Clinical Presentation and Outcomes in Real-Life Management of Elderly Patients Aged ≥75 Years Presenting with Acute Myocardial Infarction

**ABSTRACT**

**Background:** The aim of this study was to provide insight into the real-life clinical presentation and outcomes of the elderly presenting with acute myocardial infarction from the Turkish Myocardial Infarction registry database.

**Methods:** TURKMI was a nationwide, multicenter, observational, 15-day snapshot registry conducted to address the management of acute myocardial infarction patients admitted to percutaneous intervention-capable hospitals. The present analysis included the comparison of consecutively enrolled acute myocardial infarction patients aged ≥75 and <75 years.

**Results:** Of the overall 1930 patients, 362 patients were aged ≥75 years. Elderly patients were more likely to have hypertension and renal failure and less likely to have hypercholesterolemia. Elderly patients were admitted to hospitals almost 1 hour later mainly due to a late call to emergency medical service. At discharge, medical therapies were significantly less prescribed to the elderly. The proportion of patients undergoing coronary angiography was significantly lower in elderly (81.8% vs. 96.4%, P < .001). Both in-hospital and 1-year mortality were significantly higher in elderly patients (9.1% vs. 2.7% and 22.7% vs. 5.8%, P < .001 respectively). The adjusted risk of 1-year mortality was 4-fold in elderly (hazard ratio and 95% CI 4.0 [2.9-5.6], P < .001). In multivariate analysis, every 5-beat/min increase in heart rate increased mortality by 7%. Higher heart rate and use of antiplatelet agents on admission were predictors of mortality in elderly.

**Conclusion:** In real-life settings, elderly patients presenting with acute myocardial infarction are prone to prolonged total ischemic time and are subjected to less-intensive medical treatment and interventional approaches. Besides age, the increased heart rate could be the major determinant of mortality.

**Keywords:** Acute myocardial infarction, coronary artery disease, preventive cardiology, PTCA/PCI

**INTRODUCTION**

Age is an independent risk factor for adverse events after myocardial infarction (MI), and mortality rates gradually increase in elderly patients. However, elderly patients have been often underrepresented in randomized clinical trials. Despite improvements in early revascularization and medical therapy in MI, evidence-based medical treatment and revascularization remain inadequate in elderly MI patients compared to younger patients. Moreover, elderly individuals are subjected to more conservative treatment strategies contrarily to the recommendations of the guidelines.

The course of acute MI in elderly patients includes significant differences from the non-elderly patients. Diagnosis, treatment, and follow-up after discharge include various difficulties. Both the impact of co-morbidities and the real benefits of the interventions are not clear. Elderly is less likely to receive coronary angiography after MI; however, the specific subjects for the less-aggressive approach are not well defined. On the other hand, short-term clinical outcomes were decreased in these elderly patients owing to these less-optimal therapies. The aim of our study was to present the course of MI including variations in hospital admissions,
risk factors, co-morbidities, and antiplatelet regimen in elderly population in a nation-wide real-life clinical data and to determine in-hospital and 1-year mortality in this particular population.

**METHODS**

**Study Population**

The present study is generated from the nationwide TURKMI registry which was conducted to assess the management of patients with acute MI. Of note, TURKMI (clinicaltrials.gov NCT04241770) was a national, multicenter, observational study conducted in 50 percutaneous intervention (PCI)-capable cardiology centers selected from the regions according to their sampling weight. Study protocol was approved by the Ethics Committee (No: 2018-46; Date: October 09, 2018). Written informed consent was obtained from all participants. The present analysis included the comparison of those ≥75 years with younger (<75 years [non-elderly group]) consecutively admitted with acute MI to the participating hospitals.

According to TURKMI protocol, inclusion criteria were (1) being hospitalized within 48 hours from the onset of symptoms of the index event; (2) having a final (discharge) diagnosis of acute MI (either ST-elevation MI [STEMI] or non-ST-elevation [NSTEMI]) with positive troponin levels, and (3) signed informed consent. Patients unwilling or unable to consent were excluded. Patient demographic and medical history data, presenting symptoms, admission mode (self-transport, by ambulance, or transfer from other hospitals), in-hospital clinical course including cardiac medications and interventional procedures, and 1-year mortality were obtained prospectively. For the diagnosis of MI, the third universal definition was used, detail regarding MI definition is described elsewhere.

**Definitions and Outcomes**

All treatment decisions were based according to patients’ clinical settings and attending clinicians’ decisions. All definitions of risk factors and co-morbidities were described in detail in the design article of the TURKMI study. Hypertension was defined as blood pressure ≥140/90 mm Hg and/or patients taking antihypertensive therapy before MI. Hypercholesterolemia was also termed as fasting total cholesterol ≥200 mg/dL or low-density lipoprotein (LDL) cholesterol ≥130 mg/dL or taking any cholesterol-lowering drugs. Obesity was described according to the body mass index ≥30 kg/m². Diabetes mellitus (DM) was defined as the fasting glucose levels ≥126 mg/dL, glycated hemoglobin more than 6.5% where available, or a history of diabetes diagnosis/treatment. If the patient ever smoked actively before MI, he or she was termed to be a smoker. Other co-morbidities like atrial fibrillation, chronic kidney disease, peripheral arterial disease, and family history of premature coronary artery disease were defined in detail elsewhere. In-hospital death (cardiovascular or other reasons), non-fatal MI, stroke, coronary or peripheral revascularization, emergency department visit due to chest pain or dyspnea, hospitalization for heart failure was assessed during hospitalization and at the end of the first month. All-cause mortality of the elderly population was also assessed 1 year after the index event.

