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Invasive versus Conservative Treatment Approach among Older Adult Patients Admitted with Acute ST-Segment Elevation Myocardial Infarction

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Background: Primary percutaneous coronary intervention (PCI) is the preferred treatment strategy for patients with ST-elevation myocardial infarction (STEMI); however, its efficacy remains unclear in very older adult patients with STEMI. **Methods:** This retrospective single-center observational study included 530 patients aged >75 years admitted to Tel Aviv Sourasky Medical Center with a diagnosis of acute STEMI. Primary PCI was performed for patients with symptoms ≤12 hours in duration, while the other patients were conservatively treated. We evaluated 30-day mortality and complications occurring during hospitalization based on data from patient records. **Results:** Among the study patients, only 28/530 (5%) were conservatively treated. In-hospital complications, including the use of inotropes or intra-aortic balloon counterpulsation and the need for mechanical ventilation, did not differ significantly between the groups. The only parameter that showed a trend toward significance was the incidence of heart failure during hospitalization (p=0.042). The risk for 30-day mortality was substantially higher in the conservative treatment group than in the invasive treatment group (27% vs. 10%; p = 0.02). **Conclusion:** Our data suggested that despite concerns regarding the safety of the primary PCI strategy in the older adult STEMI population, this treatment strategy was associated with a survival benefit.

Key Words: ST elevation myocardial infarction, STEMI, Alder adults, Conservative treatment, Invasive treatment

INTRODUCTION

The average life expectancy of the world's population has dramatically increased in the past century. This trend is accompanied by a corresponding increase in the prevalence of ischemic heart disease in older adults.[1-3] Older age is independently associated with atherosclerosis and cardiovascular events.[4]

In clinical practice, patients aged > 75 years account for approximately 35% of all patients with acute coronary syndrome (ACS)[5,6]; however, only a minority of published clinical trials have included older adult patients.[7]

Primary percutaneous coronary intervention (PCI) is the preferred treatment strategy for patients with ST-elevation myocardial infarction (STEMI).[8,9] However, its efficacy remains unclear in older patients with STEMI because of their frailty and comorbidities, which are associated with a higher incidence of complications and mortality.[10,11] According to the current European Society of Cardiology and American College of Cardiology Foundation/American Heart Association STEMI guidelines, there is no upper age limit for reperfusion therapy, especially primary PCI.[12,13]

This study examined the effect of primary PCI versus conservative treatment in older adult patients hospitalized for STEMI.

MATERIALS AND METHODS

Patient Population

We performed this retrospective single-center observational study at Tel Aviv Sourasky Medical Center, a tertiary referral hospital

with around-the-clock primary PCI capabilities.

Among all consecutive patients with STEMI who were admitted to the cardiac intensive care unit (CICU) between January 2007 and June 2020, we included only those aged > 75 years. The cutoff age of 75 years was based on previous studies of the geriatric population that defined patients aged ≥ 75 years as older adults.[14] STEMI was diagnosed according to published guidelines, including typical history of chest pain, diagnostic electrocardiographic changes, and serial elevation of cardiac biomarker levels.[15,16] Primary PCI was performed in patients with symptoms lasting ≤ 12 hours and those with symptoms lasting 12–48 hours with pain at the time of admission. Symptom duration was defined as the time from symptom onset to admission to the emergency room or catheterization laboratory. The door-to-balloon time was defined as the time (in minute) between a patient's arrival at the hospital (taken from the computerized patient file) and the first balloon inflation or device deployment in the culprit artery, as documented in the patient's medical record. All patients received dual antiplatelet therapy. The conservatively treated patients received additional anticoagulation for up to 7 days following CICU admission. Patients undergoing PCI were administered additional anticoagulation only when clinically indicated (e.g., the presence of atrial fibrillation). Baseline demographics, cardiovascular history, clinical risk factors, treatment characteristics, and laboratory test results were retrieved from the hospital's electronic medical records. Patient records were evaluated for complications that occurred during hospitalization, including cardiogenic shock requiring inotropes or intra-aortic balloon counterpulsation (IABC) insertion, mechanical ventilation, heart failure, clinically significant tachyarrhythmias, bradyarrhythmias requiring a pacemaker, and major bleeding (requiring blood transfusion). Bleeding was defined according to the Bleeding Academic Research Consortium criteria.[17] IABC insertion was performed in patients with cardiogenic shock or mitral regurgitation. Thirty-day and 1-year mortality were determined from computerized records of the population registry bureau and were available for all included patients. The Tel Aviv Sourasky Medical Center (No. Tlv 16-0224) approved the study protocol and waived the requirement for informed consent.

