

# Clinical and Angiographic Characteristics, Therapeutic Strategies and Outcome of Young Patients with Acute Coronary Syndrome

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## ABSTRACT

### Background

Patients with acute coronary syndrome have clinical differences which are determined by the age-group to which they belong. Yet, few studies have compared young patients versus elderly patients presenting with this syndrome.

### Objectives

The aim of this study was to describe the clinical and angiographic characteristics, therapeutic strategies and outcome of young patients with acute coronary syndrome, and compare them with those of elderly patients.

### Methods

A total of 5055 patients included in the Epi-Cardio registry, with diagnosis of acute coronary syndrome, were analyzed. Men  $\leq 45$  years and women  $\leq 50$  years were considered young.

### Results

Young patients represented 10.3% of the population (519) and 89.7% (4536) were elderly patients. Among young patients, 49.9% presented ST-segment elevation acute coronary syndrome and 50.1% had non ST-segment elevation. In elderly patients, ST-segment elevation acute coronary syndrome occurred in 38.4% of patients and 61.6% had non ST-segment elevation ( $p < 0.00001$ ). Coronary angiography was performed to 2845 patients (56.3%). Among young patients, 54.2%, 20% and 9.7% had one-vessel, two-vessel and three-vessel disease, respectively, and 16.1% had non-significant lesions. Among elderly patients, 39.6%, 28.4% and 22.5% had one-vessel, two-vessel and three-vessel disease, respectively, and 9.5% had non-significant lesions ( $p < 0.001$ ). There were no significant differences in the treatments used between both age groups during hospitalization. Mortality was 1% in young patients and 3.5% in elderly patients (OR 0.26;  $p = 0.02$ ). Corrected mortality was significantly lower in young patients (OR 0.25;  $p = 0.038$ ).

### Conclusions

ST-segment elevation acute coronary syndrome was more frequent among young patients compared to elderly patients. Mortality was three to four times greater in elderly patients. The difference in clinical presentation is explained by the cardiovascular risk profile and extension of coronary artery disease in both groups.

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## Key words >

Coronary Disease - Young Adult - Myocardial Infarction

## Abbreviations >

OR	Odds ratio	ACS	Acute coronary syndrome
STEACS	ST segment elevation acute coronary syndrome	NSTEACS	Non-ST segment elevation acute coronary syndrome

## BACKGROUND

Coronary artery disease is one of the conditions producing greatest morbidity and mortality worldwide and is the leading cause of death in developed coun-

tries. (1)The acute manifestations of the disease typically occur after the sixth or seventh decade of life and symptoms appear five years later in women than in men. (2)

The clinical manifestation of plaque accident generally occurs in old age, but, atherosclerosis starts several decades before and has a silent progression. Stry and Fuster studied the evolution of atherosclerotic lesions in coronary arteries of children and young adults and demonstrated that atherosclerotic disease has a prolonged asymptomatic phase and that plaque accident is an event that occurs in long-standing lesions. (3, 4)

Between 5% and 8% of patients who develop symptomatic coronary artery disease have a premature presentation, that is, before the fifth or sixth decade of life. (5, 6) Clinical and epidemiological studies suggest that coronary risk factors, clinical presentation and the extension of coronary artery disease are different in young patients compared to elderly patients. (7-10) However, few studies have compared both age groups in the setting of acute coronary syndrome (ACS).

The primary goal of the present study was to describe the clinical and angiographic characteristics and the outcome of young patients with ACS, and to compare them with those of elderly patients. The secondary target was to analyze whether age conditions the use of different therapeutic strategies and treatment.

## METHODS

Complete data from all the patients included in the Epi-Cardio registry with diagnosis of ACS between October 2006 and January 2010 were analyzed. Epi-Cardio is a multicenter, independent and prospective registry of acute cardiovascular disease in Argentina (for more information, visit [www.epi-cardio.com.ar](http://www.epi-cardio.com.ar)). (11) Follow-up was limited to hospitalization.

## Definitions

“Young” patients were defined as men and women aged  $\leq 45$  and  $\leq 50$  years, respectively, according to the international literature. Patients aged above these limits were considered “elderly”.

Clinical presentation was defined as ST segment elevation acute coronary syndrome (STEACS) or non-ST segment elevation acute coronary syndrome (NSTEACS) according to the electrocardiographic findings in the first medical contact. Patients with persistent left bundle branch block and prolonged chest pain were classified as STEACS.

