Characteristics of Adults Older Than 75 Years in the ARGEN-IAM-ST Registry

Características de los pacientes mayores de 75 años en el Registro ARGEN-IAM-ST

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ABSTRACT

Background: Older adults represent a growing population in clinical practice.
Objectives: The aim of this study was to learn the clinical characteristics and outcome of older adults hospitalized with myocardial infarction in Argentina.
Methods: Patients included in the ARGEN-IAM-ST registry were analyzed depending on whether they were older or younger than 75 years of age.
Results: Among the 1,714 patients included in the registry, 233 (13.6%) were aged 75 years or older. These patients had greater prevalence of female sex and hypertension and lower incidence of smoking habits, while the prevalence of diabetes, dyslipidemia, anterior myocardial infarction and time from onset of symptoms was similar. They were less likely to receive reperfusion therapy and progression to heart failure (31% vs. 14%; p <0.01), reinfarction (3.9 vs. 1.4%; p=0.009), minor bleeding (7.7% vs. 3.2%; p <0.002) and mortality (21.5% vs. 6.7%, p <0.001) were more common.
Conclusions: Older adults with myocardial infarction have a more unfavorable outcome and mortality is three times greater than that of patients <75 years.

Key words: Myocardial Infarction - Aged - Aged, 80 and over - Clinical Evolution – Registries

RESUMEN

Introducción: Los adultos mayores representan una población cada vez más numerosa en la práctica clínica.
Objetivos: Conocer las características clínicas y evolución de los adultos mayores que se internan por infarto en Argentina.
Material y métodos: Se analizaron los pacientes de acuerdo con la edad mayor o menor de 75 años incluidos en el registro ARGEN-IAM-ST.
Resultados: De 1714 pacientes ingresados, 233 (13,6%) tenían una edad ≥75 años. Se observó en estos una mayor prevalencia de sexo femenino, de hipertensión arterial, menor de tabaquismo y similar de diabetes, dislipidemia, infarto agudo de miocardio de localización anterior y tiempo de evolución al ingreso. Recibieron menos tratamiento de reperfusión y evolucionaron más frecuentemente con insuficiencia cardíaca (el 31% vs. 14%; p < 0,01), reinfarto (3,9 vs. 1,4%; p = 0,009), sangrado no mayor (7,7% vs. 3,2%, p < 0,002) y muerte (21,5% vs. 6,7%, p < 0,001).
Conclusiones: Los adultos mayores con infarto tienen una evolución más tórpida y una mortalidad que triplica la de los pacientes menores de 75 años.

Palabras clave: Infarto del miocardio - Anciano - Anciano de 80 o más años - Evolución clínica - Registros

Abbreviations

AMI	Acute myocardial infarction

INTRODUCTION

Higher life expectancy has increased the number of elderly patients admitted to coronary care units. Myocardial infarction is currently the leading cause of cardiovascular mortality particularly in older patients. (1) In our country, the Ministry of Health reported that among a total of 18,228 cases of fatal myocardial infarctions in 2016, 52.25% occurred in subjects >75 years. (2) Moreover, most natural deaths in elderly patients are due to cardiovascular diseases. (3)

There are few data about this particular and increasing subgroup of patients as they are under-represented in clinical studies. (4) Therefore, the aim of this study was to learn the clinical characteristics,

presence of comorbidities, treatments used and outcome of older adults hospitalized with ST-segment elevation myocardial infarction (STEMI) in Argentina.

METHODS

Patients recorded in the National Registry of ST-segment Elevation Myocardial Infarction (ARGEN-IAM-ST) were included.

The inclusion criteria were suspected acute myocardial infarction (AMI) with any of the following: ST-segment elevation ≥1 mV in 2 limb leads or ≥2 mV in 2 contiguous precordial leads; AMI evolving with new Q waves lasting <36 hours from onset of symptoms, suspected posteroinferior AMI (horizontal ST-segment depression from V1 to V3 suggestive of acute occlusion of the circumflex coronary artery); or new or presumed new complete left bundle branch block. In each center, the patients were consecutively included during a period of 3 months between March and December 2015.

The clinical characteristics, treatments and in-hospital outcome of patients aged 75 years or older (older adults) were compared with those <75 years.

