

ARGEN-IAM-ST Registry: ST-elevation Myocardial Infarction in "New" Older Adults

Registro ARGEN-IAM-ST: infarto de miocardio con elevación del segmento ST en el "nuevo" adulto mayor

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ABSTRACT

Background: The World Health Organization (WHO) defines an Older Adult (OA) as any individual aged 60 or older. It is known that mortality due to acute myocardial infarction (AMI) increases with age, but age thresholds higher than those proposed by the WHO have been consistently used; therefore, describing the characteristics and in-hospital progress of this subgroup of patients, in accordance with the WHO definition, becomes relevant.

Objectives: 1) To know the prevalence of OA with acute ST-elevation myocardial infarction (STEMI) in Argentina according to the WHO, and 2) to compare their characteristics, reperfusion treatments, and mortality against those in young adults.

Methods: Patients included in the National Registry of ST-Elevation Myocardial Infarction (Registro Nacional de Infarto con Elevación del ST, ARGEN-IAM-ST) were analyzed. Clinical features, therapies, and progress were compared in OA versus young adults.

Results: A total of 6676 patients were enrolled, 3626 of which (54.3%) were OA. OA were mostly female (37.6% vs 31.4%, $p < 0.001$), had hypertension (67.8% vs 47%, $p < 0.001$), diabetes (26.1% vs 19.9%, $p < 0.001$), dyslipidemia (45.4% vs 37%, $p < 0.001$), and a longer coronary artery disease history (16% vs 10.3%, $p < 0.001$). The time to consultation in OA was longer (120 min vs 105 min, $p < 0.001$), with a similar total ischemic time (314 min vs 310 min, $p = 0.33$). They received less reperfusion treatment (89.9% vs 88.6%, $p = 0.04$) and more primary angioplasty (91% vs 87.4%, $p < 0.001$). Heart failure was more common in OAs (27.3% vs 18.5%, $p < 0.001$), with a similar bleeding incidence (3.7% vs 3.1%, $p = 0.33$), and significantly higher mortality (11.4% vs 5.5%, $p < 0.001$). Being an OA was an independent mortality predictor.

Conclusions: More than half the cases of AMI in our country occur in OA. Older patients are less likely to receive reperfusion, more likely to have heart failure, and show twice the rate of mortality as compared to patients under 60.

Keywords: Myocardial Infarction –ARGEN-IAM-ST Registry- Older adults – Mortality

RESUMEN

Introducción: la Organización Mundial de la Salud (OMS) considera adulto mayor (AM) a las personas que tienen 60 años o más. Es sabido que la mortalidad por infarto agudo de miocardio (IAM) aumenta a edades más avanzadas, pero siempre se han utilizado umbrales de edad mayores que el propuesto por la OMS, por lo cual describir las características y evolución intrahospitalaria de este subgrupo (de acuerdo con la definición de la OMS) se torna relevante.

Objetivos: 1) conocer la prevalencia de los AM según la OMS, con IAM con elevación del segmento ST en Argentina y 2) comparar sus características, tratamientos de reperusión y mortalidad con los adultos jóvenes.

Materiales y métodos: se analizaron los pacientes ingresados en el Registro Nacional de Infarto (ARGEN-IAM-ST). Se compararon las características clínicas, tratamientos y evolución de los AM y los adultos jóvenes.

Resultados: Se incluyeron 6676 pacientes, de los cuales 3626 (54,3%) eran AM. Los AM fueron más frecuentemente mujeres (37,6% vs. 31,4%, $p < 0,001$), hipertensos (67,8% vs. 47%, $p < 0,001$), diabéticos (26,1% vs. 19,9%, $p < 0,001$), dislipídicos (45,4% vs. 37%, $p < 0,001$), y tuvieron más antecedentes coronarios (16% vs. 10,3%, $p < 0,001$). El tiempo a la consulta de los AM fue mayor (120 min vs. 105 min, $p < 0,001$) con similar tiempo total de isquemia (314 min vs. 310 min, $p = 0,33$). Recibieron menos tratamiento de reperusión (89,9% vs. 88,6%, $p = 0,04$) y más angioplastia primaria (91% vs. 87,4%, $p < 0,001$).