**Statistical Analysis**

Categorical variables were presented as the number and percentage and were compared using the chi-square test, Fisher’s exact test, or the Mantel–Haenszel test between the independent groups such as gender and risk categories. These variables were given as the mean ± standard deviation or median and interquartile range and were compared using an independent t-test or the Mann–Whitney U test. The Kolmogorov–Smirnov test was used for the normal distribution of continuous variables. Comparison of the cumulative mortality risk between patients ≥75 years old or younger was made using the Kaplan–Meier method and compared with a log-rank test. Multiple analysis was performed with stratified Cox regression analysis, in which the diagnosis (STEMI or NSTEMI) was included in the model as a stratum. Several models were created. In the first model (baseline characteristics model), age category, sex, history of MI/coronary or peripheral revascularization, emergency department visit due to chest pain or dyspnea, hospitalization for heart failure was assessed during hospitalization and at the study center, and acetylsalicylic acid use at baseline were included in the model. To be able to consider the angiographic characteristics, the second and the third models were performed in patients who underwent coronary angiography (n = 1808). The second model included the variables of PCI (PCI performed or not performed) and the number of vessels (single vessel or multivessel), along with the variables included in the baseline model. In order to limit the variables included in the model, the number of vessel variables was replaced by the variable of left main involvement in the third model. And the last two models were compared using the Akaike information criterion (AIC). Proportional hazard assumption was assessed with log-minus-log plots and testing the Schoenfeld residuals. Log linearity was assessed by plotting Martingale residual. Analyses were conducted using Statistical Package for the Social Sciences 18.0 for Windows and Stata, and a P value of <.05 was considered significant.

**RESULTS**

Of the 1930 patients included in the TURKMI study, 362 patients aged ≥75 years (18.7%) consisted of our study population. Non-ST-elevations were more common both in elderly and non-elderly patients compared to STEMI (NSTEMI vs.
STEMI: 66.9% vs. 33.1% in the elderly and 60.8% vs. 39.2% in the non-elderly groups, \( P < .001 \).

**Baseline Characteristics**

Table 1 depicts the baseline characteristics including the laboratory measurements of the elderly patients in comparison to non-elderly. The proportion of women was higher in the elderly MI patients (46.4% vs. 21.4%, \( P < .001 \)). For risk factors, only the proportion of hypertension was higher in the elderly, hypercholesterolemia, obesity, smoking, and family history of cardiovascular disease (CVD) were all significantly more frequent in the non-elderly group. The proportion of self-reported diabetes was similar in the 2 groups. Estimated glomerular filtration rate was also higher in the non-elderly group [85.8 (68.1-101.6) vs. 60.1(45.5-78.8), \( P < .001 \)]. Prior diagnosis of coronary artery disease and CVD was similar between the groups except for atrial fibrillation and heart failure which were more frequent in the elderly patients.

| Table 1. Baseline Characteristics of the Elderly Patients (>75 years of age) in Comparison with the Non-elderly Patients |
|---------------------------------------------------------------|
| **Elderly patients (>75 years)** | **Non-Elderly patients (<75 years)** | **P** |
| n | 362 | 1568 |  
| Age, year (mean ± SD) | 81 ± 5 | 58 ± 10 | <.001 |
| Female, n (%) | 168 (46.4) | 336 (21.4) | <.001 |
| BMI (kg/m²) (mean ± SD) | 26.74 ± 4.2 | 2791 ± 4.19 | <.001 |
| **Risk factors** |  |  |  
| Hypertension, n (%) - Based on patient’s self-report | 234 (64.6) | 721 (46) | <.001 |
| Hypercholesterolemia, n (%) | 89 (32.7) | 526 (43.7) | .001 |
| Diabetes, n (%) - Based on patient’s self-report | 123 (34) | 531 (33.9) | .967 |
| Obesity (BMI ≥ 30 kg/m²), n (%) | 63 (19) | 376 (26.6) | .004 |
| Weight < 60 kg | 41 (12.3) | 43 (2.7) | <.001 |
| Smoking, n (%) | 72 (19.9) | 870 (55.5) | <.001 |
| Family history of CV disease, n (%) | 24 (6.6) | 164 (10.5) | .027 |
| **History of CV disease, n (%)** |  |  |  
| History of coronary artery disease and/or CABG and/or PCI | 107 (29.6) | 443 (28.3) | .620 |
| Myocardial infarction | 58 (16) | 204 (13) | .132 |
| PCI | 55 (15.2) | 284 (18.1) | .188 |
| CABG | 39 (10.8) | 126 (8) | .093 |
| Transient ischemic attack or stroke | 8 (2.2) | 21 (1.3) | .220 |
| Peripheral arterial disease | 4 (1.1) | 13 (0.8) | .542 |
| Heart failure | 14 (3.9) | 31 (2) | .032 |
| Atrial fibrillation | 12 (3.3) | 11 (0.7) | <.001 |
| Valve surgery | 0 (0) | 5 (0.3) | .591 |
| Pacemaker/intracardiac defibrillator | 3 (0.8) | 4 (0.3) | .127 |
| **Concomitant disease, n (%)** |  |  |  
| Cancer | 16 (4.4) | 38 (2.4) | .038 |
| Thyroid disease | 9 (2.5) | 41 (2.6) | .890 |
| Renal failure | 32 (8.8) | 71 (4.5) | .001 |
| Chronic obstructive lung disease | 29 (8) | 66 (4.2) | .003 |
| History of bleeding | 3 (0.8) | 7 (0.4) | .409 |
| **Laboratory findings (mean ± SD)** |  |  |  
| White blood cell (K/mm³) | 10.8 ± 4.3 | 11.6 ± 20.2 | .004 |
| Hemoglobin (g/dL) | 12.8 ± 2.1 | 14.1 ± 2.1 | <.001 |
| Blood glucose (mg/dL) | 136.8 ± 65.2 | 131.3 ± 59.2 | .174 |
| Creatinine (mg/dL) | 1.2 ± 0.7 | 1.1 ± 1.8 | <.001 |
| Total cholesterol (mg/dL) | 1801 ± 47.2 | 196.9 ± 51.5 | <.001 |
| LDL-cholesterol (mg/dL) | 113.9 ± 38.7 | 125.0 ± 42.8 | <.001 |
| HDL-cholesterol (mg/dL) | 42.5 ± 10.5 | 40.9 ± 10.4 | .001 |
| Triglycerides (mg/dL) | 123.5 ± 69.7 | 173.3 ± 127.9 | <.001 |

BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CV, cardiovascular; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.
compared to non-elderly. For concomitant disease, elderly patients were more likely to have renal failure, chronic obstructive pulmonary disease, and cancer.

Of the laboratory evaluation on admission, creatine levels were significantly higher in elderly patients with MI compared to the non-elderly patients (1.21 ± 0.7 vs. 1.09 ± 1.81, *P* < .001). However, white blood cell count and LDL-cholesterol levels were higher in a non-elderly group.

