

## Original Article

# Clinical and angiographic profile of young patients undergoing primary percutaneous coronary intervention

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## ABSTRACT

**Background:** The current decline observed in mortality rate among patients with ST-segment elevation acute myocardial infarction can be attributed not only to the increased use of reperfusion strategies, but also to a change in the demographic profile of this population, notably the reduction in mean age.

**Methods:** We retrospectively reviewed all patients undergoing primary percutaneous coronary intervention in the period from April 2010 to December 2014. The primary objective was the characterization of the most prevalent risk factors, the angiographic nature of the lesions, the technical aspects of the procedure, and in-hospital clinical outcomes in patients aged  $\leq 45$  years, comparing them to those aged  $> 45$  years.

**Results:** Among 489 patients with acute myocardial infarction, 54 were  $\leq 45$  years, and 435 were  $> 45$  years. Young patients exhibited a higher prevalence of smoking and obesity, while patients  $> 45$  years were more likely to have hypertension, diabetes mellitus, dyslipidemia, and previous myocardial infarction. Primary percutaneous coronary intervention in young patients was associated with the use of fewer guide catheters, shorter fluoroscopy time, and higher percentage of direct stent implantation. Young patients exhibited good in-hospital outcomes, with lower rate of adverse cardiac events (3.7% vs. 9.2%;  $p = 0.30$ ).

**Conclusions:** Patients aged  $\leq 45$  years accounted for approximately 10% of cases of ST-segment elevation acute myocardial infarction and exhibited high prevalence of modifiable risk factors.

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## Perfil clínico e angiográfico de pacientes jovens submetidos à intervenção coronária percutânea primária

## RESUMO

**Introdução:** O atual declínio observado na taxa de mortalidade entre pacientes com infarto do miocárdio com supradesnívelamento do segmento ST pode ser atribuído não apenas a maior utilização de estratégias de reperfusão, mas também a uma mudança no perfil demográfico dessa população, notadamente à redução em sua média de idade.

**Métodos:** Foram analisados retrospectivamente todos os pacientes submetidos à intervenção coronária percutânea primária no período de abril de 2010 a dezembro de 2014. O objetivo primário foi a caracterização dos fatores de risco mais prevalentes, a natureza angiográfica das lesões, os aspectos técnicos do procedimento e a evolução clínica hospitalar de pacientes jovens, com idade  $\leq 45$  anos, comparando-os àqueles com idade  $> 45$  anos.

**Resultados:** Dentre 489 pacientes com diagnóstico de infarto agudo do miocárdio, 54 tinham idade  $\leq 45$  anos e 435, idade  $> 45$  anos. Pacientes jovens exibiram maior prevalência de tabagismo e obesidade, enquanto pacientes  $> 45$  anos eram mais propensos a apresentar hipertensão arterial sistêmica, diabetes melito, dislipidemia e infarto do miocárdio antigo. Intervenção coronária percutânea primária em jovens associou-se ao uso de menor quantidade de cateteres-guia, menor tempo de fluoroscopia e maior porcentual de implante direto de stent. Pacientes jovens exibiram boa evolução hospitalar, com reduzida taxa de eventos cardíacos adversos (3,7% vs. 9,2%;  $p = 0,30$ ).

*Palavras-chave:*

Infarto do miocárdio

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**Conclusões:** Pacientes com idade  $\leq$  45 anos representaram aproximadamente 10% dos casos de infarto agudo do miocárdio com supradesnivelamento do segmento ST e exibiram elevada prevalência de fatores de risco modificáveis.

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## Introduction

Data from the National Institutes of Health and from USA government agencies indicate that coronary artery disease was responsible for one in seven deaths in that country in 2011.<sup>1</sup> It is estimated that, each year, 635,000 Americans are hospitalized for acute coronary syndrome. Although the mortality rate for ST-segment elevation acute myocardial infarction (STEMI) has decreased significantly - from 11.5%, in 1990, to 8.0%, in 2006-, this decrease can be attributed not only to advances in clinical pharmacotherapy and in reperfusion strategies, notably primary percutaneous coronary intervention (PCI), but also to changes in the demographic profile of patients.

Among these changes, the decline in the mean age of patients affected by STEMI stands out. A review of four French registries involving 6,707 people indicated a mean decrease from 66.2 to 63.3 years over the course of 15 years.<sup>2</sup> In Brazil, the National Registry of Cardiovascular Interventions (Central Nacional de Intervenções Cardiovasculares - CENIC), encompassing 20,004 procedures in a 5-year period (2006-2010), recorded a mean age of 60.8 years among patients with STEMI.<sup>3</sup>

The in-hospital and late outcomes of young patients with stable coronary artery disease in our country were recently characterized, attesting to a good long-term prognosis.<sup>4,5</sup> However, clinical and angiographic information about this population in the acute phase of STEMI are scarce. Thus, the aim of this study was to obtain more information on this subject.