When the therapeutic strategy (early invasive strategy or initial conservative strategy) and drug treatment were analyzed, patients with ST-segment elevation on admission and its rapid resolution without reperfusion therapy (patients with spontaneous reperfusion) were analyzed together with the NSTEACS group as they presented therapeutic similarity.

In patients with NSTEACS, early invasive strategy was defined as the performance of coronary angiography within the first 72 hours after admission without prior stress test.

Significant coronary artery stenosis was defined as  $\geq 70\%$  for the coronary arteries and  $\geq 50\%$  for the left main coronary artery. Also, arteries with previous percutaneous coronary intervention were considered as having significant stenosis although no significant lesions were present at the moment of coronary angiography.

## Statistical analysis

Continuous variables with non-normal distribution were expressed as median and interquartile range. Categorical variables were expressed as percentages. Differences between groups for continuous variables were assessed with the non-parametric Kruskal-Wallis test. Categorical variables were analyzed with the chi-square test or Fisher's exact test. The Cochran-Mantel-Haenzel test was used to evaluate the interaction between the age group (young/elderly) and mortality, stratified by the type of ACS. The chi-square test for trend was applied to assess the proportion in which different therapeutic strategies were used across age quartiles. Multiple logistic regression models were developed to determine the association between age group and mortality. All covariates with asymmetric distribution in both age groups and with  $p < 0.1$  in the univariate analysis were included. This analysis was repeated in the subgroup of patients undergoing coronary angiography during hospitalization. The extension of coronary artery disease was included in the model as a dichotomous variable (0-1 vs. 2-3 coronary arteries with significant stenosis). A two-tailed  $p$  value  $< 0.05$  was considered statistically significant for all the comparisons.

Statistical analysis was performed using STATA 10.0® and Epi-Info® software packages.

## RESULTS

### Follow-up

A total of 5055 patients with ACS admitted to 50 institutions in Argentina were analyzed; 519 were young patients (10.3%) and 4536 were elderly patients (89.7%). The main characteristics of the population are described in Table 1.

An audit was conducted during a month to evaluate presence of underreported patients at four randomly selected institutions, comparing patients incorporated to the Epi-Cardio registry with the hospitalization records of each institution. The proportion of underreporting was 5% or lower in all cases.

### Cardiovascular risk factors and clinical presentation

Among major cardiovascular risk factors, only active smoking was more frequent in young patients. The remaining cardiovascular risk factors, history of cardiovascular disease and previous coronary procedures were more frequent in elderly patients (see Table 1).

There were significant differences in the form of presentation of ACS between both groups. On admission, 259 (49.9%) young patients presented STEACS and 260 (50.1%) presented NSTEACS, while 1741 (38.4%) elderly patients presented STEACS and 2795 (61.6%) had NSTEACS ( $p < 0.00001$ ).

### Extension of coronary artery disease

During hospitalization, 2845 patients (56.3%) underwent coronary angiography, with a trend towards greater indication in young patients (59.7% vs. 55.9%, respectively;  $p = 0.09$ ). The extension of coronary artery disease was significantly lower in young patients (Figure 1). Among them, 16.1% had coronary arteries without significant stenosis, 54.2% had significant one-vessel disease, 20% had two-vessel disease and 9.7% had three-vessel disease. In elderly patients,

9.5% had no significant stenosis, and one-, two- and three-vessel disease was present in 39.6%, 28.4% and 22.5% of patients, respectively ( $p < 0.0001$ ). The proportion of significant stenosis of the left main coronary artery was of 3.2% in young patients and 6.7% in elderly patients.