Tuvieron más insuficiencia cardíaca (27,3% vs. 18,5%, $p < 0,001$), similar incidencia de sangrado (3,7 vs. 3,1%, $p = 0,33$) y una mortalidad significativamente mayor (11,4% vs. 5,5%, $p < 0,001$). Ser AM fue predictor independiente de mortalidad.

Conclusiones: más de la mitad de los IAM en nuestro país ocurren en AM. Los pacientes mayores tienen menor probabilidad de recibir reperusión, más insuficiencia cardíaca y el doble de la mortalidad que los pacientes menores de 60 años.

Palabras clave: Infarto de miocardio - Registro ARGEN-IAM-ST- Adultos mayores - Mortalidad

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INTRODUCTION

Increased life expectancy entails a larger population of older adults (OA) coming daily to our offices and suffering from acute myocardial infarction (AMI). The World Health Organization (WHO) and the Inter-American Convention on the Protection of the Human Rights of Older Persons currently define an OA as any individual aged 60 or older. (1) Until then, any individual aged 70-75 or older was considered an OA, and we have already described the characteristics and progress of the age range in this setting. (2) As the average age of patients hospitalized with acute ST-elevation myocardial infarction (STEMI) in the ARGEN-IAM-ST registry is 58.4 ± 11 , using this new OA definition might have a clinical impact, since patients over 60 years old are a significant group of patients who may not have the same risk as those aged 70, 75 or 80 when this is considered as a cut-off value.

The ARGEN-IAM-ST has been an ongoing registry of AMI patients developed by the Argentine Society of Cardiology and the Argentine Federation of Cardiology since 2015. Today, it includes more than 6500 patients and allows us to analyze progress of acute STEMI patients according to their age group. (3)

Our objectives were:

1) To know the percentage of new older adults hospitalized in Argentina as a result of acute STEMI.

2) To evaluate whether there are any differences in terms of clinical features, reperfusion treatments, and in-hospital progress for new OA (over 60 years old) versus young adults.

3) To analyze whether being an OA is an independent in-hospital mortality predictor.

METHODS

Patients included in the National Registry of ST-Elevation Myocardial Infarction (ARGEN-IAM-ST) were assessed. A new older adult (from now on referred to as OA) was defined as a patient aged 60 or older, and a young adult was defined as any patient under 60. The characteristics of both groups were compared, and the relationship between OAs and mortality was assessed.

Statistical analysis

Frequency tables were developed for quantitative variables, and contingency tables were developed for qualitative variables. Continuous variables were expressed as the mean and standard deviation (SD) for normal distribution variables, and as the median and 25%-75% interquartile range (IQR) for those lacking normal distribution. The statistical analysis of continuous variables was performed using the Student's t-test or the Wilcoxon rank sum test, as appropriate. Qualitative variables were expressed as percentages, and comparisons were performed using the chi-square test with Yates correction or the Fisher's exact test, as applicable.

A multiple logistic regression analysis was performed in order to determine independent associations and/or predictions among different variables involved and in-hospital mortality. Variables of statistical significance in univariate analysis with $p \leq 0.10$ were entered for evaluation in the different regression models. Each covariate value was expressed as adjusted odds ratio (OR) and its corresponding

95% confidence interval (95% CI). All statistical comparisons were two-tailed, and p-values <0.05 were considered statistically significant. Epi-info 7 was used for analysis.

Ethical considerations

The registry was approved by the Committee on Ethics of the Argentine Society of Cardiology.

RESULTS

A total of 6682 patients were enrolled, 3626 (54.3%) of which were OA, and 24.1% were aged 75 or older. Table 1 shows the overall characteristics of patients for OAs and young adults.

OAs included a significantly higher percentage of women, hypertension, diabetes, dyslipidemia, kidney failure upon admission, and coronary artery disease history. In addition, there was a higher prevalence of heart failure upon admission, a longer time to consultation, and a lower rate of reperfusion. Primary angioplasty was the most common reperfusion method, with a shorter door-to-balloon time than for young adults, though with the same total ischemic time. There were no differences in terms of bleeding complications. In-hospital mortality in OA was twice that of young adults (11.4% vs 5.5%, $p < 0.001$). The subgroup of patients aged ≥ 75 had an in-hospital mortality of 18.7%.