This study complied the ethical guidelines for authorship and publishing in the *Annals of Geriatric Medicine and Research*.[18]

Statistical Analysis

All data were summarized and presented as mean ± standard deviation or medians (25%–75% interquartile ranges) for continuous variables and as number (percentage) of patients in each group for categorical variables. Continuous variables were compared using independent sample t-tests for normally distributed data and the Kruskal-Wallis tests for non-normally distributed variables. Fisher exact tests were used to compare categorical variables.

Predictors of 30-day and 1-year mortality were determined using univariate and multivariate logistic regression models. The models were adjusted for all baseline variables that differed significantly between the treatment groups. The models included the following variables: age, sex, history of hypertension, diabetes mellitus, hyperlipidemia, family history of coronary artery disease, smoking, myocardial infarction, admission creatinine level, left ventricular ejection fraction (LVEF), and time to the emergency department. Hazard ratio (HR) and corresponding 95% confidence interval (CI) for the association between treatment assignment and 1-year mortality were estimated using the Cox proportional hazards model, which included the aforementioned independent variables. Data were censored at death, 1 year after the index date, or at the end of the study period. Kaplan-Meier survival curves were compared using log-rank tests.

Given the inherent bias in the choice of patients receiving primary PCI and the resulting differences in baseline patient characteristics, we made comparisons after propensity score nearest-neighbor matching using a logistic regression model in a 2:1 ratio. Due to the requirement for complete data in the matching process, we performed this analysis only for 30-day mortality. A two-tailed p-value < 0.05 was considered significant for all analyses. All statistical analyses were performed using R Statistical Software (version 3.6.1; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

The study population comprised 530 patients. Among those patients, only 28 (5%) were conservatively treated. Among those patients, PCI was waived due to advanced renal failure (15 patients), symptom duration > 12 hours and asymptomatic at the time of presentation (10 patients), and advanced dementia (3 patients).

The baseline characteristics of the patients stratified according to treatment strategy are shown in Table 1. Patients conservatively treated were older (mean age, 86 ± 6.3 vs. 82 ± 4.9 years; p < 0.001) and more commonly female.

In addition, creatinine levels at admission were higher among patients in the conservative treatment group. Table 2 demonstrates the in-hospital outcomes of the patients in the two groups. Patients conservatively treated were more likely to develop heart failure—12 (46%) vs. 122 (25%), p = 0.042—bradycardia, ventricular tachycardia, and ventricular fibrillation than those invasively treated. However, the use of inotropes or IABC and the need for mechanical ventilation were almost equal between the two groups. Moreover, bleeding and acute kidney injury (AKI) occurrence

Table 1. Baseline patient characteristics

	Invasive treatment group	Conservative treatment group	p-value
Age (y)	82.2±4.9	86.4±6.3	<0.001*
Sex			0.016*
Male	284 (59.8)	9 (33.3)	
Female	191 (40.2)	18 (66.7)	
Hypertension	342 (72.0)	21 (77.8)	0.522
Diabetes mellitus	146 (30.7)	12 (44.4)	0.147
Hyperlipidemia	262 (55.2)	12 (44.4)	0.435
Family history of coronary artery disease	21 (4.4)	0 (0)	0.631
Smoking history	95 (20.0)	3 (11.1)	0.327
Past myocardial infarction	101 (21.3)	6 (22.2)	0.649
Admission creatinine (mg%)	1.1 (0.4)	1.3 (0.5)	0.003*
LV ejection fraction	45.0 (10.0)	40.0 (15.0)	0.163
Time to emergency department (min)	180.0 (630.0)	900.0 (1380.0)	0.148

Values are presented as mean±standard deviation or number (%). Admission creatinine, LV ejection fraction, and Time to emergency department are presented as median (interquartile range).
LV, left ventricle
*p<0.05.