**Therapeutic strategies**

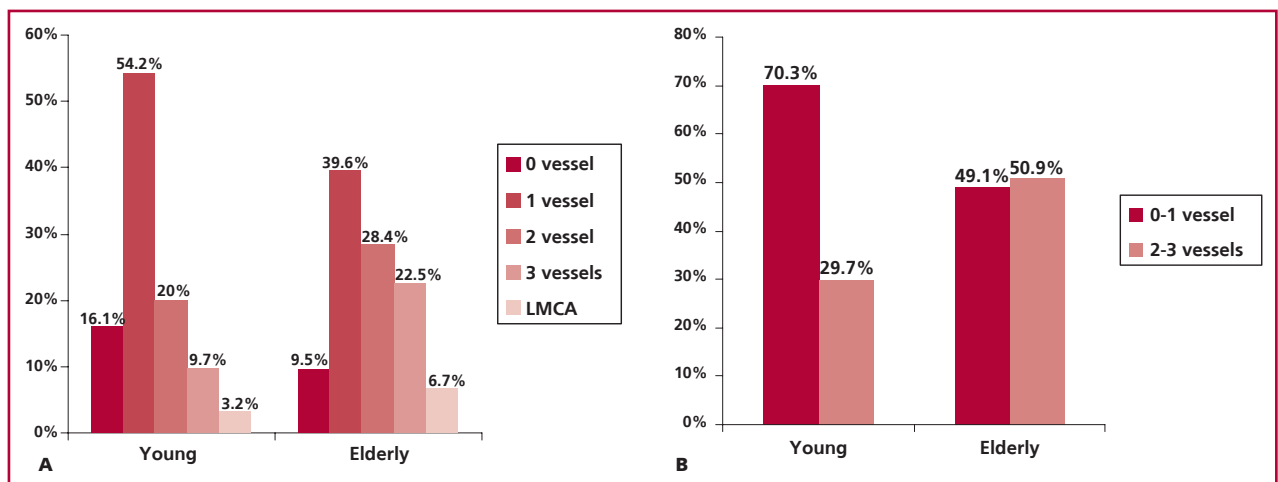
There were no significant differences between both groups in the therapeutic strategies used during hospitalization. In patients with persistent STEACS early invasive therapy was indicated in 154 young patients (53.3%) and 1514 (53%) elderly patients ( $p = 0.9$ ) (Figure 2 A). Percutaneous coronary interven-

tion was indicated in 76 young patients (26.3%) and 738 elderly patients (25.8%) ( $p = 0.8$ ), and coronary revascularization surgery was performed in 7 young patients (2.4%) and 107 elderly patients (3.7%) ( $p = 0.2$ ). In young patients, antithrombotic therapy prescribed during hospitalization included: heparin (unfractionated heparin, low-molecular-weight heparin or fondaparinux) in 136 patients (47%), clopidogrel in 159 (55%) and glycoprotein IIb-IIIa inhibitors in 2 (0.7%). Among elderly patients, 1,529 (53.5%) received heparin, 1612 (56.4%) clopidogrel and 31 (1.1%) glycoprotein IIb-IIIa inhibitors (non significant differences were found for all the comparisons between young and elderly patients).

**Table 1.** Baseline characteristics of the population

Age, median (IQR)	General n = 5055		Young patients n = 519 (10.3%) 43 (40-45)		Elderly patients n = 4536 (89.7%) 63 (56-73)		p < 0.00001
	61 (53-71)		43 (40-45)		63 (56-73)		
	n	%	n	%	n	%	
Male gender	3660	72.4	360	69.4	3300	72.7	0.1
Hypertension	3215	63.6	220	42.4	2995	66	< 0.00001
Diabetes	1026	20.3	78	15	948	20.9	0.001
Hypercholesterolemia	2353	46.5	212	40.8	2141	47.2	< 0.01
Smoking habits	1650	32.6	270	52	1380	30.4	< 0.00001
Former smoker	1223	24.2	62	11.9	1161	25.6	< 0.00001
Previous myocardial infarction	941	18.6	66	12.7	875	19.3	< 0.0001
Previous percutaneous coronary intervention	719	14.2	47	9.1	672	14.8	< 0.001
Previous coronary artery bypass graft surgery	346	6.8	6	1.2	340	7.5	< 0.00001
Previous heart failure	160	3.2	5	1	155	3.4	< 0.01
STEACS on admission	2000	39.6	259	49.9	1741	38.4	< 0.00001
NSTEACS on admission	3055	60.1	260	50.1	2795	61.6	
Coronary angiography	2845	56.3	310	59.7	2535	55.9	0.09

STEACS: ST segment elevation acute coronary syndrome. NSTEACS: Non-ST segment elevation acute coronary syndrome.



**Fig. 1.** Number of coronary arteries with severe stenosis in patients undergoing coronary angiography (n = 2845), stratified by age group. LMCA: Left main coronary artery.

An early reperfusion strategy was indicated in 143 young patients (62.2%) and 979 elderly patients (58.4%) ( $p = 0.3$ ) with STEACS (Figure 2 B). There were no significant differences in the use of thrombolytic agents or primary angioplasty as a reperfusion strategy in both age groups (27.4% vs. 22% for thrombolysis and 34.8% vs. 36.4% for primary angioplasty in young and elderly patients, respectively;  $p = 0.06$ ). However, a trend towards greater use of primary angioplasty was observed in elderly patients and of thrombolytic agents in young patients.

