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Original Article

Risk profile and in-hospital prognosis in elderly patients presenting for acute ST-elevation myocardial infarction in the Tunisian context



Walid Jomaa^{*}, Sonia Hamdi, Imen Ben Ali, Mohamed A. Azaiez, Aymen El Hraiech, Khaldoun Ben Hamda, Faouzi Maatouk

Cardiology B Department, Fattouma Bourguiba University Hospital and University of Monastir, Monastir, Tunisia

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ABSTRACT

Objectives: Little is known about the risk profile and in-hospital prognosis of elderly patients presenting for ST-elevation myocardial infarction (STEMI) in Tunisia. We sought to determine in-hospital prognosis of elderly patients with STEMI in a Tunisian center.

Methods: The study was carried out on a retrospective registry enrolling 1403 patients presenting with STEMI in a Tunisian center between January 1998 and January 2013. Patients ≥ 75 years old were considered elderly. Risk factors and in-hospital prognosis were compared between elderly and younger patients, and then predictive factors of in-hospital death were determined in elderly patients.

Results: Out of the overall population, 211 (15%) were part of the elderly group. Compared to younger patients, elderly patients were more likely to have arterial hypertension but less likely to be smokers and obese. Thrombolysis was significantly less utilized in the elderly group (22.3% vs. 36.6% in the younger group, $p < 0.001$), whereas the use primary percutaneous coronary intervention was comparable between the two sub-groups (24.2% vs. 28.8%, $p = 0.17$). The incidence of in-hospital complications was higher in the elderly group, and so was the in-hospital mortality rate (14.2% vs. 8.1%, $p = 0.005$). Heart failure on-admission, renal failure on-admission, and inotropic agents use were independently associated to in-hospital death in the elderly group.

Conclusions: In the Tunisian context, elderly patients presenting with STEMI have higher prevalence of risk factors and a worse in-hospital course in comparison to younger patients. Clinical presentation on-admission has a strong impact on in-hospital prognosis.

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^{*} Corresponding author.

E-mail address: jomaa_w@hotmail.fr (W. Jomaa).

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1. Introduction

Coronary artery disease (CAD) and acute coronary syndromes (ACS) are a leading cause of death all around the globe. The introduction of new pharmacological therapeutics along with a steady reduction in coronary revascularization delays throughout the last two decades has led to substantial improvements in both short- and long-term prognoses.^{1–3} In Western countries, where efficient primary percutaneous coronary intervention (pPCI) programs have been implemented, in-hospital mortality in patients presenting with ST-segment elevation myocardial infarction (STEMI) has decreased in a striking manner and throughout all age categories.¹ On the other hand, in developing countries, and especially with the progressive adoption of westernized lifestyles and the increase of life expectancy, CAD is more frequently encountered in older age groups and patients presenting with STEMI in healthcare structures have a changing epidemiology and outcomes over time. Published data from Middle East and North Africa addressing the in-hospital prognosis of STEMI specifically in the elderly are scarce. Available data put the emphasis on the changing risk profile in this region of the world and often seek to compare patients' characteristics and STEMI prognosis with that in Western series in a general manner.^{4,5} Studies from North African countries addressing the specific issue of CAD in the elderly are nearly absent.

Therefore in this study, we sought to determine in-hospital outcomes for elderly patients presenting with STEMI in a Tunisian center and to study factors related to in-hospital death in this population.

2. Methods

2.1. Study population and design

The analyses were performed on data from the STEMI registry of the cardiology B department of Fattouma Bourguiba University Hospital (Monastir, Tunisia). The registry includes retrospectively all consecutive patients presenting to our center via the emergency department or the SAMU (*Service d'Aide Médicale Urgente* for Emergency Medical Service) and for whom the final diagnosis established was STEMI, regardless to the therapeutic strategy implemented. The diagnosis of STEMI was established in the presence of 2 mm (in precordial leads) or 1 mm (in frontal leads) ST-segment elevation in two adjacent leads or a new left bundle branch block concurrently to a typical prolonged chest pain (>20 min). The registry is updated for new patients and outcomes in a yearly fashion.