Table 2. Complications stratified according to the treatment group

Complication	Invasive treatment group	Conservative treatment group	p-value
30-day mortality	48 (9.7)	7 (26.9)	0.021*
1-year mortality	66 (13.3)	9 (34.6)	0.007*
IABC/inotropes treatment	53 (10.7)	3 (11.5)	1.000
Mechanical ventilation	50 (10.1)	3 (11.5)	0.753
Heart failure	122 (24.5)	12 (46.2)	0.042*
Bradycardia	48 (9.7)	3 (11.5)	0.745
VT/VF	36 (7.2)	4 (15.4)	0.153
In-hospital CABG	11 (2.2)	0 (0.0)	1.000
Acute kidney injury	110 (22.1)	6 (23.1)	1.000
Bleeding	54 (10.9)	3 (11.5)	1.000

Values are presented as number (%).
IABC, intra-aortic balloon counterpulsation; VT, ventricular tachycardia; VF, ventricular fibrillation; CABG, coronary artery bypass graft.
*p<0.05.

were almost equal between the two groups—54 (10.8%) vs. 3 (11.5%), p=1.00 and 110 (22.1%) vs. 6 (23.1%), p=1.00, respectively (Table 2).

The risks for 30-day and 1-year mortality were significantly higher in the conservative treatment group than in the invasive treatment group—7 (27%) vs. 48 (10%), p=0.02 and 9 (35%) vs. 66 (14%), p=0.007, respectively (Table 2, Fig. 1).

In the univariate analysis, conservative treatment was associated with increased 1-year mortality—hazard ratio (HR)=2.7; 95% confidence interval (CI), 1.34–5.41; p=0.005 (Table 3).

However, this association was not statistically significant in the multivariate analysis. In the multivariate analysis, the independent variables associated with mortality risk in the first year after STEMI were age, admission creatinine level, and LVEF. After 2:1 matching, we identified 81 patients, among whom 27 (33%) were conservatively treated and 54 (67%) underwent primary PCI. The patient characteristics did not differ significantly between the groups after matching.

In a multivariate analysis using the matched cohort, conservative treatment was associated with a higher mortality risk in the first 30 days after STEMI—HR=27.2; 95% CI, 2.53–1026.63; p=0.023 (Table 4).

DISCUSSION

This observational study of older adult patients with STEMI

demonstrated that invasive primary treatment is associated with better outcomes. Older adults are a heterogeneous group of patients with marked differences in chronological and biological age, which are explained by comorbidities and biological situations such as frailty.[19] Mortality owing to ACS at all ages has dramatically decreased during the last decade due to aggressive risk factor reduction, optimized medical therapy, and early coronary revascularization. However, not all therapeutic approaches are equally suitable for all age groups. More consideration is needed in the older adult population to select a treatment strategy based on procedural risks.[20]

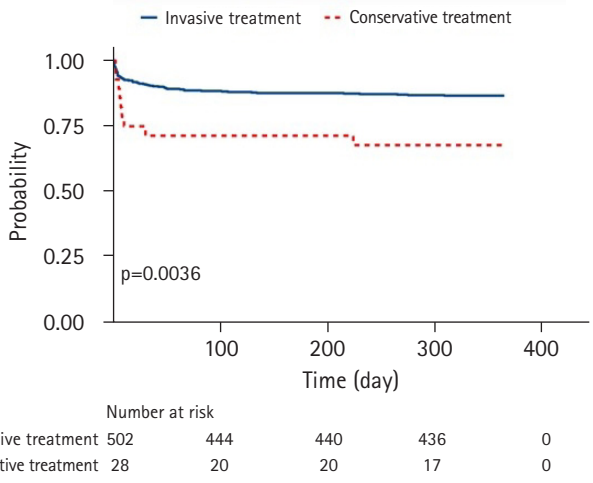

Fig. 1. Kaplan-Meier plot for survival in the first year following ST-elevation myocardial infarction by treatment strategy.