### Admission Symptoms, Mode of Admission, and Timings

Variables related to hospital admissions including symptoms and timings are given in Table 2. Among the admission symptoms, dyspnea was reported significantly more in the elderly patients than non-elderly (30.1% vs. 15.1%, *P* < .001), whereas all other symptoms and admission systolic blood pressure did not differ between the groups. However, heart rate was significantly higher in the elderly group on admission (84.75 ± 19 vs. 81.8 ± 19 bpm, *P* = .001). The mode of admission did not differ between the groups. In elderly patients with STEMI, median total ischemic time was 86 minutes longer than non-elderly population. This delay was mainly due to the late call of the emergency medical services (EMS). In the STEMI patients, door to balloon time was similar between the groups. Also, all the timings of patients with NSTEMI did not differ between the groups.

#### Electrocardiographic Findings on Index Admission

Comparisons of the groups according to electrocardiogram (ECG) findings on index admission are presented in Supplementary Table 1. Abnormal ECG findings such as left bundle branch block, right bundle branch block, non-Q wave MI, non-specific ST/T abnormalities, and higher heart rates were more frequent in elderly patients. Although T wave inversion was similar in both groups, ST-depression in 2 adjacent derivations of ≥1 mm was more common in the elderly group (50.8 % vs. 42.2% *P* = .003). Atrial fibrillation was also more common in the elderly group compared to younger patients (12.7% vs. 4.1% *P* < .001).

### Medications Before Admission and Prescribed at Discharge

All medications before admission and prescribed at discharge are summarized in Table 3. Before hospital admission of the index event, almost 1/3 of the elderly patients were already on acetylsalicylic acid therapy. The proportion of elderly patients on treatment including beta-blockers, Ca
antagonists, nitrates, and angiotensin-converting enzyme (ACE) inhibitors were significantly higher compared to those non-elderly patients at baseline (Table 3). However, the use of lipid-lowering medications was similar between the groups. The evaluation of medications prescribed at discharge revealed that clopidogrel was preferred in 71.2% of elderly patients, while almost half of the non-elderly patients have prescribed ticagrelor (45%). At discharge, beta-blockers, ACE inhibitors, and anti-lipid drugs were significantly less prescribed to the elderly patients compared to those non-elderly. However, calcium antagonists, nitrates, and diuretics were prescribed in the elderly more often. The dual antiplatelet strategy was prescribed less frequently to the elderly group than non-elderly (91.4% vs. 94.5%, P = .032).

**Coronary Angiography and Percutaneous Coronary Intervention**

The proportions of elderly patients either evaluated by coronary angiography or underwent primary PCI were significantly lower than non-elderly (81.8% vs. 96.4%, P < .001 and 33.7% vs. 41.2%, P = .01, respectively) (Table 4). Thrombolysis in myocardial infarction (TIMI)-0 flow after PCI was more frequent in the elderly (5.6% vs. 2.2%, P = .009).

**Complications After the Myocardial Infarction**

All adverse events were more frequently observed in the older age group. Cardiogenic shock, arrhythmias including sustained ventricular tachycardia, and ventricular fibrillation leading to cardiac arrest were observed more in the elderly patients with MI than non-elderly patients (Table 4).

---

### Table 3. Medications Before Admission and Prescribed at Discharge

|                         | Aged >75 years, n = 362 | Aged < 75 years, n = 1568 | P     |
|-------------------------|-------------------------|---------------------------|-------|
| **Medications before admission, n (%)** |                         |                           |       |
| Antiplatelet agents     |                         |                           |       |
| Acetyl salicylic acid   | 112 (34.8)              | 422 (28.8)                | .033  |
| Clopidogrel             | 37 (10.2)               | 148 (9.4)                 | .649  |
| Ticagrelor              | 0 (0.0)                 | 1 (0.1)                   | *     |
| Prasugrel               | 0 (0.0)                 | 3 (0.2)                   | *     |
| Beta blockers           | 103 (32)                | 294 (20.0)                | <.001 |
| Calcium antagonists     | 61 (18.9)               | 162 (12.4)                | .002  |
| Nitrates                | 29 (9.0)                | 41 (2.8)                  | <.001 |
| Anti-lipid agents       | 39 (12.1)               | 217 (14.8)                | .214  |
| ACE inhibitors          | 65 (20.2)               | 219 (14.9)                | .019  |
| **Medications prescribed at discharge, n (%)** |                         |                           |       |
| Anti-platelet agents    |                         |                           |       |
| Acetyl salicylic acid   | 322 (98.8)              | 1508 (99.5)               | .243  |
| Clopidogrel             | 232 (71.2)              | 698 (46.0)                | <.001 |
| Ticagrelor              | 68 (20.9)               | 682 (45.0)                | <.001 |
| Prasugrel               | 1 (0.3)                 | 57 (3.8)                  | .001  |
| Dual antiplatelet       | 298 (91.4)              | 1433 (94.5)               | .032  |
| Anti-coagulants         | 25 (6.9)                | 43 (2.7)                  | *     |
| Warfarin                | 8 (2.3)                 | 20 (1.3)                  | *     |
| Dabigatran              | 2 (0.6)                 | 5 (0.3)                   | *     |
| Rivaroxaban             | 4 (1.1)                 | 5 (0.3)                   | *     |
| Apiksaban               | 9 (2.6)                 | 11 (0.7)                  | *     |
| Edoxaban                | 2 (0.6)                 | 2 (0.1)                   | *     |
| Beta blockers           | 274 (78.1)              | 1272 (82.5)               | .053  |
| Calcium antagonists     | 62 (17.7)               | 184 (11.9)                | .004  |
| Anti-lipid agents       | 300 (92.6)              | 1456 (97.1)               | <.001 |
| Diuretics               | 75 (21.4)               | 223 (14.5)                | .001  |
| ACE inhibitors          | 165 (47.0)              | 897 (58.2)                | <.001 |
| Angiotensin receptor blockers | 32 (91)                | 112 (7.3)                 | .237  |
| Digitalis               | 2 (0.6)                 | 7 (0.5)                   | .676  |
| Anti-arrhythmic         | 8 (2.3)                 | 16 (1.0)                  | .067  |
| Nitrates                | 44 (12.5)               | 109 (7.1)                 | .001  |
| Anti-diabetic agents    | 34 (9.7)                | 174 (11.3)                | .388  |

*not analyzed
ACE, angiotensin converting enzyme
In-hospital mortality was 3 times higher in elderly patients compared to non-elderly patients (9.1% (n = 33) vs. 2.7% (n = 42), P < .001). Among 362 elderly patients, 82 (22.7%) patients died during the 1-year follow-up. The incidence rate of mortality was higher in the elderly in both NSTEMI and STEMI (for NSTEMI patients aged < 75 years 1.79 per 10,000 and patients aged ≥ 75 years 7.61 per 10,000; for STEMI patients aged < 75 years 1.62 per 10,000 and patients aged ≥ 75 years 8.34 per 10,000). Figure 1 shows the cumulative risk of 1-year mortality in patients with STEMI and NSTEMI.