The present study included patients enrolled during the period between January 1998 and January 2013. The overall study population was divided into two groups according to age; patients, who were ≥ 75 years old, were considered elderly. Demographic features, cardiovascular risk factors, clinical presentation, and in-hospital course were compared between the two study groups. Given the relatively small number of patients in the two age sub-groups, temporal trends for reperfusion therapy and in-hospital mortality were reported

for the four four-year sub-periods of the study (1998–2001, 2002–2005, 2006–2009 and 2010–2013). Anemia was defined as a hemoglobin rate < 12 g/dL in men and < 11 g/dL in women. Heart failure on-admission was defined as a Killip class II or III upon presentation. Renal failure on-admission was defined as a creatinine clearance < 45 mL/min using the Modification of Diet in Renal Disease (MDRD) formula in patients not previously known to suffer from chronic kidney disease (CKD); in patients known to have CKD, renal failure on-admission was defined as an increase of $\geq 30\%$ of baseline serum creatinine rate. Patients on dialysis were excluded. All patients received 100 IU per kg of weight of unfractionated heparin upon diagnosis, 250 mg aspirin and a loading dose of 300 or 600 mg clopidogrel according to the reperfusion strategy chosen (thrombolysis or pPCI). If no reperfusion modality was decided, patients received only 75 mg clopidogrel upon presentation. Medications at discharge included aspirin for life, clopidogrel for 3–12 months in addition to statins, beta-blockers, and angiotensin-converting enzyme (ACE) inhibitors, when indicated. Spontaneous fibrinolysis was defined as complete ST-segment resolution concomitant to the disappearance of any chest discomfort in the few minutes upon presentation and before the initiation of any reperfusion therapy (thrombolysis or pPCI). Relevant factors associated to in-hospital death in the elderly group were studied in univariate analysis. Multivariate analysis was performed to determine factors that were independently associated to in-hospital death in the elderly group.

2.2. Statistical analysis

Categorical variables are presented in absolute values and proportions. Continuous variables are presented as mean standard deviation as appropriate. When indicated, the Student t-test was used to compare means. The Pearson chi-square test was used to compare proportions between the two subgroups of the study population as a whole and in each study sub-period. It was also used to determine factors in the elderly group that were associated with in-hospital death in univariate analysis. Multivariate analysis was performed using binary logistic regression for variables that were significantly associated to in-hospital death in univariate analysis. The Hosmer and Lemeshow test was applied to discard variables that were not significantly associated with in-hospital death in the intermediate analysis. Multivariable adjusted odds ratio (OR) with accompanying 95% confidence intervals were reported. A p value of < 0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 17.0 version.

3. Results

A total of 1403 patients were enrolled during the study period. Out of the overall study population, 1155 (82.3%) were male, 421 (30%) had arterial hypertension and 495 (35.3%) a history of diabetes mellitus. Two hundred eleven (15%) patients were part of the elderly group. Clinical characteristics and cardiovascular risk factors of the patients are presented in [Table 1](#). In summary, compared to younger patients, patients in the elderly group were less frequently male with a lower

Table 1 – Patients characteristics in the overall population and according to age category.

	Population (n = 1403)	Age < 75 (n = 1192)	Age ≥ 75 (n = 211)	p
Male gender	1155 (82.3%)	1011 (84.8%)	144 (68.2%)	<0.001
Hypertension	421 (30%)	329 (27.6%)	92 (43.6%)	<0.001
Diabetes mellitus	495 (35.2%)	431 (36.2%)	64 (30.3%)	0.103
Tobacco smoking	938 (66.8%)	842 (70.6%)	96 (45.5%)	<0.001
Obesity	178 (12.6%)	168 (14.1%)	10 (4.8%)	<0.001
History of heart failure	33 (2.3%)	25 (2.1%)	8 (3.8%)	0.134
History of PCI or CABG	55 (3.9%)	51 (4.3%)	4 (1.9%)	0.1
Anemia	216 (15.4%)	174 (16.1%)	42 (22.5%)	0.033
Anterior localization	647 (46.1%)	553 (50.7%)	94 (49.7%)	0.8

CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention.

Table 2 – Management of patients and in-hospital prognosis according to age category.

