RESEARCH ARTICLE

Which treatment strategy is preferred in the octogenarians with acute coronary syndrome?

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Abstract

Objective: To compare the efficacy of invasive and conservative strategy in the management of octogenarians with acute coronary syndrome.

Methods: The retrospective study was conducted after approval from the ethics review committee of University of Health Sciences, Derince Training and Research Hospital, Turkey and comprised data from April 2020 to April 2021 related to octogenarian patients of either gender admitted to University of Health Sciences, Darica Farabi Training and Research Hospital, Turkey with acute coronary syndrome diagnosis. The data was divided into invasive group A and conservative group B. Data was analysed using SPSS 25.

Results: Of the 168 patients with median age 84(interquartile range: 81-86 years), there were 25(14.9%) in group A; 14(56%) males and 11(44%) females. There were 143(85.1%) patients in group B; 70(49%) males and 73(51%) females. Overall mortality was 111(66.1%); 11(44%) in group A, and 100(69.9%) in group B (p=0.012). Elevated alanine aminotransferase and invasive strategy were independent factors associated with mortality (p<0.05).

Conclusion: The invasive strategy in the management of octogenarian patients presenting with acute coronary syndrome was found to be more efficient compared to the conservative strategy.

Keywords: Octogenarians, Acute coronary syndrome, Mortality. (JPMA 73:1800; 2023)

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Introduction

Improvements in living standards, improved treatment of acute and chronic diseases and increased access to healthcare services have contributed to gradual increase in the number of older adults. As a result, the most rapidly growing population is the oldest age group in Turkey.[1] Older adults constitute a very heterogenous population, ranging from independent, robust older adults to frail or completely dependent ones. The presence of geriatric syndromes, such as frailty, malnutrition and polypharmacy, adversely affect survival[2] and hence, should be taken into account whilst managing these patients. Such geriatric syndromes are more common with advancing age, especially in the population aged ≥80 years.

The primary cause of mortality in such patients in countries with high living standards is ischaemic heart disease (IHD).[3] The proportion of the elderly is increasing in Turkey, with 9.5% of the population being 65 years or older in 2020, comprising approximately 8 million older adults. The proportion of octogenarians was also significant at 16.4%. In terms of death statistics, 41.5% of the older adults who died in 2019 in Turkey died due to circulatory system diseases.[1]

Acute coronary syndrome (ACS) can be managed with either conservative or invasive strategy. The conservative strategy includes optimal anti-ischaemic medical management. The invasive strategy includes invasive coronary angiography, percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery.

University of Health Sciences, Darica Farabi Training and Research Hospital is a secondary care facility with no coronary angiography unit. Demographic and clinical data of the patients is taken down manually on in the emergency room (ER). Patients diagnosed with ACS are referred to a tertiary hospital via the designated emergency call centre for invasive coronary angiography. Echocardiography is not routinely performed in the ER, and patients in need of invasive coronary angiography are referred quickly without wasting time. In order for the referral to be made, the patient must be accepted by the invasive cardiologist in the tertiary healthcare institution. Complications related to the application of invasive strategy include stroke, renal failure and haemorrhage, which are more common in elderly patients. For these reasons, invasive cardiologists often do not accept patients for the procedure.[4] The octogenarians diagnosed with ACS

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are followed in the coronary intensive care unit (CICU) in this hospital.

The current study was planned to compare the efficacy of invasive and conservative strategy in the management of octogenarians with ACS. It was hypothesised that invasive strategy would decrease mortality in the specific patient population.

Materials and Methods

The retrospective study was conducted from May 21, 2021, to April 16, 2022, after approval from the ethics review committee of Derince Training and Research Hospital, Turkey, and comprised data from April 15, 2020, to April 15, 2021, related to octogenarian patients of either gender who were diagnosed with ACS. The data of those outside the 80-90 years age range were excluded. The sample was raised using consecutively sampling technique, and data of all patients who met the inclusion criteria was reviewed. ACS was defined as per the international criteria.[5]

The data was divided into invasive group A and conservative group B. Patients who were referred to external hospitals for invasive strategy constituted group A, and those who were provided optimal medical management constituted group B. All causes of death in Turkey are recorded in a central death declaration system. Mortality data was obtained through that system.[6]

Laboratory data noted included haematocrit (Hct), haemoglobin (Hb), white blood cells (WBCs), C-reactive protein (CRP), creatinine (Cr), alanine aminotransferase (ALT), glucose, high-sensitive cardiac troponin T (hs-cTnT) and estimated glomerular filtration rate (eGFR) values at the time of presentation.