A trend analysis stratified by age quartiles demonstrated a lower proportion of invasive strategy in NSTEMACS (quartile 1: 56.9%, quartile 2: 55.9%, quartile 3: 55% and quartile 4: 44.5%) and of reperfusion strategy in STEACS (quartile 1: 63.8%, quartile 2: 61.7%, quartile 3: 59.8% and quartile 4: 50.5%) (chi square test for trend  $< 0.0001$  in both cases) (Figure 2 C and D).

At discharge, use of aspirin, clopidogrel or prasugrel, beta blockers and statins was 94.6%, 80.5%, 69.9% and 85.2%, respectively, in young patients and 94.5%,

84.5%, 69.2% and 86.4%, respectively, in elderly patients ( $p = 0.01$  for beta blockers, and non significant differences for aspirin, clopidogrel or prasugrel and statins). The difference in use of beta blockers at discharge was due to its lower prescription (55.8% in young patients and 67.2% in elderly patients) in the subgroup of patients without significant angiographic stenosis, a finding which was more prevalent in young patients.

**Mortality**

Five young patients (1%) and 161 elderly patients (3.5%) died (odds ratio [OR] 0.26, 95% CI 0.11 to 0.65;  $p = 0.02$ ) (Figure 3 A). In-hospital mortality was greater in patients with STEACS (5.5% overall mortality, 1.2% in young patients and 6% in elderly patients, OR 0.18, 95% CI 0.05 to 0.6;  $p = 0.001$ ) compared to patients with NSTEMACS (1.9% overall mortality, 0.8% in young patients and 2% in elderly patients, OR 0.38, 95% CI 0.06 to 1.59;  $p = 0.1$ ), with a non significant interaction test ( $p = 0.4$ ). Mortality adjusted for clinical covariates (diabetes, previous heart failure, type