	Population (n = 1403)	Age < 75 (n = 1192)	Age ≥ 75 (n = 211)	p
Spontaneous fibrinolysis	140 (9.9%)	125 (10.5%)	15 (7.1%)	0.131
Conservative medical therapy	435 (31%)	344 (28.9%)	91 (43.1%)	<0.001
Thrombolysis	483 (34.4%)	436 (36.6%)	47 (22.3%)	<0.001
Symptoms to thrombolysis delay (h)	3.79 ± 4.03	4.2 ± 4.24	3.68 ± 2.08	0.402
pPCI	394 (28%)	343 (28.8%)	51 (24.2%)	0.17
Symptoms to pPCI delay (h)	4.88 ± 4.23	4.9 ± 4.17	5.07 ± 4.57	0.811
Heart failure on-admission	306 (21.8%)	243 (20.4%)	63 (29.9%)	0.002
Renal failure on-admission	115 (8.2%)	83 (7%)	32 (15.2%)	<0.001
Hyperglycemia on-admission	468 (33.3%)	401 (40.1%)	67 (36%)	0.291
Cardiogenic shock	33 (2.4%)	21 (1.8%)	12 (5.7%)	0.001
New onset atrial fibrillation	90 (6.4%)	65 (5.5%)	25 (11.8%)	<0.001
Atrioventricular block	133 (9.4%)	99 (8.3%)	34 (16.1%)	0.002
Hemorrhage	38 (2.7%)	30 (2.5%)	8 (3.9%)	0.265
Inotropic agents use	206 (14.6%)	164 (13.8%)	42 (19.9%)	0.02
CCU length of stay (days)	4.74 ± 3.5	4.7 ± 3.46	4.98 ± 4	0.332
In-hospital death	127 (9%)	97 (8.1%)	30 (14.2%)	0.005

CCU, coronary care unit; pPCI, primary percutaneous intervention.

prevalence of tobacco smoking and obesity. Nevertheless, elderly patients were more frequently hypertensive and presented more frequently with heart failure and renal failure on-admission. New-onset atrial fibrillation and atrioventricular block in the hospital course were more frequently encountered in the elderly group. Concerning therapeutics implemented (Table 2), thrombolysis in the acute phase of myocardial infarction was the reperfusion option in 22.3% of the cases in the elderly group compared to 36.6% in the younger group ($p < 0.001$). Conservative medical therapy with

no reperfusion treatment was chosen in 43.1% of the cases in the elderly group (vs. 28.9% in younger patients, $p < 0.001$). The use of pPCI as the reperfusion strategy was slightly lower in the elderly group but with no statistical significance (24.2% vs. 28.8%, $p = 0.17$). No significant difference could be demonstrated in terms in reperfusion delays (either by thrombolysis or pPCI) between the two sub-groups. In-hospital mortality rate in the overall study population was at 9% and was significantly higher in the elderly group in comparison with younger patients (14.2% vs. 8.1%, $p = 0.005$). When looking at temporal

Table 3 – Temporal trends in reperfusion therapies used and in-hospital mortality for elderly and younger patients during the study period. Percentages express rates in the corresponding age category for the indicated study period.

		1998–2001 (n = 281)	2002–2005 (n = 349)	2006–2009 (n = 382)	2010–2013 (n = 392)
pPCI	Young (334)	19 (8.1%)	76 (25.2%)	154 (48.4%)	95 (28.1%)
	Elderly (51)	5 (11.1%)	6 (12.5%)	24 (37.7%)	16 (29.6%) [‡]
Thrombolysis	Young (436)	107 (45.3%)	130 (43.2%)	60 (18.9%)	139 (41.1%)
	Elderly (47)	12 (26.7%)	14 (29.2%)	6 (9.4%)	15 (27.8%) [∞]
In-hospital mortality	Young (97)	11 (4.7%)	26 (8.6%)	28 (8.8%)	33 (9.8%)
	Elderly (30)	4 (8.9%)	12 (25%) [†]	7 (10.9%)	7 (13%) [∞]

pPCI, primary percutaneous coronary intervention.

[†] $p = 0.001$ vs. in younger patients for the same period.

[‡] $p = 0.025$ vs. in elderly patients for 1998–2001 period.

[†] p non-significant vs. in younger patients for the same period.

[∞] p non-significant vs. in elderly patients for 1998–2001 period.

Table 4 – Factors associated to in-hospital death in elderly patients in univariate analysis.