Data was analysed using SPSS 25. Kolmogorov-Smirnov test was used to determine data normality. Chi-square test and Fisher's exact test were used to compare categorical variables, as appropriate. Mann-Whitney U test was used to compare numerical parameters of the two groups. After analysing the factors associated with mortality with univariate analyses, binary logistic regression analyses were performed to assess independent associates of mortality. The variables detected as significant in univariate analyses and the factors known to be associated with mortality were evaluated using regression analyses. As a result of the logistic regression analyses, odds ratios (ORs) and 95% confidence intervals (CIs) were obtained. P<0.05 was considered statistically significant.

Results

Of the 168 patients with median age 84(interquartile range: 81-86 years), there were 25(14.9%) in group A; 14(56%) males and 11(44%) females. There were 143(85.1%)

Table-1: Demographic and pathological data of the study groups.

Variables	Conservative Strategy	Invasive Strategy	Total	*p*-value
	n (%)	n (%)	n (%)	
	143 (85.1)	25 (14.9)	168 (100)	
Gender (male/female)	70/73 (49/51)	14/11 (56/44)	84/84 (50/50)	0.515
Age years*	84 (81–86)	84 (81–86)	84 (81–86)	0.762
Glucose mg/dL*	148 (115–205)	168 (122–258)	151 (118–209)	0.142
ALT U/L*	18 (11–34)	15 (12–27)	18 (11–30)	0.641
Creatinine mg/dL*	1.4 (0.8-3.1)	1.2 (0.8-1.7)	1.3 (0.8-3.0)	0.030
CRP mg/L*	51.2 (13.6–122.0)	11.0 (3.7–46.1)	43.2(9.8–106.5)	0.001
WBC 10^3/L*	9.6 (7.1–14.2)	10.3 (8.5–12.5)	9.80 (7.20–13.85)	0.740
Haemoglobin g/dL*	11.3 (9.8–13.0)	12.0 (9.9–13.5)	11.4 (8.6–13.2)	0.376
Haematocrit %*	34.8 (30.5–40.0)	37.1 (31.7–41.2)	34.9 (30.6–40.3)	0.527
eGFR mL/min/1.73 m^2*	42 (24–59)	51 (44–71)	45 (25–62)	0.020
hs-cTnT ng/L*	100 (47–307)	356.0 (39.3–1865.0)	107.5 (45.4–361.3)	0.046
Anaemia	92 (64.3)	12 (48)	104 (61.9)	0.121
Decreased eGFR	111 (77.6)	17 (68)	128 (76.2)	0.297
Elevated ALT enzyme	35 (24.5)	4 (16)	39 (23.2)	0.350
Elevated CRP	125 (87.4)	17 (68)	142 (84.5)	0.030
Elevated WBC	70 (49.0)	16 (64)	86 (51.2)	0.165
Lower WBC	4 (2.8)	1 (4)	5 (3)	0.558
Non-survivors	100 (69.9)	11 (44.0)	111 (66.1)	0.012

n: number, IQR: Interquartile range, hs-cTnT: High-sensitivity cardiac troponin T, ALT: Alanine aminotransferase, CRP: C-reactive protein, WBC: White blood cell, eGFR: Estimated glomerular filtration rate, *: median (IQR).

Table-2: Comparison of demographic characteristics, pathological findings and the applied strategy between non-survivors and survivors.