The treatment approaches for older adult patients diagnosed with STEMI have recently changed. The use of primary PCI in older adults has consistently increased globally. Until 2010, only 17% of older adult patients with STEMI had been treated with a primary PCI strategy.[21,22] In comparison, 95% of these patients were treated with a primary PCI strategy at our medical center in 2020, and a similar trend was demonstrated in the United States, with a shift from 19.7% in 2007 to 31.2% in 2010. These numbers have significantly increased worldwide over the last decade.[23]

Current clinical guidelines for STEMI in older adults state that there is no upper age limit for reperfusion, especially with primary PCI, and recommend that the decision regarding treatment strategy should balance ischemic risk and bleeding risk.[24] Previous studies have demonstrated that PCI reduces in-hospital mortality, even in STEMI patients aged ≥80 years. Despite existing guidelines and evidence for mortality benefits from other registries, there remains uncertainty about the use of reperfusion strategies in older adults due to concerns of higher periprocedural complication risk in this population, especially contrast nephropathy and bleeding.[22] Primary PCI among older adult patients was associated with consistent rates of major bleeding events (3%–5%) and intracranial hemorrhages (1.4%).[2,3,25] Periprocedural bleeding is also a major determinant of poor prognosis, including myocardial in-

Table 3. Associations between treatment strategy (conservative vs. primary percutaneous coronary intervention) and survival during the first year following STEMI

	All	Univariable		Multivariable	
		HR (95% CI)	p-value	HR (95% CI)	p-value
Age (y)	82.5±5.1	1.10 (1.05–1.14)	0.001	1.07 (1.02–1.13)	0.006
Sex					
Male	312 (100)	-		-	
Female	218 (100)	1.35 (0.86–2.11)	0.195	1.32 (0.79–2.23)	0.289
Hypertension	384 (100)	1.25 (0.74–2.12)	0.411	1.18 (0.62–2.27)	0.612
Diabetes mellitus	174 (100)	1.39 (0.88–2.20)	0.160	0.97 (0.54–1.73)	0.912
Hyperlipidemia	292 (100)	1.01 (0.64–1.59)	0.955	0.89 (0.50–1.57)	0.690
Family history of coronary artery disease	24 (100)	1.23 (0.45–3.36)	0.688	1.29 (0.40–4.23)	0.670
Smoking history	101 (100)	0.69 (0.36–1.30)	0.250	0.81 (0.41–1.58)	0.532
Past myocardial infarction	118 (100)	1.09 (0.64–1.85)	0.750	1.02 (0.55–1.86)	0.959
Admission creatinine (mg%)	1.3±0.6	1.56 (1.31–1.85)	0.001	1.70 (1.32–2.19)	0.001
LV ejection fraction	44.7±8.9	0.92 (0.90–0.95)	0.001	0.93 (0.91–0.96)	0.001
Time to emergency department (min)	543.1±853.9	1.00 (1.00–1.00)	0.260	1.00 (1.00–1.00)	0.675
Treatment group					
Invasive	502 (100)	-		-	
Conservative	28 (100)	2.70 (1.34–5.41)	0.005	1.26 (0.51–3.09)	0.614

Values are presented as mean±standard deviation or number (%).
STEMI, ST-elevation myocardial infarction; LV, left ventricle; HR, hazard ratio; CI, confidence interval.

Table 4. Associations between treatment strategy (conservative vs. primary percutaneous coronary intervention) and survival during the first 30 days following STEMI in the matched-cohort population

	No	Yes	Univariable		Multivariable	
			OR (95% CI)	p-value	OR (95% CI)	p-value
Age (y)	85.2±6.1	86.9±6.6	1.05 (0.95–1.16)	0.385	0.99 (0.78–1.25)	0.950
Sex						
Male	22 (91.7)	2 (8.3)	-		-	
Female	47 (82.5)	10 (17.5)	2.34 (0.56–16.07)	0.298	42.33 (1.80–6368.52)	0.067
Hypertension	49 (83.1)	10 (16.9)	2.04 (0.48–14.05)	0.384	0.35 (0.02–5.01)	0.436
Diabetes mellitus	29 (85.3)	5 (14.7)	0.99 (0.27–3.40)	0.981	0.38 (0.02–4.26)	0.457
Hyperlipidemia	31 (81.6)	7 (18.4)	1.72 (0.50–6.30)	0.394	4.04 (0.53–43.47)	0.197
Family history of coronary artery disease	0 (0)	1 (100)	NA		NA	
Smoking history	14 (100)	0 (0)	NA		NA	
Past myocardial infarction	13 (81.2)	3 (18.8)	1.44 (0.29–5.63)	0.622	0.32 (0.01–3.52)	0.409
Admission creatinine (mg%)	1.3±0.7	2.3±2.4	1.69 (1.05–3.24)	0.067	3.04 (1.33–14.18)	0.047
LV ejection fraction	43.9±8.6	36.2±9.1	0.90 (0.81–0.97)	0.011	0.80 (0.60–0.94)	0.038
Time to emergency department (min)	1140.6±1798.9	772.5±867.3	1.00 (1.00–1.00)	0.496	1.00 (1.00–1.00)	0.366
Treatment group						
Invasive	49 (90.7)	5 (9.3)	-		-	
Conservative	20 (74.1)	7 (25.9)	3.43 (0.98–12.83)	0.055	27.18 (2.53–1026.63)	0.023

