segment depression** **T wave depression** **No change**	 2 (4.5%) 29 (65.9%) 13 (29.5%)	 19 (95%) 1 (5%) 0 (0%)	MC	<0.001**
	Conservative technique (medical treatment) **N=34 (%)**	Invasive technique **N=20 (%)**	χ^2	p
Cerebrovascular stroke	0 (0%)	0 (0%)	0	>0.999
Heart failure	3 (6.8%)	9 (45%)	Fisher	0.001**
Serious arrhythmia	4 (9.1%)	10 (50%)	Fisher	0.001**
Reinfarction	1 (2.3%)	0 (0%)	Fisher	>0.999
Mortality	2 (3.7%)	6 (6.7%)	Fisher	0.094
MACE	6 (13.6%)	11 (55%)	12.06	<0.001**

χ^2Chi square test t independent sample t test Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant BMI body mass index IQR interquartile range MC Monte Carlo test.

Table 5: Comparison between management techniques among patients regarding MACE

	No MACE (n=100)	MACE (n=44)	t	p
	Mean ± SD	Mean ± SD		
Age (year)	58.66 ± 7.96	60.82 ± 9.41	-1.416	0.159
BMI (kg/m^2)	26.85 ± 2.3	26.86 ± 3.23	-0.033	0.974
Heart rate (/minute)	86.15 ± 9.27	92.43 ± 13.31	-2.842	0.006*
LVEDD (cm)	4.87 ± 0.51	4.95 ± 0.56	-0.919	0.316
LVESD (cm)	3.75 ± 0.49	3.68 ± 0.51	-2.331	0.021*
EF (%)	55.24 ± 7.07	48.27 ± 7.48	5.351	<0.001**
Wall motion index	1.48 ± 0.28	1.47 ± 0.28	0.212	0.832
Hemoglobin (g/dl)	13.27 ± 1.34	12.61 ± 1.56	2.569	0.011*
Serum creatinine	1.13 ± 0.28	1.21 ± 0.36	-1.325	0.19
	Median (IQR)	Median (IQR)	Z	p
CK-MB	82(49 – 99.75)	90.5(69.25–110.75)	1.798	0.072
	N=100(%)	N=44 (%)	χ^2	p
Troponin (+ve)	**82 (82%)**	**41 (93.2%)**	3.067	0.08
Smoking	10 (10%)	6 (13.6%)	Fisher	0.569
Family history	78 (78%)	35 (79.5%)	0.043	0.835
Diabetes	41 (41%)	19 (43.2%)	0.06	0.807
Hypertension	43 (43%)	27 (61.4%)	4.125	0.042*
Dyslipidemia	39 (39%)	21 (47.7%)	0.958	0.328
ST abnormalities: **Anterior ST elevation** **Inferior ST elevation** **ST segment depression** **T wave depression**	 33 (33%) 20 (20%) 10 (10%) 26 (26%)	 17 (38.6%) 10 (22.7%) 11 (25%) 4 (9.1%)	MC	0.021*

No change	11 (11%)	2 (4.5%)		
Type				
STEMI	53 (53%)	27 (61.4%)	0.866	0.352
Non-STEMI	31 (31%)	15 (34.1%)	0.134	0.714
Unstable angina	16 (16%)	2 (4.5%)	3.665	0.056
Management				
Conservative	44 (44%)	10 (22.7%)	5.9	0.015*
Invasive	56 (56%)	34 (77.3%)		

χ^2Chi square test t independent sample t test Z Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant BMI body mass index IQR interquartile range MC Monte Carlo test.

Table 6: Multivariate analysis of factors associated with MACE.