Variables	Non-survivors	Survivors	Total	*p*-value
	n (%)	n (%)	n (%)	
	111 (66.1)	57 (33.9)	168 (100)	
Gender (male/female)	53/58 (48/52)	31/26 (54/46)	84/84 (50/50)	0.415
Age, years*	84 (82–86)	84 (81–86)	84 (81–86)	0.568
Glucose mg/dL*	157 (122–209)	141 (113–209)	151 (118–209)	0.503
ALT U/L*	20 (12–41)	15 (11–23)	18 (11–30)	0.036
CRP mg/L*	55.0 (17.0–128.0)	15.6 (5.8–71.5)	43.2 (9.8–106.5)	0.001
WBC 10^3/L*	10.04 (7.10–15.07)	9.60 (7.45–11.84)	9.80 (7.20–13.85)	0.437
Haemoglobin g/dL*	11.0 (9.5–13.0)	11.7 (10.7–13.4)	11.4 (8.6–13.2)	0.113
Haematocrit %*	34.4 (29.6–40.5)	35.4 (32.9–40.5)	34.9 (30.6–40.3)	0.130
eGFR mL/min/1.73 m^2*	39 (24–58)	51 (37–70)	45 (25–62)	0.012
hs-cTnT ng/L*	107 (50–350)	119 (35–385)	107.5 (45.4–361.3)	0.908
Anaemia n (%)	73 (65.8)	31 (54.4)	104 (62)	0.150
Decreased eGFR	90 (81.1)	38 (66.7)	128 (76)	0.038
Elevated ALT enzyme	33 (29.7)	6 (10.5)	39 (23.2)	0.010
Elevated CRP	99 (89.2)	43 (75.4)	142 (85)	0.020
Elevated WBC	56 (50.5)	30 (52.6)	86 (51)	0.789
Lower WBC	3 (2.7)	2 (3.5)	5 (3)	1.000
Invasive Strategy	11 (9.9)	14 (24.6)	25 (15)	0.012

n: number, IQR: Interquartile range, hs-cTnT: High-sensitivity cardiac troponin T, ALT: Alanine aminotransferase, CRP: C-reactive protein, WBC: White blood cell, eGFR: Estimated glomerular filtration rate, *: median (IQR).

Table-3: Univariate analyses and multivariate binary logistic regression analyses for independent factors associated with mortality.

Parameter	*p*-value	Odds Ratio	95% Confidence Interval
Univariate			
Presence of elevated CRP	0.020	2.69	1.15-6.29
Presence of elevated ALT enzyme	0.010	3.29	1.28–8.45
Presence of decreased eGFR	0.038	2.14	1.04–4.43
Application of invasive strategy	0.012	0.34	0.14-0.80
Multivariate			
Presence of elevated CRP	0.153	1.94	0.78–4.80
Presence of elevated ALT enzyme	0.043	2.76	1.03–7.40
Presence of decreased eGFR	0.320	1.49	0.68–3.24
Application of invasive strategy	0.046	0.40	0.16-0.98

ALT: Alanine aminotransferase, CRP: C-reactive protein, eGFR: Estimated glomerular filtration rate.

patients in group B; 70(49%) males and 73(51%) females. Cr, CRP, eGFR and hs-cTnT values were significantly different between the groups ($p<0.05$). Overall mortality was 111(66.1%); 11(44%) in group A, and 100(69.9%) in group B ($p=0.012$) (Table 1).

The mortality status was assessed after a median follow-up time of 129 days (20-238). Between the survivors and non-survivors, ALT, CRP, eGFR values were significantly different ($p<0.05$). There was no significant difference between the non-survivors and survivors in terms of age, gender, serum glucose, WBC, Hb, Hct and hs-cTnT levels (Table 2).

Further analysis revealed that the presence of elevated ALT (OR; 2.76, 95%CI: 1.03-7.40; $p=0.043$) and application of invasive strategy (OR: 0.40, 95%CI: 0.16-0.98; $p=0.046$) were independent factors associated with mortality (Table 3).

Discussion

The current study comprised 168 octogenarians presenting with ACS, and conservative strategy was applied more commonly than invasive strategy (85.1% versus 14.9%). The reasons for low application of invasive strategy included the fact that the study site was a secondary care hospital, the operators who perform invasive procedures at the referred hospital tended to have reservations due to the high rate of complications related to invasive procedures, there has not been enough time to adapt to updated ACS management guidelines[5] and because of the coronavirus disease-2019 (COVID-19) pandemic.[7] Application of conservative strategy, however, emerged as one of the two independent factors associated with higher mortality. Until recently, the conservative treatment regimen was preferred after ACS diagnosis in patients aged >80 years.[8,9]

Hs-cTnT levels were lower at admission in the conservative strategy arm in the current study. This may be due to the smaller infarct area.

The 'After Eighty' prospective study,[10] conducted in 2016, compared the invasive strategy with the conservative strategy in patients older than 80 years diagnosed with non-ST segment elevation myocardial infarction (NSTEMI) and unstable angina pectoris who were admitted to 16 centres without a coronary angiography unit in Norway between 2010 and 2014. A total of 457 patients were included in this study; 229(50.1%) in the invasive group and 228(49.9%) in the conservative group. Death from any cause was 25% in the invasive group and 27% in the conservative group. The current study had a much smaller sample size and the rate of application of the invasive strategy was lower. In addition, mortality was significantly higher in both arms of the study.