Table 2 shows that OA received more clopidogrel and less prasugrel. Use of ticagrelor was very low in the overall population (15%), with no age-based differences. OA received less beta-blockers and vasodilators upon admission, but at discharge showed no differences in the use of angiotensin-converting enzyme inhibitor (ACEI)/angiotensin receptor blockers (ARB), which was higher than 75% in the population. Table 3 displays the multivariate analysis to predict mortality. Being an OA was an independent mortality predictor. A Killip and Kimball score $>A$, a creatinine value >2 mg/dL upon admission, absence of reperfusion, female sex, and diabetes were also mortality predictors.

DISCUSSION

Most AMI patients are currently in the age range considered as OA by the WHO. For projections based on life expectancy, it is known that this number will be even higher in a not very distant future. (4) New OA (i.e., with a cut-off value of 60 years) with acute STEMI also have a higher risk of complications and death as compared to patients under 60, though lower than OAs when the cut-off value is 75 or older.

Many of the characteristics of this specific group of patients affect progress, such as the patients' own features and other healthcare system characteristics. While most of them are male, the percentage of women significantly increases with age, probably due to their higher life expectancy, as observed in other population registries as well. (5)

Age increases prevalence of all risk factors, the most common of which is hypertension. (6) Kidney failure (defined by a creatinine value higher than 2

Table 1. Population characteristics and progress based on age

	Young adults n = 3056	Older adults n = 3626	p
Age, years. Median (IQR 25-75)	52 (47-56)	67.5 (63-74)	<0.001
Female (%)	31.4	37.6	<0.001
Hypertension (%)	47	67.8	<0.001
Diabetes (%)	19.9	26.1	<0.001
Dyslipidemia (%)	37	45.4	<0.001
Documented coronary artery disease history (%)	10.3	16	<0.001
Previous AMI (%)	54.5	51.7	0.014
Killip and Kimball >A (%)	18.5	27.3	<0.001
Reperfusion (%)	89.9	88.6	0.045
Primary PTCA (%)	87.4	91	<0.001
Creatinine >2 mg/dL upon admission (%)	4.3	6.6	<0.001
Time to consultation, minutes. Median (IQR 25-75)	105 (45-233)	120 (59-270)	<0.001
Total ischemic time, minutes. Median (IQR 25-75)	310 (182-600)	314 (190-610)	0.332
Door-to-balloon time, minutes. Median (IQR 25-75)	105 (60-197)	96 (55-190)	0.017
Non-major bleeding* (%)	3.1	3.7	0.224
Major bleeding** (%)	0	1	0.235
Mortality (%)	5.5	11.4	<0.001

*: 3 to 5 mg/dL Hb drop; **: >5 mg/dL Hb drop (as evaluated in 2424 patients)

AMI: acute myocardial infarction; IQR: interquartile range

PTCA: percutaneous transluminal coronary angioplasty

Table 2. Medication upon admission and discharge.

	Young adults n = 3056	Older adults n = 3626	p
Medication upon admission			
ASA (%)	99.1	98.7	0.083
P2Y12 inhibitor (%)	95.9	96.2	0.274
Clopidogrel (%)	74.3	79	<0.001
Prasugrel (%)	12.2	7.2	<0.001
Ticagrelor (%)	15.8	15.3	0.312
Betablockers (%)	61.7	53.4	<0.001
ACEI/ARB (%)	58.8	55.5	0.004
Aldosterone antagonists (%)	11.9	13.3	0.063
Medication upon discharge			
ASA (%)	96.7	94.9	<0.001
P2Y12 inhibitor (%)	93	92.5	0.225
Clopidogrel (%)	68.8	74.2	<0.001
Prasugrel (%)	14.5	8.8	<0.001
Ticagrelor (%)	16.7	16.2	0.313
Betablockers (%)	87.4	81.5	<0.001
ACEI/ARB (%)	76.3	76	0.404
Aldosterone antagonists (%)	19.7	22	0.023
Statins (%)	94.7	93.9	0.095