## Methods

### Study population

All patients diagnosed with STEMI undergoing primary PCI in a single center performing a large volume of procedures ( $> 70$  primary PCIs/year) were analyzed retrospectively. Patients aged  $\leq 45$  years were classified as young patients, based on previous publications on the subject.<sup>6-8</sup>

The primary aim of this study was the characterization of the most prevalent risk factors in young patients with STEMI, angiographic nature of lesions, technical details of primary PCI, and in-hospital clinical evolution, with emphasis on mortality rate, reinfarction, stroke, stent thrombosis, and the occurrence of major bleeding, comparing them to patients aged  $> 45$  years.

### Procedures

A 12-lead electrocardiogram, plus  $V_3R$ ,  $V_4R$ ,  $V_7$ , and  $V_8$  leads in inferior infarction, were performed at hospital admission and 30-60 minutes after the procedure. Therapeutic interventions followed recommendations and practices established by the existing guidelines.<sup>9,10</sup> Anticoagulation was obtained with unfractionated heparin (UFH) 100 U/kg IV and dual antiplatelet therapy with a loading dose of 300 mg of acetylsalicylic acid, plus clopidogrel 600 mg or ticagrelor 180 mg. The radial approach was the first choice of vascular access. Manual thrombus aspiration and use of glycoprotein IIb/IIIa inhibitors were at the discretion of the operator. Dosages of creatine

kinase MB isoenzyme (CK-MB) were performed every 6 hours, until a decrease in the level of this marker was observed.

### Definitions

The following risk factors were assessed: smoking - active smoker, or abstinence from smoking occurring in less than 6 months; hypercholesterolemia (low density lipoprotein-cholesterol - LDL-C  $> 160$  mg/dL); systemic arterial hypertension (systolic blood pressure  $> 140$  mmHg and/or diastolic blood pressure  $> 90$  mmHg); diabetes mellitus (two fasting plasma glucose levels  $> 125$  mg/dL on different days); family history of heart disease (atherosclerosis diagnosed in parents or siblings  $< 55$  years for men and  $< 65$  for women); prior manifestation of atherosclerotic disease (previous myocardial infarction, percutaneous or surgical revascularization procedure, stroke); and chronic renal failure (glomerular filtration rate  $< 60$  mL/min or serum creatinine  $> 1.5$  mg/dL).

Regarding electrocardiographic location, acute myocardial infarction was classified as an anterior (anteroseptal, anterior, anterolateral, and extensive anterior) or inferior (inferior, lateral, and dorsal) event. Door-to-balloon time was defined as the interval between hospital admission and crossing of the lesion with a predilation balloon, manual thrombus aspiration catheter, or stent. Angiographic success was defined as a PCI with reduction of target stenosis to  $< 20\%$  diameter, maintaining or restoring normal antegrade flow (Thrombolysis in Myocardial Infarction - TIMI grade 3). Major bleeding was defined as a Type 3 or 5 bleeding according to the definition of the Bleeding Academic Research Consortium: type 3 - (3a) bleeding with hemoglobin decrease  $\geq 3$  and  $< 5$  g/dL or with red blood cell transfusion; (3b) bleeding with hemoglobin decrease  $\geq 5$  g/dL, or cardiac tamponade, or bleeding requiring surgical intervention, or bleeding requiring the use of intravenous vasoactive drugs; (3c) intracranial hemorrhage, or subcategories confirmed by autopsy, imaging studies, or lumbar puncture, or intraocular bleeding with vision impairment; Type 5 - (5a) likely fatal bleeding; (5b) final fatal bleeding.<sup>11</sup>

### Statistical analysis

Qualitative variables were summarized in absolute frequencies and percentages, and quantitative data were expressed as mean  $\pm$  standard deviation. To compare groups, the Chi-squared test or Fisher's exact test for qualitative variables and Student's *t*-test or the Mann-Whitney test for quantitative variables were used. Results with  $p < 0.05$  were considered statistically significant.

## Results

From April 2010 to December 2014, 2,674 PCIs were carried out; of these, 489 (18.3%) occurred in patients with STEMI in the first 12 hours of symptom onset. Of these patients, 54 (11%) were aged  $\leq 45$  years (mean 40.7 years, range 36-45 years), and 435 were aged  $> 45$  years (mean 64.2 years, range 46-96 years).