Univariate comparison of patients who died or survived among the elderly population according to baseline characteristics is presented in Table 5. The patients who died were older, had a higher heart rate, and lower blood pressure during the index event compared to those survived elderly patients. Although the predominant symptom was chest pain, the proportion of dyspnea was relatively higher in non-survived patients. Prior history of renal disease and being on acetylsalicylic acid therapy before the index event and depressed baseline left ventricular ejection fraction were significantly associated with increased 1-year mortality in the elderly group.

In the multiple model 1 (adjusted for baseline characteristics), the risk of 1-year mortality was 4 times higher in the elderly group (HR and 95% CI 4.00 [2.86-5.59]; P < .0001). Also, higher heart rate, late hospital admission, and antiplatelet use on admission were significantly associated with higher mortality when the whole study population was taken into the analysis (Table 6a). In patients who underwent...
coronary angiography, the addition of the multivessel disease (model 2) or left main coronary artery involvement (model 3) improved the statistical model (based on the AIC values), however, provided similar results for elderly people (HR and 95% CIs were 3.94 [2.64-5.88], and 4.11 [2.76-6.13]; \( P < .001 \)) (Table 6a). As a sensitivity analysis, patients with a history of cancer were excluded from the analysis. Hazard ratio and 95% CIs for the elderly group were 4.35 (3.06-6.17) in model 1, 4.44 (2.93-6.73) in model 2, and 4.62 (3.05-6.98) in model 3 (\( P < .001 \)).

However, when only patients aged \( \geq 75 \) years were taken into account, the multivariate analysis revealed that higher heart rate and use of antiplatelet agents on admission were the 1-year mortality predictors in patients presenting with acute MI (Table 6b). Additionally, every 5-beat increase per minute in heart rate increased mortality by 7% when we considered only the elderly population (Table 6b).

**DISCUSSION**

Our contemporary data showed that the risk of in-hospital and 1-year mortality was 3.4 and 4 times higher in the elderly patients (aged \( \geq 75 \) years) with MI compared to those aged < 75 years, respectively. Increased heart rate and antiplatelet use on admission were the major determinants of mortality in elderly patients with MI. Elderly patients are admitted to the hospitals almost 1 hour later mainly due to late calls to EMS leading to prolonged total ischemic time compared to patients aged < 75 years. Moreover, elderly patients are still less treated with coronary invasive strategies and evidence-based medical therapies including dual antiplatelet therapies, anti-hyperlipidemia drugs, and renin-angiotensin system (RAS) blockers compared to those younger than 75 years.

In accordance with the previous data, our study showed that the elderly patients were more likely to have NSTEMIs (66.9% vs. 60.8%, \( P = .032 \)) as compared to the non-elderly patients. \(^8\) Mortality after MI tends to increase progressively with aging, and the risk of death especially during hospitalization or within the first month after acute coronary events increase with advanced age. \(^9,11\) The prevalence of conventional CVD risk factors in the elderly was different from non-elderly in the present database. According to a previous study, although the mortality of women with STEMI was found to be higher than that of men, \(^12\) this may be explained by the advanced age of women presenting with STEMI. In our

**Table 5. Univariate Predictors of 1-Year Mortality in Elderly Patients**

|                     | Survived Elderly n = 280 (77.3%) | Died Elderly n = 82 (22.7%) | \( P \) |
|---------------------|---------------------------------|-----------------------------|--------|
| Age, mean (SD)      | 80.65 (4.67)                    | 82.02 (5.19)                | .023   |
| Male gender, n (%)  | 154 (55.0)                      | 40 (48.8)                   | .321   |
| Weight, mean (SD)   | 73.38 (11.37)                   | 71.49 (14.55)               | .255   |
| STEMI, n (%)        | 92 (32.9)                       | 28 (34.1)                   | .827   |
| Anterior STEMI localization, n (%) | 44 (48.4) | 14 (50) | .879 |
| Angina on admission, n (%) | 271 (96.8) | 73 (89.0) | .004 |
| Dyspnea on admission, n (%) | 69 (24.6) | 40 (48.8) | .0001 |

**Mode of hospital admission, n (%)**

|                     | Survived Elderly n = 280 (77.3%) | Died Elderly n = 82 (22.7%) | \( P \) |
|---------------------|---------------------------------|-----------------------------|--------|
| Self-transport      | 142 (50.7)                      | 29 (35.4)                   | .037   |
| By ambulance        | 26 (9.3)                        | 15 (18.3)                   |        |
| Transfer from other hospital | 101 (36.1) | 35 (42.7) | .911 |
| Other *             | 11 (3.9)                        | 3 (3.7)                     |        |
| History of hypercholesterolemia, n (%) | 33 (11.8) | 7 (8.5) | .409 |
| History of diabetes, n (%)    | 91 (32.5)                      | 32 (39.0)                   | .273   |
| History of smoking, n (%)     | 56 (20.0)                      | 16 (19.5)                   | .922   |
| Family history of CVD, n (%)  | 11 (3.9)                       | 3 (3.7)                     | .843   |
| History of AF, n (%)         | 9 (3.2)                        | 3 (3.7)                     |        |
| History of renal disease, n (%) | 20 (71)                        | 12 (14.6)                   | .036   |
| Prior acetyl salicylic acid use, n (%) | 77 (30.9) | 35 (47.9) | .007 |
| HR (bpm) on admission, mean (SD) | 83.40 (17.4)                  | 89.42 (22.9)                | .011   |
| Systolic BP (mm Hg) on admission, mean (SD) | 138.1 (25.3) | 124.8 (28.3) | .0001 |
| Coronary angiography and/or PCI, n (%) | 238 (85.0) | 56 (68.3) | .001 |
| LVEF**, % mean (SD) | 46.1 (10.9)                    | 41.2 (11.8)                 | .003   |
| Acute renal failure, n (%)  | 11 (3.9)                       | 13 (15.9)                   | .0001  |
| Major bleeding, n (%)      | 1 (0.4)                        | 3 (3.7)                     | .012   |

*Transfer from other departments of the same hospitals or myocardial infarction detected during the examinations in the outpatient clinics of the same hospitals. **Data for ejection fraction was available for 78.5% of the elderly population.