	Surviving (n = 181)	Dead (n = 30)	p
Female gender	53 (29.3%)	14 (46.7%)	0.058
Hypertension	77 (42.5%)	15 (50%)	0.44
Diabetes mellitus	51 (28.2%)	13 (43.3%)	0.09
Obesity	9 (5%)	1 (3.3%)	0.69
History of CAD	17 (9.4%)	3 (10%)	0.31
History of heart failure	7 (3.9%)	1 (3.3%)	0.88
Heart failure on-admission	44 (24.3%)	19 (63.3%)	<0.001
Anterior localization	77 (48.1%)	17 (58.6%)	0.29
Spontaneous fibrinolysis	14 (7.7%)	1 (3.3%)	0.385
Conservative medical therapy	74 (40.9%)	17 (56.7%)	0.211
Thrombolysis	42 (23.2%)	5 (16.7%)	0.425
Symptoms to thrombolysis delay (h)	3.66 ± 2.1	3.8 ± 2.16	0.894
Primary PCI	43 (23.8%)	8 (26.7%)	0.581
Symptoms to pPCI delay (h)	5.15 ± 4.84	4.63 ± 2.92	0.769
Anemia	126 (79.7%)	19 (65.5%)	0.091
Renal failure on-admission	21 (11.6%)	11 (36.7%)	<0.001
Hyperglycemia on-admission	50 (31.8%)	17 (58.6%)	0.006
Cardiogenic shock	5 (2.8%)	7 (23.3%)	<0.001
New onset atrial fibrillation	17 (9.4%)	8 (26.7%)	0.019
Atrioventricular block	24 (13.3%)	10 (33.3%)	0.006
Hemorrhage	5 (2.9%)	3 (10%)	0.063
Inotropic agents use	20 (11%)	22 (73.3%)	<0.001

trends across the four pre-specified sub-periods (Table 3), reperfusion therapies (thrombolysis or pPCI) were numerically more used in younger patients, and in-hospital mortality remained numerically higher in the elderly subgroups except for 2002–2005 period, where it reached statistical significance. When comparing the last (2010–2013) period to the early one (1998–2001), no significant difference could be reached in in-hospital mortality and thrombolysis use between the two periods. On the other hand, a significant increase was noted in pPCI use between the early and the last period ($p = 0.025$).

Factors associated to in-hospital death in the elderly group were studied in univariate analysis (Table 4). When compared to surviving patients ($n = 181$), those who died ($n = 30$) had more frequently heart failure and renal failure on admission (63.3% vs. 24.3%, $p < 0.001$ and 36.7% vs. 11.6%, $p < 0.001$, respectively). In died patients, new-onset atrial fibrillation and atrioventricular block occurred more frequently in the hospital course (26.7% vs. 9.4%, $p = 0.019$ and 33.3% vs. 13.3%, $p = 0.006$, respectively). The recourse to inotropic agents during hospital stay was more frequent in the elderly group (73.3% vs. 11%, $p < 0.001$).

In multivariate analysis (Table 5), the only factors that were independently associated with in-hospital death in elderly patients were heart failure on-admission (OR = 3.24, 95% CI: 1.15–9.13, $p = 0.026$), renal failure on-admission (OR = 3.67, 95%

CI: 1.11–12.11, $p = 0.033$) and inotropic agents use (OR = 13.33, 95% CI: 4.78–37.03, $p < 0.001$).

4. Discussion

This study is, to our knowledge, the largest published series addressing specifically the issue of STEMI in the elderly population in Tunisia. Furthermore, it presents an actual depiction of risk profile, management strategies and in-hospital prognosis of STEMI in this age group. Results are issued from a fifteen-year experience population and some of them deserve careful consideration.

Male gender preponderance in STEMI patients is maintained over age categories even though less striking in the elderly group. This finding is well explained by the difference in the risk profile between the two genders and is reported in some Middle-Eastern and larger Western studies as well.^{5–8} In our study, tobacco smoking as a risk factor is alarmingly prevalent. Its prevalence remains higher than that reported in other studies^{5,8} and mandate specific intervention at the population scale. Other traditional coronary risk factors are more prevalent in the elderly group except for obesity, which was less frequent in this group.

As reported in other studies,^{3,9} in our study, elderly patients presenting for STEMI are more likely to have HF upon presentation. This fact is obviously related to a higher prevalence of other HF risk factors in the elderly population such as hypertension. Likewise, elderly patients are more likely to have multivessel disease in the setting of ACS in general, a factor that is highly associated to HF in CAD both in the acute and chronic settings.¹⁰

Similar to that reported in others, in the present study, elderly people presenting for STEMI are more likely to be managed conservatively (i.e. with no reperfusion therapy) in comparison to younger patients. That is well accounted for by

Table 5 – Factors independently associated to in-hospital death in elderly patients in multivariate analysis.