Values are presented as mean±standard deviation or number (%).
STEMI, ST-elevation myocardial infarction; LV, left ventricle; OR, odds ratio; CI, confidence interval; NA, not available.

farction, procedure failure, and all-cause mortality in older patients undergoing primary PCI.[26]

Older adults are more susceptible to the detrimental effects of bleeding due to hypovolemia, hypoxia, reduced oxygen-carrying capacity, and hypotension.[27] Moreover, chronic kidney disease (CKD) is more prevalent in older people and increases the risk of contrast-induced nephropathy.[28] CKD may also lead to the overdosing of antithrombotic drugs and an increased risk of bleeding.[29]

Renal dysfunction is generally associated with a higher mortality rate in patients with STEMI who undergo primary PCI.[30] Several studies have also shown that functional status is strongly associated with mortality.[31] Therefore, a clinical frailty assessment may improve patient selection for primary PCI. In the older adult population, a delay in the arrival time to the hospital from symptom onset may be related, at least in part, to cognitive decline and alterations in perception and reaction to pain.[32]

In this study, we examined patients aged >75 years who were more likely to have comorbidities that could affect their prognosis, including diabetes mellitus, hypertension, previous myocardial infarction, previous heart failure symptoms, and CKD.[33] Previous studies have also shown that patients of these ages tend to develop more complications.[34-36] However, we observed a higher risk of clinical heart failure and 30-day mortality in the conservative treatment group (27%) than in the invasive treatment group (10%). The findings were similar when we examined 1-year mortality (35% vs. 14%).

These findings suggest that an invasive strategy should be the default strategy in older adult patients with STEMI and that older age should not limit the use of reperfusion therapy, especially primary PCI. Nevertheless, as older adult patients are likely to have numerous comorbidities, functional and cognitive status must be assessed before determining a treatment strategy.

The main strengths of our study are that it was based on real-world data and included unselected consecutive patients with STEMI admitted to our hospital over 13 years. Our study had several limitations. First, as an observational study, it was subject to confounding factors. For instance, there was a selection bias in choosing the primary PCI strategy. Thus, conservative treatment may be chosen for older and sicker patients. This limitation was addressed by propensity score matching; however, residual bias could not be excluded. Second, we had no information regarding the patients' status on admission, which could have affected the treatment decision. Although our results demonstrated the survival advantage of primary PCI, owing to the small number of patients in the conservative treatment arm, the study was not powered to demonstrate differences in other outcomes between the groups. Third, this was a single-center clinical study, which could have caused a selection bias. Fourth, accurate survival analysis could be limited by the relatively small number of patients and adverse

events. Finally, as the population registry bureau did not include information about the cause of death, we could not differentiate between cardiac and noncardiac deaths in this population.

In conclusion, our findings suggested that despite concerns regarding the safety of the primary PCI strategy in the population of older adults with STEMI, this treatment strategy is associated with a survival benefit. Further studies are required to determine the best treatment approach for this population.

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CONFLICT OF INTEREST

The researchers claim no conflicts of interest.

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None.

AUTHOR CONTRIBUTIONS

Conceptualization, KLR, LL; Data curation, KLR, LL; Investigation, KLR; Methodology, KLR, LL, YS; Project administration, IM, SM; Supervision, SB, YS; Writing original draft, KLR, LL; Writing review and editing, YS, KLR, LL.

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