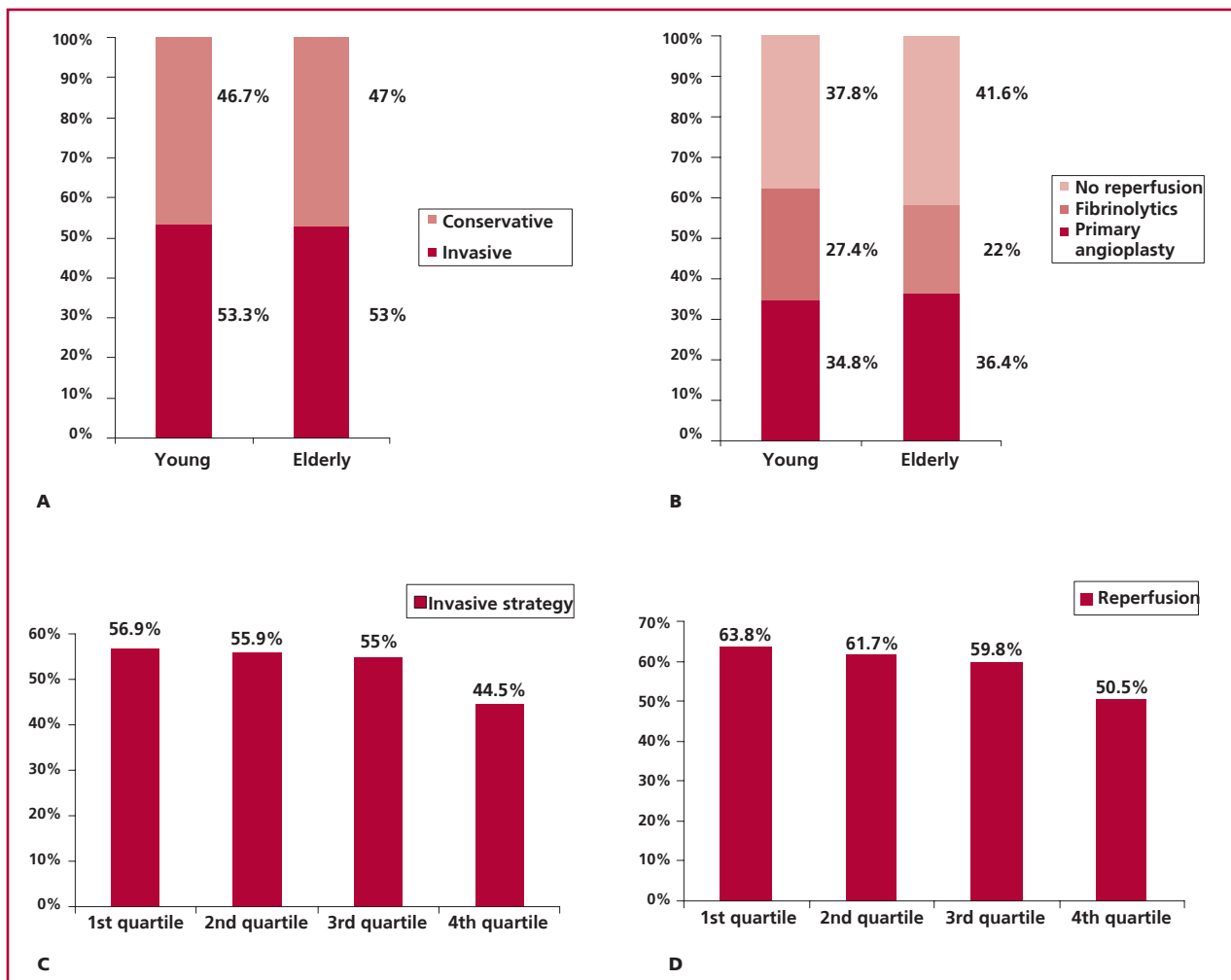


Fig. 2. Use of early invasive strategy (NSTEMACS) and early reperfusion (STEACS) stratified by age group and quartile.

of ACS, gender, active smoking and dyslipidemia) was significantly lower in young patients (OR 0.25, 95% CI 0.10 to 0.62; p = 0.038) (Figure 3 B) (Table 2).

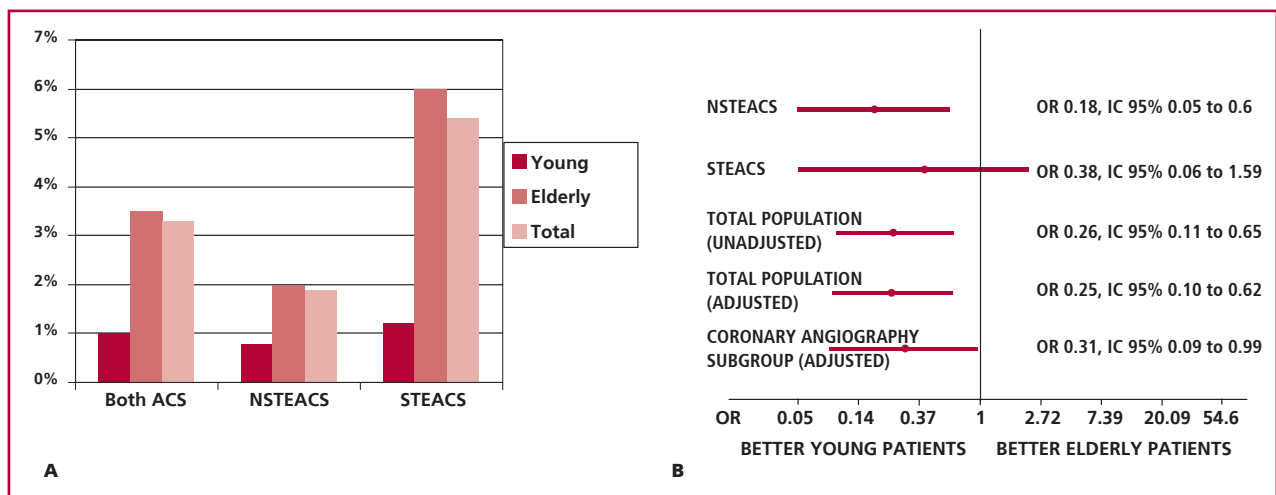
In the subgroup of patients undergoing coronary angiography during hospitalization, mortality was also adjusted for the same clinical variables and the extension of coronary artery disease was included in the model. Mortality was significantly lower in young patients, though the association had a borderline p value (OR 0.31, 95% CI 0.09 to 0.99; p = 0.049) (Figure 3 B and Table 2).

**DISCUSSION**

**Age-related differences in the clinical presentation**

The results of our study show significant differences in the form of presentation of ACS between young and elderly patients. Compared to the elderly, STEACS

was more frequent in young patients. Traditionally, NSTEMACS has been correlated with extensive coronary artery disease, and some of these episodes are due more to an imbalance in coronary artery circulation than to acute thrombotic occlusion secondary to atherosclerotic plaque accident. Conversely, the pathophysiology of STEACS corresponds to thrombotic occlusion in more than 90% of the episodes, and in these cases, the extension of coronary artery disease is an essential variable for the development of this condition, which is more dependent on the presence of young and vulnerable plaques with subsequent plaque accident. The different prevalence of risk factors in both groups supports this clinical and pathophysiological reasoning. In elderly patients, ACS develops in the setting of a much more extensive atherosclerotic disease due to the accumulation of risk factors acting over many



**Fig. 3. A.** Total in-hospital mortality and mortality by age group, stratified by the type of acute coronary syndrome. **B.** Odds ratio for in-hospital mortality.