STEmI, ST-elevation myocardial infarction; CVD, cardiovascular disease; AF, atrial fibrillation; HR, heart rate; BP, blood pressure; PCI, percutaneous coronary intervention; LVEF, left ventricle ejection fraction.
elderly population, the effect of gender on 1-year mortality of MI could not be demonstrated. As expected, elderly were more likely to have risk factors like hypertension, heart failure, and renal failure which are known to increase with age, whereas the elderly were less likely to have hypercholesterolemia, smoking, obesity, and family history of CVD. Patients with higher lipid levels and family history of CVD who could be more likely to have familial hypercholesterolemia or those with higher life-long CVD risk would probably not live long till the older ages. As the cumulative effect of LDL cholesterol leads to CVD events in early ages, hypercholesterolemia may not be a strong predictor of CVD in the elderly as in young adults. However, SCORE risk charts developed for older people (SCORE-OP) revealed that even though hypercholesterolemia and other traditional risk factors do not strongly predict CVD risk as in the younger population, more effective management of these risk factors such as LDL-cholesterol lowering with statins and blood pressure treatment is still effective in terms of lowering CVD events in the elderly. Of note, SCORE-OP was developed for the age group of 65-80 years from the SCORE-risk calculation model and validated to predict CVD mortality better than the standard risk scales. It is clear that risk estimation by taking into account the older individuals such as in SCORE OP reduces excessive use of medication in the elderly population by decreasing the overestimation of the risk. However, in our elderly population with a mean age of 81 ± 5 years, smoking and hypercholesterolemia were no longer presented as risk factors for 1-year mortality. Therefore, in this late elderly group, the attenuation of the association between traditional risk factors and CVD risk might be more pronounced probably due to increased co-morbidities as in our elderly MI patients.

Recently, the SCORE2-OP model covering the age interactions for risk factors was introduced. This new model also highlighted the necessity to improve the accuracy of risk prediction in elderly patients, due to the wide distribution of 10-year CVD event risk in these patients. Likewise, low body weight (<60 kg) was significantly more common in our elderly patients compared to those younger aged. It is well known that being underweight is associated with

| Table 6a. Baseline Characteristics of Fully Adjusted Model of Whole Study Population |
|---------------------------------|-----------------|--------|
| Characteristics                 | Adjusted HR, CI | P      |
| Model 1*                         |                 |        |
| Being aged ≥75 years             | 4.0 (2.86-5.59) | .0001  |
| Male                            | 0.96 (0.68-1.37)| .828   |
| Heart rate*                     | 1.09 (1.05-1.14)| .000   |
| Time from symptom-onset to hospital arrival** | 1.01 (1.0-1.03) | .022   |
| Acetyl salicylic acid use at baseline | 1.32 (0.90-1.93) | .158   |
| Model 2**                        |                 |        |
| Being aged ≥75 years             | 3.94 (2.64-5.88)| .0001  |
| Male                            | 0.97 (0.64-1.48)| .886   |
| Heart rate*                     | 1.11 (1.06-1.15)| .0001  |
| Time from symptom onset to hospital arrival** | 1.01 (1.0-1.03) | .102   |
| Acetyl salicylic acid use at baseline | 1.08 (0.67-1.73) | .747   |
| Percutaneous coronary intervention | 0.72 (0.45-1.14) | .161   |
| Multi vessel disease             | 1.71 (0.97-3.04)| .066   |
| Model 3***                      |                 |        |
| Being aged ≥75 years             | 4.11 (2.76-6.13)| .0001  |
| Male                            | 0.97 (0.64-1.49)| .905   |
| Heart rate*                     | 1.11 (1.06-1.16)| .000   |
| Time from symptom-onset to hospital arrival** | 1.01 (1.0-1.03) | .100   |
| Acetyl salicylic acid use at baseline | 1.07 (0.66-1.71) | .793   |
| Percutaneous coronary intervention | 0.74 (0.46-1.19) | .219   |
| Left main coronary artery involvement | 1.56 (1.03-2.35) | .034   |

Cox proportional hazard regression model, significance at P < .01. Stratified by diagnosis.
*Adjusted for age, gender, history of myocardial infarction, coronary bypass, percutaneous coronary intervention, heart rate at admission, time between symptom onset and arrival at the study center, and acetylsalicylic acid use at baseline.
*Every 5 beats increase per minute in heart rate.
**Every 30 minutes delay from symptom-onset to hospital arrival.
***Adjusted for age, gender, history of myocardial infarction, coronary bypass, percutaneous coronary intervention, heart rate at admission, time between symptom onset and arrival at the study center, and acetylsalicylic acid use at baseline, percutaneous coronary intervention at any time, multivessel disease.
### Adjusted for age, gender, history of myocardial infarction, coronary bypass, percutaneous coronary intervention, heart rate at admission, time between symptom onset and arrival at the study center, and acetylsalicylic acid use at baseline, percutaneous coronary intervention at any time, left main coronary artery involvement.
both poor outcomes and also with increased risk of frailty in the elderly, and addition of frailty indices or at least low body weight could improve the CVD risk estimation in the elderly patients.

Another important finding of our analysis was the late arrival of the elderly patients. Both in STEMI and NSTEMIs, the elderly were almost 60 min and 50 min, respectively, late to admit compared to those younger than 75 years of age. The major component of late arrival was the late EMS call after symptom onset in our cohort. Late admissions due to delayed contact with EMS especially in the elderly patients with STEMI could lead to increased total ischemic time which is directly related to mortality. Elderly patients who were admitted to the hospital during the index event by self-transport rather than ambulance and/or transferring from another hospital were reported to survive more after 1-year follow-up. This was probably due to more preference for self-transportation by less severe patients.