	β	P	AOR	95% C.I.	
				Lower	Upper
Hemoglobin	-.169	.274	.845	.624	1.143
Ejection fraction	-.114	.004*	.892	.826	.964
Heart rate	.034	.093	1.035	.994	1.077
LVESD (cm)	-.617	.265	.540	.183	1.595
Hypertensive	.795	.083	2.214	.902	5.437
Conservative technique	.703	.347	2.020	.466	8.751
ST abnormalities (No change)		.647			
ST abnormalities (anterior ST elevation)	.926	.406	2.524	.284	22.435
ST abnormalities (inferior ST elevation)	.711	.514	2.036	.241	17.232
ST abnormalities (ST segment depression	.970	.405	2.638	.268	25.937
ST abnormalities (T wave depression)	-.454	.644	.635	.092	4.360

*AOR adjusted odds ratio CI Confidence interval *p<0.05 is statistically significant.*

Table 7: Multivariate backward analysis of factors associated with MACE.

	β	p	AOR	95% C.I.	
				Lower	Upper
Hypertensive	1.007	0.013*	2.738	1.233	6.077
Heart rate	0.058	0.002*	1.060	1.021	1.100
Hemoglobin	-.279	0.037*	0.757	0.582	0.984

AOR adjusted odds ratio CI Confidence interval.
*p<0.05 is statistically significant

DISCUSSION

The current study reported non-statistically significant difference between patients treated with various management techniques as regard age or BMI (non-significantly higher in patients underwent invasive technique).

The current study found statistically significant difference in the incidence of between the two study groups heart failure (7.4% versus 21.1% within conservative and invasive techniques, respectively), and MACE (18.5% versus 37.8% within conservative and invasive techniques respectively). Nonetheless, there was a non-statistically significant variation in the occurrence of serious arrhythmia or mortality. No one of the studied patients developed cerebrovascular stroke.

In disagreement with current findings**,** Savonitto et al [9] study sought to compare initially conservative (IC) strategy versus an early aggressive (EA) strategy for older patients with acute coronary syndromes that do not exhibit ST-segment elevation. Patients in the IC arm had significantly higher cases of severe recurrent ischemia, while those in the EA arm had slightly more incidences of heart failure and death.

Specifically, the current study included 80 patients had STEMI; (of them 10 underwent conservative techniques while remaining 70 ones underwent PCI) and 64 patients had NSTEMI; (of them, 44 patients underwent conservative therapy while twenty patients underwent PCI).

Among STEMI group, the current non-statistically significant difference was detected in the study between conservative group and invasive group as regard age, BMI, heart rate, risk factors, Echo findings (LVEDD, LVESD, EF or wall motion index), laboratory data (hemoglobin, troponin, or CK-MB) and ST segment elevation. But there was statistically significant difference regarding serum creatinine (significantly higher in patients underwent invasive technique).

Also, among STEMI group, the current study found non-statistically significant difference between 2 groups as regard incidence of serious arrhythmia, heart failure, re-infarction, MACE, or mortality. No one of the studied patients developed cerebrovascular stroke.

On the other hand, Rozenfeld et al [10] performed in this retrospective, single-center observational analysis, 530 patients between the ages of >75 years admitted with a diagnosis of acute STEMI. They reported statistically significant difference between conservative group and invasive group as regard admission creatinine (mg %) (Significantly higher in patients underwent conservative technique) and Heart failure but found non-statistically significant difference as regard incidence of LV ejection fraction.

Among NSTEMI group, the current study found statistically significant difference between conservative group and invasive group as regard age, and heart rate (both are significantly higher in patients underwent invasive technique) and both serum creatinine (significantly higher in patients underwent invasive technique) and hemoglobin (significantly lower in patients underwent invasive technique) and ECG abnormalities (ST segment depression and T wave depression) and LVESD (significantly lower in conservative technique) and EF% (significantly higher in conservative technique).

While there was non-statistically significant difference as regard BMI, risk factors, laboratory data (troponin, or CK-MB), LVEDD, or wall motion index.

In disagreement with our findings, Li et al [11] evaluated A meta-analysis of seven published studies indicated that, in comparison to a conservative method, an invasive technique could improve NSTE-ACS patients' short- or long-term survival rates. Furthermore, they did not differentiate between problems, risk factors, age, gender, or the two methods.

Furthermore, a related meta-analysis showed that the benefits of an invasive method for lowering the composite end point of death, MI, or NSTE-ACS re-hospitalization were similar in men and high-risk women [12].