Variable	Odds ratio	95% CI	p
<b>Total population</b>			
Young (yes/no)	0.25	0.10-0.62	0.038
Gender (M/F)	0.55	0.40-0.77	< 0.001
Current smoking	0.59	0.40-0.87	< 0.01
Hypercholesterolemia	0.65	0.47-0.91	0.01
Diabetes	1.47	1.02-2.11	0.04
Previous heart failure	2.06	1.04-4.07	0.04
STEACS/NSTEMACS	3.58	2.65-5	< 0.0001
<b>Total population</b>			
Young (yes/no)	0.31	0.09-0.99	0.049
Gender (M/F)	0.43	0.26-0.69	< 0.001
Hypercholesterolemia	0.50	0.31-0.80	0.004
Previous heart failure	2.95	1.09-7.98	0.03
STEACS/NSTEMACS	3.04	1.87-4.29	< 0.0001
Number of vessels (2-3/0-1)	3.59	2.13-6.07	< 0.001

**Table 2.** Multivariate analysis of in-hospital mortality

M: Male. F: Female. STEACS: ST segment elevation acute coronary syndrome. NSTEMACS: Non-ST segment elevation acute coronary syndrome.

years. On the contrary, in young patients the extension of coronary artery disease is lower. Structural differences in atherosclerotic plaques in both age groups have been demonstrated by histopathologic studies. (12, 13) Young patients present a large amount of lipid-containing foam cells (lipid-laden macrophages) and relative decrease of collagen extracellular matrix. This relation is inverted in elderly patients. In turn, complex plaques are more common in young patients with coronary artery disease compared to elderly patients. All this information may be put together in a logical sequence: the risk factor profile is different in both age groups, conditioning the extension and the angiographic and histopathologic characteristics of atherosclerotic plaques which will induce the type of presentation of acute coronary artery disease in both groups. In young patients, the presence of soft, lipid-rich plaques, together with the higher prevalence of prothrombotic factors, such as more frequent active smoking, may facilitate the mechanism of plaque accident and subsequent thrombosis, leading to acute coronary artery occlusion and more prevalent STEACS clinical presentation.

This hypothesis is consistent with the results of our study.

#### Strategies and treatments used

There were no significant differences in the treatments used between both age groups during hospitalization. In the group of patients with NSTEMACS, the proportion of invasive strategy and antithrombotic treatments was similar in young and elderly patients. In patients with STEACS, a trend towards greater indication of early reperfusion was noted in young patients, with no significant differences between both age groups. Although age is a variable that has been inversely associated with the probability of receiving some kind of reperfusion or invasive strategy, (14, 15) the comparison between both age groups did not show significant differences. This may be due to the division of the population into two dichotomous age groups (young - elderly). The analysis by age quartiles showed a significant trend towards lower use of reperfusion and invasive strategies in the higher quartiles, in agreement with previously published studies.

At discharge, the prescribed proportion of aspirin, clopidogrel or prasugrel and statins was similar in young and elderly patients. Beta blockers were more frequently indicated in elderly patients. This was due to the greater proportion of young patients submitted to angiography without coronary artery stenosis, a subgroup that received the lowest percentage of beta blocker indication.

Owing to the geographic distribution of the participating centers and their heterogeneous complexity, we consider that our results represent how ACS is treated in the real world in Argentina.

#### Mortality and age

In-hospital mortality was lower in the group of young patients. Mortality was higher in elderly patients in both types of ACS. Univariate analysis showed that the difference in mortality between both age groups reached statistical significance in the total population and in STEACS. In the NSTEMACS group, the power was insufficient to obtain statistically significant differences because of the low number of events and because the unadjusted OR of mortality in young patients was higher than in the STEACS group. Multivariate analysis showed that the risk of death in elderly patients was four times greater than in young patients and that there was a significant association between age group and mortality ( $p = 0.003$ ). When the analysis was limited to patients undergoing coronary angiography during hospitalization, the extension of the disease had a significant prognostic relevance, and when it was included in the analysis model, the relationship between age and mortality decreased to a borderline  $p$  value ( $p = 0.049$ ). The result of the second analysis should be considered with caution, as the population is smaller compared to that of the first model and the absolute number of events is lower because it is a subgroup. However, it shows that part of the strong association between age and mortality may be due to the confounding effect of the extension of coronary artery disease in elderly patients.