Sui et al.[11] conducted a retrospective study with patients aged 80 and over who were diagnosed with ST segment elevation myocardial infarction (STEMI) between 2014 and 2017 at a centre in China with PCI facility. The study had 232 patients, and invasive strategy was applied in 60% of the patients. The in-hospital mortality was 32.3% in the conservative group and 9.4% in the invasive group. Patients in the invasive treatment group had a better prognosis, a lower incidence of adverse events and lower death rates ($p<0.05$). The rate of invasive strategy application was lower in the current study. Sui et al.[10] reported only the in-hospital mortality rate, while the current study described all-cause mortality up to one-year follow-up post-discharge.

Patients diagnosed with STEMI aged 75 years and older were included in a study called the Chinese Acute Myocardial Infarction (CAMI) Registry,[12] which was conducted between 2013 and 2014, with more than 100 hospitals in China participating. The sample comprised 3,082 patients. In-hospital cardiac and non-cardiac death rates were: 7.7% in the primary PCI group, 15% in the fibrinolysis arm, and 19.9% in the no reperfusion group ($p<0.001$). Since primary PCI was performed on STEMI patients, no patient was given fibrinolytic therapy in the current study.

In the Korean Acute Myocardial Infarction Registry (KAMIR) study, Lee et al.[13] compared clinical outcomes, clinical characteristics and management of 270 nonagenarian acute myocardial infarction (AMI) patients with 2,145 octogenarian AMI patients diagnosed between 2005 and 2007. An invasive strategy was used in 71.7% of the octogenarian cases and 57.2% of the nonagenarians. PCI was preferred more among the octogenarians. The combination of one-year mortality, in-hospital mortality, and in-hospital adverse outcomes were higher in the nonagenarian group than in the octogenarian. One-year clinical results were better in the nonagenarian group treated with PCI. A higher mortality rate in the

nonagenarian group was detected during hospital follow-up (15.7%). The invasive strategy was applied in octogenarian cases at a relatively high rate compared to the current study.

In the current study, regardless of the conservative or invasive strategy, the presence of elevated ALT enzyme was independently related with higher mortality. Li et al.[14] and Gao et al.[15] reported similar findings.

Moon et al.[16] found that 22% of STEMI patients seen in the emergency department had hypoxic liver injury. In these patients, mortality rate and major adverse cardiovascular event (MACE) frequency after PCI were higher. Similarly, Baars et al.[16] pointed out that ALT enzyme levels showed high importance in terms of predicting mortality in patients after AMI over a long follow-up. The current study lacked detailed information about liver morbidities, such as viral hepatitis or other liver diseases. However, together with the results reported in literature[16,17] the current findings suggested that ALT enzyme level might improve prognosis in terms of mortality in AMI patients.

Larsen et al.[18] recently conducted a study comprising 11,226 patients who underwent primary PCI for STEMI. Of them, 1,400 patients were over 80 years old. The mortality rate in patients aged <80 years was 5.6% at 30-day follow-up and 7.6% at 1-year follow-up; for patients aged 80 years and older, it was 15% and 24.2%, respectively (p<0.0001). The time from electrocardiogram (ECG) diagnosis to sheath insertion was strongly associated with mortality, and this was especially true in the octogenarian group. When the time from ECG diagnosis to sheath insertion was >90 minutes, it was associated with an even worse prognosis in those aged ≥80 years compared to those aged <80 years. This confirmed that meeting time targets of <90 minutes recommended in the guidelines was associated with a large survival benefit, especially among the octogenarians.[18]

The current findings as well as those reported in literature[10,18] indicated better survival through invasive strategy even in older patients.[5]

The current study has limitations as it was a single-centre, observational, retrospective study, and STEMI and NSTEMI patients were not separately compared because of the small sample size. Also, not enough data was available related to risk factors, such as hypertension, diabetes mellitus, history of coronary artery disease, and obesity, owing to which statistical comparison could not be made. Finally, propensity score matching was not done.

Prospective studies with larger sample sizes are needed to validate the findings of the current study.

Conclusion

In ACS patients aged 80-90 years, the application of invasive strategies was found to be very low. The mortality rate was lower in patients who underwent invasive procedures. ALT enzyme levels significant importance in terms of predicting mortality in octogenarians with ACS.

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