Statistical analysis

Quantitative variables are expressed as mean and standard deviation, or median and 25%-75% interquartile range, according to their distribution. Qualitative variables are presented as frequency tables and percentages. Continuous variables with normal and non-Gaussian distribution were compared using Student's t test or the Wilcoxon rank sum test, respectively. Discrete variables were compared using the chi-square test or Fisher's exact test. Univariate and multivariate logistic regression analyses were performed in order to identify independent predictors of in-hospital mortality. The multiple logistic regression analysis included all the variables that predicted in-hospital mortality in univariate analysis with a p value <0.05.

All the calculations were performed using Epi Info version 7.2.

Ethical considerations

The protocol design of the ARGEN-IAM-ST registry was evaluated and approved by the Bioethics Committee of the Argentine Society of Cardiology, and was subjected to evaluations of the participating center committees, depending on local regulations and institutional policies.

RESULTS

The ARGEN-IAM-ST registry included 1,714 patients, 233 (13.6%) of which were ≥75 years. Table 1 shows the clinical characteristics of the patients according to age.

In patients undergoing reperfusion, there were no differences in the indication of primary percutaneous coronary intervention (PCI) [82% (149/181) vs. 78% (974/1,254); p=0.3] or in the use of thrombolytic therapy [17% (32/181) vs. 22% (280/1,254); p=0.07]. Delays in reperfusion were reported in 65% of older adult patients (126/181) vs. 67.4% in the rest of patients (806/1,254) (p=0.25) and there were no differences with age in the percentage of patients who were transferred to other centers for reperfusion therapy (17%) (219/1,254 p <75 years vs. 30/181 >75 years, p=0.4).

With regard to adjuvant therapy during hospitalization, the indication of aspirin and thienopyridines (particularly clopidogrel) was similar in those >75 years and <75 years, but older patients were less likely to receive beta blockers and angiotensin-converting enzyme inhibitors than those <75 years. At discharge, the indication of aspirin, thienopyridines (also predominantly clopidogrel), beta blockers, angiotensin-

Table 1. Clinical characteristics of the patients according to age

Median age (IQR 25-75)	≥75 years n=233 (13.6%) 81 (78 - 85)		<75 years n=1,481 (86.4%) 59 (52 - 65)		p
	n	%	n	%	
Women	109	46.8	278	18.7	<0.001
Hypertension	155	66.5	829	56.0	0.002
Diabetes	43	18.5	286	19.3	0.76
Dyslipidemia	86	36.9	568	38.4	0.67
Smoking habits	33	14.2	729	49.2	<0.001
COPD	8	3.4	60	4.1	0.65
Previous CABGS	7	3.0	23	1.6	0.12
Previous PCI	22	9.4	138	9.3	0.95
Chronic kidney failure	15	6.4	23	1.6	<0.001
Anterior AMI	109	46.8	646	43.6	0.36
Time from symptom onset at admission (median, IQR 25-75), in minutes	150 (70- 412)		135 (61-315)		0.26
Reperfusion	181	77.7	1,254	84.7	0.007
Killip and Kimball class II-III-IV	91	39.1	347	23.4	<0.001

COPD: Chronic obstructive pulmonary disease; CABGS: Coronary artery bypass graft surgery; PCI: Percutaneous coronary intervention; AMI: Acute myocardial infarction.

converting enzyme inhibitors or angiotensin II receptor blockers and statins was similar in both groups, but older adults were more likely to receive diuretics (Table 2

During hospitalization, the use of Swan Ganz catheter was similar in both groups of patients (3%), but requirement of mechanical ventilation and temporary pacing was twofold higher in older adults: 14% vs. 7% (p <0.001) and 6% vs. 2.7% (p <0.01), respectively.

Mechanical complications occurred in 1% (n=17) of the general population: 4 patients presented ventricular septal defect, 8 presented mitral regurgitation and 5 had external mechanical rupture. Only two of these complications occurred in patients >75 years.

The incidence of heart failure and mortality was significantly greater in older adults (30.4% vs. 14%; p=0.02 and 50/233, 21.5% vs. 99/1,481, 6.7%; p <0.0001, respectively); 48% were women. In addition, non-major bleeding was more than twice higher in older adults (7.7% vs. 3.2%; p=0.02) with no differences in the incidence of major bleeding (Table 3).