Variable	Odds ratio	95% CI	p
Hyperglycemia on-admission	2.67	0.97–7.38	0.057
Heart failure on-admission	3.2	1.15–9.13	0.026
Renal failure on-admission	3.6	1.11–12.11	0.033
Inotropic agents use	13.3	4.78–37.03	<0.001

a significantly lesser recourse to thrombolysis in this population and a slight trend, although not statistically significant to less pPCI implementation. Reperfusion strategies for STEMI had been addressed in some Middle-Eastern reports.^{11,12} In the Gulf RACE registry,¹¹ among 8176 enrolled ACS patients, 3202 (39%) presented with STEMI; only 1584 (19%) patients underwent coronary angiography during the index hospitalization and age category failed to stand out as an independent predictor of coronary angiography use in multivariate analysis. More recently, in a 20-year analysis carried-out in Qatar, Ahmed et al.¹² reported a trend to a lesser use of thrombolysis as the reperfusion option for STEMI in the last two decades. Contrarily, pPCI prevalence increased from 2.5% to 14.6% of the overall study population and an age >70 years arose as an independent predictor of in-hospital death. These rates are lower than those noticed in our study, where even for patients older than 75 years, pPCI was used in nearly the quarter of the cases. In the large European Euroheart Acute Coronary Syndrome survey,³ pPCI was not the preferred reperfusion therapy in patients presenting with acute STEMI across the whole age spectrum, and a reperfusion therapy (pPCI or thrombolysis) was implemented in less than 20% of patients aged 75 years or more. More recently in the British Myocardial Ischemia National Audit Project (MINAP),⁸ pPCI use in the very elderly (≥ 85 years) rose from 0.5% in 2003–2004 to 32.2% in 2009–2010, and use of in-hospital thrombolysis in the elderly (≥ 75 years) was remarkably frequent ($\geq 50\%$ either in men or women).

In the present study, in-hospital prognosis in elderly patients presenting with STEMI remains poor and in-hospital mortality rate is significantly higher than in younger patients. In-hospital mortality rates in patients presenting with STEMI were reported in several Middle-Eastern studies but no specific data for the elderly are available. Ahmed et al. reported a 3.6 fold higher mortality rate in patients older than 70 years when compared to those who were 50 or younger,¹² whereas in Western reports, in-hospital mortality rate across the whole age spectrum remains quite low. For example, in Scandinavian countries, where pPCI program is well established and high standards of care is applied, 30-days mortality rates in old and very old patients managed invasively was around 3%.^{13,14} Prognosis improvement in STEMI patients in Europe could be explained by the introduction of new medications in ACS improvement in clinical management in general and in the setting of pPCI in particular as well as early invasive management strategy specifically in the elderly population.^{1,15} Another explanation for the worse prognosis in STEMI patients in the present study, when compared to Western studies is the remarkable difference in cardiovascular risk profile in old Tunisian patients: prevalence of classic cardiovascular risk factors such as diabetes mellitus and hypertension in the study population is significantly higher than that reported in major Western series.^{14,16,17}

4.1. Study limitations

This is a retrospective observational study in one Tunisian tertiary care center. Although depicting a somewhat realistic picture of STEMI management and prognosis in the elderly, data are issued from an urban population with a relatively

westernized lifestyle for many of the patients enrolled. These data could not be generalized to the overall Tunisian population neither to the whole North African countries, in particular because of an important rural population in this part of the world. Contemporary therapeutic strategies are implemented only in regions benefitting from tertiary health care facilities and prognosis of old patients presenting for STEMI in far-off primary care centers with no reperfusion therapeutic option could be quite different. Likewise, the small sample size in the elderly group accounts for the lack of statistical relationship between some factors (reperfusion therapeutics, in-hospital complication) and in-hospital death. Also, the lack of precise information about all the medications at discharge taken by elderly and younger patients makes it difficult to interpret long-term outcomes in the two sub-groups. Finally, multicenter studies have to be conducted to better describe regional management and prognostic particularities and adjust intervention strategies at a nationwide scale.

5. Conclusions

In this single center Tunisian registry, elderly patients presenting with STEMI have a higher prevalence of cardiovascular risk factors in comparison to younger patients. Management strategies were different between the two groups with less recourse to reperfusion therapy in the elderly group. In-hospital prognosis was poor in elderly. Heart failure and renal failure on-admission as well as inotropic agents use were highly predictive of in-hospital death.

Conflicts of interest

The authors have none to declare.

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