#### Study limitations

Some limitations should be mentioned. Although the results are similar to those of other studies, and clinical reasoning is supported by previous pathophysiological and histopathologic studies, our results are only the expression of clinical, electrocardiographic and angiographic arguments, without absolute certainty in the resulting clinical-pathophysiological and clinical-histopathologic correlation accuracy.

The presence of family history of coronary artery disease or history of drug abuse was not investigated. Family history, drug abuse and active smoking are the most prevalent risk factors among young subjects with coronary artery disease. (8-10)

No information was reported about the angiographic condition of the culprit or probably culprit coronary artery involved in the ACS. Patency or occlusion of the culprit vessel could have provided more information to differentiate ACS in both age groups.

Underreporting of patients cannot be ruled out due to the voluntary nature of the registry. However, an audit performed in a small number of randomly selected centers showed that the proportion of underreporting was 5% or lower in all cases.

#### CONCLUSIONS

Acute coronary artery disease had a different manifestation in young patients compared to elderly patients.

STEACS was most frequent in young than in elderly patients. The different cardiovascular risk profile, coronary artery anatomy and, probably, the anatomy of atherosclerotic lesions in young patients explain these differences. Despite the lack of significant differences in the treatment received, mortality was three to four times greater in elderly patients.

## RESUMEN

### Características clínicas, angiográficas, estrategias terapéuticas y pronóstico de pacientes jóvenes con síndrome coronario agudo

#### Introducción

Los pacientes con síndrome coronario agudo presentan diferencias clínicas según el grupo etario al que pertenezcan. No obstante, son pocos los estudios que han comparado pacientes jóvenes versus mayores en el contexto de este síndrome.

#### Objetivos

Describir las características clínicas y angiográficas, los usos terapéuticos y el pronóstico de los pacientes jóvenes con síndrome coronario agudo y compararlos con los pacientes mayores.

#### Material y métodos

Se analizaron 5.055 pacientes incluidos en el registro Epi-Cardio con diagnóstico de síndrome coronario agudo. Se consideraron jóvenes los hombres  $\leq 45$  años y las mujeres  $\leq 50$  años.

#### Resultados

De los pacientes incluidos, 519 eran jóvenes (10,3%) y 4.536 eran mayores (89,7%). El 49,9% de los jóvenes presentaron síndrome coronario agudo con elevación del segmento ST y el 50,1% sin elevación del segmento ST. Entre los mayores, el 38,4% presentaron el síndrome con elevación del segmento ST y el 61,6% sin elevación del segmento ST ( $p < 0,00001$ ). Se realizó cateterismo coronario a 2.845 pacientes (56,3%). Entre los jóvenes, el 54,2% tenían enfermedad significativa de un vaso, el 20% de dos vasos, el 9,7% de tres vasos y el 16,1% no tenían lesiones significativas. Entre los mayores, el 39,6% tenían enfermedad de un vaso, el 28,4% de dos vasos, el 22,5% de tres vasos y el 9,5% sin lesiones significativas ( $p < 0,001$ ). No existieron diferencias significativas en los tratamientos entre ambos grupos etarios durante la internación. La mortalidad fue del 1% en jóvenes y del 3,5% en mayores (OR 0,26;  $p = 0,02$ ). La mortalidad corregida fue significativamente menor entre los jóvenes (OR 0,25;  $p = 0,038$ ).

#### Conclusiones

Los pacientes jóvenes con síndrome coronario agudo presentaron más frecuentemente elevación del segmento ST que los mayores. La mortalidad de los mayores fue tres a cuatro veces mayor que en los jóvenes. El perfil de riesgo cardiovascular y la extensión de la enfermedad coronaria de ambos grupos justifican la diferencia en la presentación clínica.

**Palabras clave** > Enfermedad coronaria - Adulto joven  
Infarto del miocardio

## Conflicts of interest

None declared.