Our real-life data showed that elderly patients are still subjected to more conservative treatment strategies, despite the evidence-based recommendations in the guidelines. Although elderly patients were more aggressively treated with beta-blockers and ACE inhibitors compared to non-elderly patients before MI, after the infarction the proportion of patients prescribed beta-blockers, ACE inhibitors, and lipid-lowering agents were less in the elderly patients. These results could be due to reduced renal functions, higher risk of drug interactions, and higher risk of drug-induced adverse effects in elderly patients. Moreover, the use of clopidogrel was significantly higher in our elderly group (71.2% vs. 46.0%, P < .001), while almost half of the non-elderly patients have prescribed ticagrelor (45%) at discharge from the hospital. Nevertheless, selecting the antiplatelet therapy and tailoring the dosage of the antithrombotic therapy is of importance in the elderly considering the increased bleeding risk and reduced renal functions. Considering the risk of bleeding in the elderly, clopidogrel, a less potent drug, might have been preferred naturally in this group. Indeed, the low use of dual antiplatelet strategy in the elderly supported this idea. The higher rates of co-morbidities including atrial fibrillation and renal failure might have also affected the antiplatelet drug choice.

In our study, elderly patients underwent coronary angiography and primary PCI less than non-elderly. This might be due to a higher proportion of multivessel disease, left main disease, comorbidities, and late admission in the elderly.

### Table 6b. Multiple Analysis of 1-Year Mortality Predictors in Patients Aged >75 Years Presenting with Acute Myocardial Infarction

| Characteristics                                      | Adjusted HR, CI | P     |
|------------------------------------------------------|-----------------|-------|
| **Model-1**                                           |                 |       |
| Male                                                 | 0.93 (0.58-1.51)| .776  |
| Heart rate*                                          | 1.07 (1.00-1.14)| .041  |
| Time from symptom-onset to hospital arrival**        | 1.01 (1.0-1.03) | .105  |
| Acetyl salicylic acid use at baseline                | 1.89 (1.13-3.15)| .015  |
| **Model-2**                                           |                 |       |
| Male                                                 | 0.73 (0.41-1.32)| .299  |
| Heart rate*                                          | 1.10 (1.02-1.19)| .016  |
| Time from symptom-onset to hospital arrival**        | 1.01 (0.99-1.04)| .193  |
| Acetyl salicylic acid use at baseline                | 1.62 (0.84-3.10)| .147  |
| Percutaneous coronary intervention                   | 0.62 (0.31-1.22)| .166  |
| Multi vessel disease                                 | 1.23 (0.48-3.18)| .669  |
| **Model-3**                                           |                 |       |
| Male                                                 | 0.73 (0.41-1.32)| .299  |
| Heart rate*                                          | 1.10 (1.02-1.19)| .016  |
| Time from symptom-onset to hospital arrival**        | 1.02 (0.99-1.04)| .182  |
| Acetyl salicylic acid use at baseline                | 1.58 (0.83-3.04)| .165  |
| Percutaneous coronary intervention                   | 0.67 (0.34-1.33)| .248  |
| Left main coronary artery involvement                | 1.51 (0.81-2.78)| .191  |

Cox proportional hazard regression model, significance at P < .01. Stratified by diagnosis.

*Adjusted for age, gender, history of myocardial infarction, coronary bypass, percutaneous coronary intervention, heart rate at admission, time between symptom-onset and arrival at the study center, and acetylsalicylic acid use at baseline.

**Every 5 beats increase per minute in heart rate.

***Every 30 minutes delay from symptom-onset to hospital arrival.

*Adjusted for age, gender, history of myocardial infarction, coronary bypass, percutaneous coronary intervention, heart rate at admission, time between symptom-onset and arrival at the study center, and acetylsalicylic acid use at baseline, percutaneous coronary intervention at any time, multivessel disease.

**Adjusted for age, gender, history of myocardial infarction, coronary bypass, percutaneous coronary intervention, heart rate at admission, time between symptom-onset and arrival at the study center, and acetylsalicylic acid use at baseline, percutaneous coronary intervention at any time, left main coronary artery involvement.
Though merge at the end of 1 year, the course of mortality curves differed according to the type of MI. The cumulative risk of 1-year mortality was increased steeply during the first 3 months then followed by a plateau in STEMI patients. Meanwhile, mortality has increased gradually in the NSTEMI. Mortality curves came closer in 1-year in patients with STEMI and NSTEMI (Figure 1). A rapid increase in the cumulative risk of mortality in the early period after STEMI could be explained by a higher frequency of mechanical complications and arrhythmias in the first 3 months, and the more depressed myocardium in the early period after STEMI.

Although in-hospital mortality was higher in elderly patients in our study (9.1%) compared to non-elderly patients (2.7%), it is obvious that the cut-off age for defining the elderly affects the mortality rates following MI in this population. In EuroHeart ACS Survey, in-hospital death was 16.8% in patients aged > 85 years.²⁰ In a recent study of STEMI, although the primary PCI was performed in 78% of the patients, overall, in-hospital mortality was 24% in the elderly aged ≥90 years.²¹ In another study²² including both STEMI and NSTEMI patients, 10.2% of patients aged 80 years old died during the index hospitalization, and it was comparable with 9.1% in-hospital mortality in our elderly acute MI patients aged ≥75 years. Defining the cut-off age for the determination of the elderly age limit could be a matter of debate. Although many guidelines do not define elderly by any specific age criteria, studies mostly describe patients aged 65 years or older as elderly patients and those aged ≥75 years as “late elderly patients.” However, currently, it is proposed to change the definition of elderly to those over 75 years of age instead of the current 65 years in accordance with the aging of the population.²³ Therefore, the 75 years we used in our database is currently the most preferred cutoff, whereas older data suggested lower cutoffs, such as 65 years.²⁴