Mortality was due to cardiovascular causes in 90.6% of the cases (135/149) and to extracardiac causes in 9.4% (14/149), without differences by age. Only 6% of the deaths were due to mechanical complications.

On univariate analysis, the following variables were identified as predictors of mortality: age ≥75 years (21.5 vs. 6.7; p <0.01), bleeding (18.2 vs. 8.3%; p=0.005), female sex (11.4% vs. 7.9%; p=0.034), diabetes (14.3% vs. 7.4%; p <0.0001) and absence of reperfusion (13.3% vs. 7.8%; p=0.003).

On multivariate analysis including age ≥75 years, bleeding, sex, diabetes and absence of reperfusion, age (OR: 3.67; 95% CI: 2.48-5.45, p <0.001), diabetes (OR: 2,19; 95% CI: 1.5-3.21; p <0.0001), bleeding (OR: 2.09; 95% CI: 1.06-4.11, p=0.033) and absence of reperfusion (OR: 1.63; 95% CI: 1.08-2.45; p=0.019) remained as independent predictors of mortality.

DISCUSSION

The increase in life expectancy has produced a demographic shift in patients with myocardial infarction, with a percent expansion in the elderly population. As this population is not adequately represented in clinical trials, the choice of specific treatments in daily practice is more difficult. (5)

In addition to the episode of acute coronary syndrome, older patients are more likely to have chronic coronary disease, greater frailty, cognitive impairment, polypharmacy, anemia, some degree of kidney impairment, neurological disorders, special family contexts and cancer, among other disorders (6), which adds difficulty in determining the best treatment

Table 2. Adjuvant treatment on admission and discharge

	≥75 years (n=225)		<75 years (n=1,454)		p
Treatment on admission					
ASA	224/225	99.6	1,437/1,454	98.8	0.33
Any thienopyridine	220/225	97.8	1,413/1,454	97.2	0.61
Clopidogrel	195/221	88.2	1,054/1,368	77.1	0.0001
Ticagrelor	27/195	13.8	233/1,236	18.9	0.09
Prasugrel	2/187	1.1	150/1,209	12.4	<0.0001
GP IIb/IIIa inhibitors	13/192	6.8	104/1,217	8.6	0.41
Beta blockers	104/210	49.5	854/1,352	63.2	0.0001
ACEI/ARB	97/225	43.1	816/1,454	56.1	0.0002
ACEI	85/207	41.1	750/1,324	56.7	<0.0001
ARB	14/195	7.5	69/1,201	58.8	0.43
Statins	195/221	88.2	1,304/1,413	92.3	0.04
Medication at discharge (n = 1,535)					
ASA	146/148	98.7	1,152/1,169	98.6	0.92
Any thienopyridine	135	76.7	1,070	78.7	0.54
Clopidogrel	118	67.1	753	55.4	0.003
Ticagrelor	15	8.5	186	13.7	0.06
Prasugrel	2	1.1	135	9.9	0.0001
ACEI/ARB	107	60.8	897	66.0	0.17
ACEI	92	52.3	822	60.5	0.04
ARB	16	9.1	89	6.6	0.21
Beta blockers	124	70.5	999	65	0.39
Diuretics	25	14.2	86	6.3	0.0001
Statins	143	81.3	1,092	80.4	0.77

ASA: Acetylsalicylic acid; ACEI: Angiotensin-converting enzyme inhibitor; ARB: Angiotensin II receptor blocker; GP: Glycoprotein.

	≥75 years n: 233	<75 years n: 1,481	RR	95% CI	p
PIA	6 (2.5%)	37 (2.5%)	1.03	0.44-2.41	0.54
Reinfarction	9 (3.8%)	21 (1.42%)	2.72	1.26-5.87	0.01
HF	71 (30.4%)	207 (14%)	2.18	1.73-2.74	<0.0001
Major bleeding	3 (1.28%)	5 (0.33%)	3.81	0.91-15.85	0.08
Non-major bleeding	18 (7.7%)	48 (3.2%)	2.38	1.41-4.02	0.02
In-hospital mortality	50 (21.5%)	99 (6.7%)	3.21	2.35-4.38	<0.0001

Table 3. In-hospital outcome according to age

PIA: Postinfarction angina. HF: Heart failure.

strategy in these cases. (7)

Why did we consider older adults as those >75 years?