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## APPENDIX

Institution	City	Province	Investigator
CEMIC	Autonomous City of Buenos Aires		Dr. Javier Guetta
Centro Gallego	Autonomous City of Buenos Aires		Dr. Sergio Varini
Clínica 25 de Mayo	Mar del Plata	Buenos Aires	Dr. Jorge Tévez
Clínica Bazterrica	Autonomous City of Buenos Aires		Dr. Carlos Barrero
Clínica Colón	Mar del Plata	Buenos Aires	Dr. Miguel García
Clínica Constituyentes	Morón	Buenos Aires	Dr. Daniel Null
Clínica de Nefrología y CCV	Santa Fe	Santa Fe	Dr. Guillermo Heredia
Clínica del Sol	Autonomous City of Buenos Aires		Dr. Juan Gagliardi
Clínica Independencia	Vicente López	Buenos Aires	Dr. Horacio Pomés Iparraguirre
Clínica Santa Isabel	Autonomous City of Buenos Aires		Dr. Adrián Charask
HIGA Eva Perón	San Martín	Buenos Aires	Dr. Alejandro Saied
HIGA Dr. Luis Güemes	Haedo	Buenos Aires	Dr. Silvia Ferreira
HIGA San Martín	La Plata	Buenos Aires	Dr. Néstor Ruiz
Hospital Dr. Teodoro Álvarez	Autonomous City of Buenos Aires		Dr. Karina Palacios
Hospital Dr. Cosme Argerich	Autonomous City of Buenos Aires		Dr. Alfredo Piombo
Hospital Evita Pueblo	Berazategui	Buenos Aires	Dr. Néstor Gorini
Hospital Dr. Eduardo Castro Rendón	Neuquén	Neuquén	Dr. Marianela Gutiérrez
Hospital Dr. Horacio Cestino	Ensenada	Buenos Aires	Dr. Adrián Lamarque
Hospital de Clínicas Gral. José de San Martín	Autonomous City of Buenos Aires		Dr. Sandra Swieszkowski
Hospital El Cruce - Néstor Kirchner	Florencio Varela	Buenos Aires	Dr. Carlos Tajer
Hospital Escuela Gral. San Martín	Corrientes	Corrientes	Dr. Julio Ibáñez
Hospital Español	Autonomous City of Buenos Aires		Dr. Liliana Nicolosi
Hospital Español	La Plata	Buenos Aires	Dr. Daniel De Sagastizábal
Hospital Juan A. Fernández	Autonomous City of Buenos Aires		Dr. Simón Salzberg
Hospital Dr. Felipe Glasman	Bahía Blanca	Buenos Aires	Dr. Fernando Sierra
Hospital Lucio Molas	Santa Rosa	La Pampa	Dr. Mario Kohan
Hospital Delicia Concepción Masvernat	Concordia	Entre Ríos	Dr. Carlos Pedroza
Hospital Dr. José Penna	Bahía Blanca	Buenos Aires	Dr. Gustavo Carrasco
Hospital Regional Río Grande	Río Grande	Tierra del Fuego	Dr. Raúl Maltez
Hospital Donación F. Santojanni	Autonomous City of Buenos Aires		Dr. José Suárez
INCOR	La Rioja	La Rioja	Dr. Pablo Santander
Instituto Alexander Fleming	Autonomous City of Buenos Aires		Dr. Marcelo Zylberman
Instituto Cardiovascular San Luis	San Luis	San Luis	Dr. Juan Albisu
Instituto Médico Central	Ituzaingó	Buenos Aires	Dr. Mariano Ferrer
ITEC	S. M. de Tucumán	Tucumán	Dr. Esteban Ávila
Policlínico Rafaela	Rafaela	Santa Fe	Dr. Eduardo Marzioni
Sanatorio Anchorena	Autonomous City of Buenos Aires		Dr. Miguel González
Sanatorio Belgrano	Mar del Plata	Buenos Aires	Dr. Héctor Moreno
Sanatorio Boratti	Posadas	Misiones	Dr. Mariela Fontana
Sanatorio de la Mujer	Rosario	Santa Fe	Dr. Pablo Milanesio
Sanatorio de la Providencia	Autonomous City of Buenos Aires		Dr. Esteban Carfagna
Sanatorio Dupuytren	Autonomous City of Buenos Aires		Dr. Paula Pérez Terns
Sanatorio El Carmen	Salta	Salta	Dr. Edmundo Falú
Sanatorio Franchín	Autonomous City of Buenos Aires		Dr. Rafael DiZeo
Sanatorio Garat	Concordia	Entre Ríos	Dr. Ezequiel Forte
Sanatorio Güemes	Autonomous City of Buenos Aires		Dr. Álvaro Sosa Liprandi
Sanatorio de la Trinidad Mitre	Autonomous City of Buenos Aires		Dr. Carlos Pellegrini
Sanatorio Municipal Dr. Julio Méndez	Autonomous City of Buenos Aires		Dr. Ada Abad Monetti
Sanatorio Otamendi	Autonomous City of Buenos Aires		Dr. Carlos Rodríguez Pagani
Sanatorio San Carlos	Bariloche	Río Negro	Dr. Mariano Trevisán