In the China Acute Myocardial Infarction (CAMI) registry, primary PCI was safe and effective with a reduction of mortality in patients ≥75 years old.²⁵ In our study, 81.8% of the elderly patients with MI underwent coronary angiography and 33.7% underwent primary PCI. Likewise, in KAMIR-NIH registry, PCI was performed in 87.4% of elderly patients, and in-hospital and 1-year mortality were much lower (3.9% and 4.3%, respectively).²⁶ It is obvious that invasive revascularization in the geriatric population is more complicated and challenging due to the increased frequency of multi-vessel disease, left main coronary involvement, calcified lesions, and decreased left ventricular systolic functions with age.²⁷ The proportion of TIMI flow rate of zero was reported more in our elderly group, and it could be related with increased in-hospital mortality rates in this population. This finding could be the result of late hospital admissions and longer total ischemic times in our elderly patients. On the other hand, it should be noted that PCI was not associated with mortality in a multivariate model. The risk of 1-year mortality was 4 times higher in the elderly group. Besides from being elderly, increased heart rate and late hospital admission were the major drivers for mortality. All of these findings could trigger each other and complicate the picture of the MI. Late hospital admissions which are more frequent in the elderly MI patients could lead to increased myocardial damage and acute heart failure, resulting with increased heart rates. Especially, in elderly patients with late presentations, increased heart rates could be the important indicator of mortality.

**Strengths and Limitations**

The major strength of the present study is representation of a nationwide real-life clinical practice for the management of elderly patients with acute MI. The prospective enrollment of MI patients consecutively within a 2-week period is another strength. As the elderly patients are mostly excluded from the clinical trials, our study is of importance to fill the gap by depicting the impact of the implementation of the latest guideline-recommended treatments in the elderly population.

Our study has several limitations. First, we enrolled only primary PCI-capable hospitals and assumed that all the patients with acute MI are eventually directed to these sites. Consequently, in these primary PCI-capable hospitals, the elderly patients with MI mostly underwent coronary angiograms contrary to the previous data. We did not include patients who died before admission to the study centers. The elderly patients who died (n = 82) represent a relatively small group and multiple analyses should be carefully evaluated accordingly.

**CONCLUSION**

Our nationwide real-life data with a prospective enrollment of MI patients revealed important information about the management of acute MI in elderly patients. Both in-hospital and 1-year mortality rates are higher in elderly patients compared to non-elderly patients. Mortality determinants for in-hospital and 1-year follow-up periods could differ among the elderly and the non-elderly patients with MI, in terms of baseline patient characteristics, prior comorbidities and medications, admission features, and treatment strategies. Elderly patients with acute MI admit to hospitals with longer total ischemic times and are still subjected to less-intensive medical therapies including dual antiplatelet therapies. Increased heart rate is an important determinant of survival in elderly patients presenting with MI. Related to the aging population, it is crucial to understand the risk factors and clinical presentations of elderly patients to develop appropriate primary and secondary prevention strategies for these high-risk individuals.

**Ethics Committee Approval:** Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of University of Health Sciences, Istanbul Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital (No: 2018-46; Date: 09.10.2018).

**Informed Consent:** Written informed consent was obtained from all participants who participated in this study.

**Peer-review:** Externally peer-reviewed.
Author Contributions: MKE, MKa, and MKi wrote the study protocol; MKE, MKa, MKi, AAY conceived the study; MKE, MKi, and MKa completed the files for application to Institutional Review Board and Ministry of Health; MKE, MKa, and MKi coordinated the data collection and study; MKE, MKa, and MKi completed the data cleaning; MKi revised the statistical analysis of the data; OO and MKa drafted the manuscript; OO, MKE, MKa, CE, MKU, and MK conducted the main interpretation of the data, and all other authors commented and helped the interpretation of the data; All authors collected the data, revised the literature search, read and certified the proof of the draft; All authors contributed to the interpretation of data, critically revised and approved the final version of the manuscript.

Acknowledgments: Statistical analyses were conducted by Omega CRO, Ankara, Turkey. The electronic case report form and the data capture program (OpenClinica LLC and collaborators, Waltham, MA, USA) hosted were by Omega CRO, Ankara, Turkey.

TURKMI registries are investigator-initiated trials and sponsored by the Turkish Society of Cardiology, which receives major unrestricted funding from Astra-Zeneca Company for this project. The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Declaration of Interests: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Dr. Özdoğan reports grants from Abbot, Doiichi Sankyo, Phizer, Servier, Bayer, Astra Zeneca, Menarini, Abdi Ibrahim, Recoradati outside the submitted work. Dr. Kayıkçıoğlu reports grants from Aegerion, other from Astra Zeneca, other from Menarini, non-financial support and other from Abbott, outside the submitted work.

Funding: All other authors report non-financial support from Astra Zeneca, during the conduct of the study.