It was discovered that the debate over the invasive vs conservative treatment in NSTE-ACS patients has not ended after ten years. Some studies found that an invasive therapy for NSTE-ACS patients yielded similar advantages to a conservative method, and that it decreased the rates of hospital readmission and Re-infarction, whether deadly or nonfatal, but not all-cause mortality [13].

Other research, however, indicated that as compared to conservative therapy, an intrusive approach decreased the rate of revascularization and was not associated with increases in long-term survival [14].

When CAD patients undergo PCI, major adverse cardiac events (MACE) are a major source of morbidity and mortality. To increase longevity and quality of life, MACE risk factor identification and treatment are essential. The conventional risk factors for CAD, such as systolic blood pressure, age, sex, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and smoking, are naturally linked to the advancement of the disease [15].

Remarkably, the present investigation assessed the factors associated with MACE and discovered a statistically significant distinction between the occurrence of MACE and hypertension (43% of patients with no MACE versus 61.4% of those with MACE had hypertension), heart rate (significantly higher in patients with MACE), hemoglobin (significantly lower in patients with MACE),

ECG abnormalities (ST segment depression prevailed in 10% within No MACE patients versus 25% in patients with MACE, T wave depression prevailed in 26% within No MACE patients versus 9.1% in patients with MACE) and LVESD (significantly lower in patients with MACE) and EF (significantly higher in conservative technique) and type of management technique (About 23%, and 77.3% of patients with MACE underwent conservative and invasive management technique, respectively).

However, Incidence of MACE did not change statistically significantly with either age, BMI, other risk factors, LVEDD, or wall motion index, studied laboratory data (creatinine, troponin, or CK-MB) or diagnosis (STEMI, NSTEMI or stable angina).

Like our findings, In FRISC-II and RITA-3, In the TACTICS-TIMI 18 study, as long as the troponin level was elevated, the advantage of early revascularization was equivalent for men and women. However, only men had a better outcome in the early intrusive arm. On the other hand, low-risk men did not benefit or suffer any harm from early revascularization therapy was more effective in high-risk women, but low-risk women had poorer outcomes, including a higher risk of serious bleeding [16].

In contrast with our findings, the use of an early invasive technique, as opposed to an initial conservative strategy, is currently supported by a meta-analysis of recent randomized trials including patients with NSTEMI to improve long-term mortality and morbidity [17].

Specifically, the current study, on doing multivariate regression, found that being hypertensive, increasing heart rate, conservative management, anterior, inferior ST segment elevation, and ST segment depression, non-significantly increased risk of MACE by 2.214, 1.035, 2.02, 2.524, 2.036, and 2.638 folds respectively.

While, increasing hemoglobin level, LVESD, and wave depression decreases risk of MACE. Increased ejection fraction significantly decreases that risk.

On Multivariate backward analysis, the current study found that being hypertensive, increasing heart rate significantly increased risk of MACE by 2.738 and 1.06 folds respectively. Increasing hemoglobin level decreases risk of MACE.

The study of Diaz et al [18] demonstrated that, in individuals with suspected or confirmed CAD, HR was a predictor of all-cause and CV mortality independent of other established risk factors such smoking, diabetes, and hypertension.

Additionally, Tsai et al [15] study found triple vessel disease, using multivariate Cox regression analysis, was one of the independent variables linked to the development of MACE hypertension, and eGFR in ACS patients.

The discrepancies in the findings of the above-mentioned studies can be explained by several factors including differences in sample size, follow up period, the etiology of ACS, dissimilar populations, and selection of patients.

CONCLUSIONS

According to the findings of our research, it is possible to conclude "Compared to the non-invasive approach, the invasive option is associated with worse outcomes in patients with NSTEMI. The non-invasive strategy is linked to more favorable results than the invasive choice. While the outcomes for those with STEMI are not significantly different between the two methods.

We recommend future research on NSTEMI patients that should be expanded to include additional cases from various cardiology centers. These investigations ought to assess long- and intermediate-term results.

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