There is no universally accepted definition of "older adults". In our population, 36.7% were ≥65 years, 23.3% were ≥70 years, 13.6% were ≥75 years and 7.9% were ≥80 years. We decided to consider 75 years for our study as it is the most widely used in the contemporary medical literature.

Moreover, 75 years is the age considered to change the therapeutic indication in anticoagulant drugs, antiplatelet therapy and thrombolytic therapy in STEMI. (8)

The guidelines recommend using lower doses of fibrin-specific thrombolytic agents in patients >75 years, adjusting the enoxaparin dose and avoiding a loading dose of clopidogrel before thrombolysis.

Prasugrel is not recommended in patients >75 years, at least in full doses.

All these interventions focus on reducing bleeding, a common event in elderly patients.

In our registry, we found a significant increase in non-major bleeding among older adults.

Bleeding itself is a prognostic marker, since it leads to a reduction or withdrawal of anticoagulation or antiplatelet medication which may contribute to increase mortality. (9)

The importance of adjusting the doses of these drugs in this population should be emphasized in order to prevent bleeding. Despite the recommendation to reduce the dose of thrombolytic agents by 50% in patients >75 years had not been launched at the time of the survey, no cases of brain hemorrhage were detected. This could be attributed to the fact that PCI was the reperfusion strategy mostly used and that streptokinase was the fibrinolytic agent administered.

Worldwide, the percentage of elderly patients with myocardial infarction varies according to the populations analyzed, ranging from 12.3% to 19% in randomized clinical trials (10) and from 28% to 31% in large registries such as the GRACE (11) registry or the French national registry (FAST AMI) (12), or is even 40% in some reports. (13)

In elderly populations, female sex is more prevalent, reaching 46% in our work, probably because life expectancy for women is 4.5 years longer than for men. (14)

The prevalence of hypertension was greater and fewer patients were current smokers, but, as opposed to other studies, the incidence of diabetes, dyslipidemia and history of revascularization was similar. (15)

Kidney dysfunction was the only comorbidity more common in older adults, and the incidence could have been greater if glomerular filtration had been calculated using formulas. Kidney dysfunction increases the risk of bleeding (which was twice greater than that of younger patients in our study), is associated with mortality and is the reason why some patients cannot receive some medications recommended.

The percentage of reperfusion therapy was high and may constitute a bias, as most of the centers participating in the registry are institutions with academic or community motivation and are related with scientific societies, have residency programs or PCI capabilities. However, despite the high rate of reperfusion, similar times of ischemia and of anterior infarctions, older adults doubled the incidence of heart failure, and mortality was three times greater compared with younger patients. This could be due to the presence of more extended coronary artery disease, lower tolerance to ischemia, less ventricular compliance or greater microcirculatory injury.

The diagnosis of infarction is later in older adults as chest pain is mild or atypical. In our series, time from onset of symptoms was not statistically different, but perhaps there may be a trend toward a longer time in the elderly that was not detected due the sample size.

The ACC/AHA guidelines for the management of AMI patients suggest use of aspirin, clopidogrel, beta blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers and statins for most of the patients after a myocardial infarction regardless of age. However, the indication of these medications is lower in older adults in clinical practice, probably due to the presence of contraindications, hypotension or adverse events, similarly to what happens in other countries. (16)

The greater in-hospital mortality found in older adults in our study is similar to other real-life registries and faces us with the clinical challenge of trying to improve our quality of care to change the outcome of this large and vulnerable population.

Study limitations

The Argen-IAM-ST study is a voluntary registry of institutions close to scientific societies and may not be representative of the healthcare universe of patients with myocardial infarction. As we have mentioned, the majority of the institutions have cardiology residency programs and PCI capabilities. A second limitation is that the data were not monitored, they were based only on information provided by the institutions and, therefore, there may be some level of under-reporting. This is a characteristic of community-based registries.

CONCLUSIONS

The elderly population has its own characteristics, with greater comorbidities and complications of myocardial infarction. Mortality is three times greater than that of patients <75 years and one out of every three deaths in patients hospitalized due to myocardial infarction occurs in elderly patients. It is highly relevant that clinical trials also include elderly patients and evaluate different age-adjusted therapeutic strategies for this particular age group, which, considering the progression of the population will become more and more frequent.

Conflicts of interest

None declared.

(See authors conflicts of interest forms on the website/ Supplementary material).

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