REFERENCES

1. Lopes RD, Gharacholou SM, Holmes DN, et al. Cumulative incidence of death and rehospitalization among the elderly in the first year after NSTEMI. Am J Med. 2015;128(6):582-590. [CrossRef]
2. Vitale C, Fini M, Spoletrini I, Lainscak M, Seferovic P, Rosano GM. Under-representation of elderly and women in clinical trials. Int J Cardiol. 2017;232:216-221. [CrossRef]
3. Gurwitz JH, Col NF, Avorn J. The exclusion of the elderly and women from clinical trials in acute myocardial infarction? JAMA. 1992;268(11):1417-1422.
4. Rich MW, Bosner MS, Chung MK, Shen J, McKenzie JP. Is age an independent predictor of early and late mortality in patients with acute myocardial infarction? Am J Med. 1992;92(1):7-13. [CrossRef]
5. Stafford RS, Radley DC. The underutilization of cardiac medications of proven benefit, 1990-2002. J Am Coll Cardiol. 2003;41(1):56-61. [CrossRef]
6. Bradley EH, Herrin J, Elbel B, et al. Hospital Quality for acute myocardial infarction: correlation among process measures and relationship with short-term mortality. JAMA. 2006;296(1):72-78. [CrossRef]
7. Erol MK, Kayıkçıoğlu M, Kılıçkap M. Rationale and design of the Turkish acute myocardial infarction registry: the TURKMI Study. Anatol J Cardiol. 2020;23(3):169-175. [CrossRef]
8. Avezzu A, Mokdisse M, Spencer F, et al. Impact of age on management and outcome of acute coronary syndromes observations from the Global Registry of Acute Coronary Events (GRACE). Am Heart J. 2005;149(1):67-73. [CrossRef]
9. Maggioni AP, Maseri A, Fresco C, et al. Age-related increase in mortality among patients with first myocardial infarctions treated with thrombolysis. The Investigators of the Gruppo Italiano per lo Studio della Sopravvivenza nell’Infarto Miocardico (GISSI-2). N Engl J Med. 1993;329(20):1442-1448. [CrossRef]
10. Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the global registry of acute coronary events. Arch Intern Med. 2003;163(19):2345-2353. [CrossRef]
11. DeGeare VS, Stone GW, Grines L, et al. Angiographic and clinical characteristics associated with increased in-hospital mortality in elderly patients with acute myocardial infarction undergoing percutaneous intervention (A pooled analysis of the primary angioplasty in myocardial infarction trials). Am J Cardiol. 2000;86(1):30-34. [CrossRef]
12. Zachur M, Wilczek K, Janion M, Gajsior M, Gierlotka M, Sadowski M. Long-term outcomes in men and women with ST-segment elevation myocardial infarction and incomplete reperfusion after a primary percutaneous coronary intervention: a 2-year follow-up. Coron Artery Dis. 2019;30(3):171-178. [CrossRef]
13. Ciriq MH, Langer RD, Fronke A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. N Engl J Med. 1992;326(6):381-386. [CrossRef]
14. Everett BM, Zeller T, Glynn RJ, Ridker PM, Blankenberg S. High-sensitivity cardiac troponin I and B-type natriuretic peptide as predictors of vascular events in primary prevention: impact of statin therapy. Circulation. 2015;132(1):1851-1860. [CrossRef]
15. Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. Lancet. 2002;360(9346):1623-1630. [CrossRef]
16. Cooney MT, Seimer L, Lindman A, et al. Cardiovascular risk estimation in older persons: SCORE O.P. Eur J Prev Cardiol. 2016;23(10):1093-1103. [CrossRef]
17. SCORE2-OP working group and ESC Cardiovascular risk collaboration. SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions. Eur Heart J. 2021;42(25):2455-2467. [CrossRef]
18. Bowen ME. The relationship between body weight, frailty, and the disablement process. J Gerontol B Psychol Sci Soc Sci. 2012;67(5):618-626. [CrossRef]
19. Briasoaulis A, Asleh R. Cardiovascular risk prediction in older adults with the use of biomarkers. Ann Transl Med. 2018;6(Suppl 1):550. [CrossRef]
20. Rosengren A, Wallentin L, Simoons M, et al. Age, clinical presentation, and outcome of acute coronary syndromes in the Euro–heart acute coronary syndrome survey. Eur Heart J. 2006;27(7):789-795. [CrossRef]
21. Petroni T, Zaman A, Georges JL, et al. Primary percutaneous coronary intervention for ST elevation myocardial infarction in nonagenarians. Heart. 2016;102(20):1648-1654. [CrossRef]
22. Seguchi M, Sakakura K, Tsukui T, et al. Determinants of inhospital death among the very elderly with acute myocardial infarction. Int Heart J. 2020;61(5):879-887. [CrossRef]
23. Orito H, Itō H, Suzuki T, Arai A, Hosi T, Sawabe M. Reviewing the definition of ‘elderly’. Geriatr Gerontol Int. 2006;6(3):149-158. [CrossRef]
24. Roe MT, Goodman SG, Ohman EM, et al. Elderly patients with acute coronary syndromes managed without revascularization insights into the safety of long-term dual antiplatelet therapy
with reduced-dose prasugrel versus standard-dose clopidogrel. Circulation. 2013;128(8):823-833. [CrossRef]

25. Peiyuan H, Jingang Y, Haiyan X, et al. The comparison of the outcomes between primary PCI, Fibrinolysis, and no reperfusion in patients $\geq$ 75 years old with ST-segment elevation myocardial infarction: results from the Chinese acute myocardial infarction (CAMI) registry. PLoS ONE. 2016;11(11):e0165672. [CrossRef]

26. Kim JH, Chae SC, Oh DJ, et al. Multicenter cohort study of acute myocardial infarction in Korea- interim analysis of the Korea acute myocardial infarction registry-national institutes of health registry. Circ J. 2016;80(6):1427-1436. [CrossRef]

27. Thompson RC, Holmes DR Jr, Gersh BJ, Mock MB, Bailey KR. Percutaneous transluminal coronary angioplasty in the elderly: early and long term results. J Am Coll Cardiol. 1991;17(6):1245-1250. [CrossRef]
### Supplementary Table 1. Comparison of the Elderly and Non-elderly Patients According, Electrocardiography Findings on Index Admission

| Electrocardiography Findings on Admission, n (%) | Elderly patients (Age 75 years) | Non-Elderly patients (Age < 75 years) | P      |
|------------------------------------------------|-------------------------------|---------------------------------------|--------|
| Sinus rhythm                                   | 307 (84.8)                    | 1455 (92.8)                           | <0.001 |
| Atrial fibrillation / Flutter                  | 46 (12.7)                     | 64 (4.1)                              | <0.001 |
| Pace-maker                                     | 2 (0.6)                       | 3 (0.2)                               | 0.237  |
| Ventricular fibrillation / Flutter             | 1 (0.3)                       | 8 (0.5)                               | 1.000  |
| Others                                         | 4 (1.1)                       | 19 (1.2)                              | 1.000  |
| New LBBB, n (%)                                | 24 (6.8)                      | 44 (2.9)                              | <0.001 |
| New RBBB n (%)                                 | 12 (3.4)                      | 22 (1.5)                              | 0.013  |
| AV Block, n (%)                                | 11 (3.1)                      | 33 (2.2)                              | 0.302  |
| ST segment elevation in 2 adjacent derivations ≥1mm, n (%) | 126 (35.1) | 626 (40.7) | 0.052 |
| ST segment depression in 2 adjacent derivations ≥1mm, n (%) | 181 (50.8) | 648 (42.2) | 0.003 |
| T wave inversion, n (%)                        | 98 (27.6)                     | 379 (24.8)                            | 0.266  |
| Non-specific ST / T changes, n (%)             | 95 (26.8)                     | 336 (22.0)                            | 0.057  |

LBBB, Left Bundle Branch Block; RBBB, Right Bundle Branch Block; AV, Atrioventricular Block