ACEI: angiotensin-converting enzyme inhibitor

ARB: angiotensin receptor blocker

ASA: acetylsalicylic acid

Table 3. Independent mortality predictors

	OR (CI 95%)	p
Older adults	1.67 (1.27-2.17)	<0.001
Diabetes	1.30 (1.00-1.69)	0.047
Female	0.77 (0.64-0.98)	0.036
No reperfusion	1.64 (1.38-1.96)	0.036
Creatinine >2 mg/dL	2.59 (1.75-3.83)	<0.001
Killip and Kimball score >A	9.12 (7.07-11.76)	<0.001

mg/dL upon admission) was significantly higher in OAs. It is known that kidney failure increases the risk of bleeding (7) and sometimes prevents using drugs which are useful to reduce mortality; therefore, its presence becomes relevant. The percent use of P2Y12 inhibitors was similar in OA and young adults, with no difference in the incidence of bleeding, probably since use of clopidogrel was more widespread among OA (at the expense of little use of more potent platelet aggregation inhibitors), with very little use of thrombolytic drugs.

In our study, the percentage of global reperfusion was high regardless of age, while it was significantly lower in OAs than in young adults. Primary angioplasty was the most common strategy for OAs, following current treatment guidelines and likely influenced by the type of sites in the ARGEN-IAM-ST registry, where the institutions involved are affiliated to scientific societies, and most of them have a hemodynamics department. Despite the low rate of reperfusion, OA had a higher incidence of heart failure and death. This might relate to more extensive coronary artery disease, less tolerance to ischemia, greater ventricular stiffness, or microcirculation damage associated with older age. (8)

Mortality in OAs is twice that of young adults, and this also happens with other real-life registries. (9) It was 11.4% in our study and higher than mortality recently reported in STREAM 2 for this group of patients treated with primary angioplasty, reaching 8.2% within 30 days. (10)

Mortality in OA is associated with age-specific aspects, such as a higher prevalence of coronary artery disease, and more diffuse coronary lesions. However, in case of a similar lesion, an OA's response might differ, as it may be affected by microcirculation and the capacity to develop collateral circulation. In addition, OA have concomitant clinical conditions leading to worse prognosis, such as comorbidities, nutritional risk, sarcopenia, polypharmacy, the inability to perform daily life activities, and fragility. (11,12) Multiple morbidity makes patients less likely to receive invasive treatments versus younger patients. (13) Charlson comorbidity index (14) is one of the instruments that might be used to evaluate impact on patients' prognosis. It has been validated in aortic stenosis, (15) infectious endocarditis, (16) thromboembolic venous

disease, (17) heart transplantation, (18) and coronary angioplasty, where a Charlson index of ≥ 2 was associated with mortality and major cardiac events in the short and long term. (19) More recently, a Danish index (DANCAMI) has been developed to evaluate AMI comorbidities; (20) this index has been validated in a large American population with good results. (21) Barthel index is used in OA to evaluate the degree of dependence when performing daily life activities. It has shown to be a one-year mortality predictor in patients with acute coronary syndrome (ACS) under coronary angioplasty. (22)

While these indexes may serve to stratify risk, their application becomes complex in the context of acute STEMI, where immediate treatment is required, particularly when there are no relatives to confirm the patient's baseline condition.

Although the latest European guideline on ACS management describe the importance of comorbidities and other geriatric syndromes, e.g., fragility in OAs, they fail to establish any specific scoring at this time. (23) However, we believe it might be necessary to perform a comprehensive assessment of OAs.

Limitations

The ARGEN-IAM-ST study is a voluntary registry of institutions closely related to scientific societies that may not be representative of the healthcare setting for patients with infarction. As stated above, there are many institutions with cardiology internships and hemodynamic care availability 24/7.

CONCLUSIONS

More than half the cases of acute STEMI in our country occur in OA, who have a higher prevalence of risk factors and more extensive coronary artery disease. They have lower chances of receiving reperfusion, but if they do, it is mostly through primary angioplasty and with door-to-balloon times shorter than to those in younger patients. Total ischemic time is also long in all patients. OA are more likely to experience heart failure and bleeding and have twice the mortality rate of patients under 60. Given this epidemiology, it might be convenient to include variables such as geriatric syndromes and fragility screening among the data we normally record for a wider view. (24,25) The new OA definition continues to involve higher mortality, despite the lower age threshold. However, the OA group has heterogeneous clinical characteristics, which might make it more adequate to regard age from a "biological" rather than from a "chronological" perspective.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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