Young patients exhibited a higher prevalence of smoking (72.2% vs. 40.5%;  $p < 0.0001$ ) and obesity (35.2% vs. 21.6%;  $p = 0.04$ ), while patients > 45 years showed a greater propensity to present systemic arterial hypertension (69.7% vs. 40.7%;  $p < 0.0001$ ), diabetes mellitus (33.3% vs. 14.8%;  $p = 0.005$ ), dyslipidemia (34.0% vs. 13.0%;  $p = 0.002$ ), and previous myocardial infarction (9.4% vs. 0.0%;  $p = 0.02$ ; Table 1).

Anterior wall infarction was more frequent (50.9%), with stenting in 90.4% of procedures, predominantly with bare-metal stents (98.6%); manual aspiration thrombectomy, radial access, and glycoprotein IIb/IIIa inhibitors were used in 57.5%, 94.3%, and 47.0% of the cases, respectively, with no difference between groups (Table 2). Primary PCI in young patients was associated with the use of fewer guide catheters (1.1 vs. 1.3,  $p = 0.02$ ), shorter fluoroscopy time ( $10.0 \pm 4.4$  vs.  $15.3 \pm 23.1$  min;  $p = 0.09$ ), and a higher percentage of direct stenting (61.1% vs. 47.1%;  $p = 0.06$ ).

The overall angiographic success rate was high (92.2%); and young patients exhibited good in-hospital evolution, with reduced mortality (1.9% vs. 6.7%;  $p = 0.23$ ) and reinfarction (1.9% vs. 1.8%;  $p > 0.99$ ) rates and no occurrence of stroke, stent thrombosis, and major bleeding (Table 3).

## Discussion

Although hospitalizations for acute myocardial infarction currently present a downward trend, this is not observed in young patients.<sup>12</sup> Consequently, the statistics show a decline in the mean age of STEMI cases, as well as in mortality rate, and these findings are justified by the prognostic impact of advanced age in this high-risk scenario, representing one of its main determinants of morbidity and mortality.<sup>13</sup>

**Table 1**  
Basal clinical and demographic characteristics.

Variable	General (n = 489)	Age ≤ 45 years (n = 54)	Age > 45 years (n = 435)	p-value
Male gender, n (%)	338 (69.1)	34 (63.0)	304 (69.9)	0.35
Age, years	61.6 ± 12.4	40.7 ± 3.7	64.2 ± 10.5	< 0.0001
Body mass index, kg/m <sup>2</sup>	27.0 ± 4.9	28.5 ± 5.3	26.8 ± 4.8	0.02
Obesity, n (%)	113 (23.1)	19 (35.2)	94 (21.6)	0.04
Systemic arterial hypertension, n (%)	325 (66.5)	22 (40.7)	303 (69.7)	< 0.0001
Diabetes mellitus, n (%)	153 (31.3)	8 (14.8)	145 (33.3)	0.005
Insulin user	23 (15.0)	2 (25.0)	21 (14.5)	0.34
Dyslipidemia, n (%)	155 (31.7)	7 (13.0)	148 (34.0)	0.002
Current smoker, n (%)	215 (44.0)	39 (72.2)	176 (40.5)	< 0.0001
Positive family history of CAD, n (%)	91 (18.6)	15 (27.8)	76 (17.5)	0.09
Previous myocardial infarction, n (%)	41 (8.4)	0 (0.0)	41 (9.4)	0.02
Prior PCI, n (%)	42 (8.6)	1 (1.9)	41 (9.4)	0.07
Prior CABG, n (%)	7 (1.4)	0 (0.0)	7 (1.6)	> 0.99
Stroke, n (%)	17 (3.5)	0 (0.0)	17 (3.9)	0.24
Chronic renal failure, n (%)	15 (3.1)	0 (0.0)	15 (3.4)	0.39

CAD: coronary artery disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft.

**Table 2**  
Angiographic and procedural characteristics.

Variable	General (n = 489)	Age ≤ 45 years (n = 54)	Age > 45 years (n = 435)	p-value
De novo injury, n (%)	483 (98.8)	53 (98.1)	430 (98.9)	0.51
In-stent restenosis, n (%)	6 (1.2)	1 (1.9)	5 (1.1)	0.51
Location, n (%)				0.56
Anterior	249 (50.9)	30 (55.6)	219 (50.3)	
Inferior	240 (49.1)	24 (44.4)	216 (49.7)	
Duration of the procedure, minutes	41.6 ± 19.1	38.1 ± 14.6	42.0 ± 19.6	0.16
Fluoroscopy time, minutes	14.5 ± 19.0	10.0 ± 4.4	15.3 ± 23.1	0.09
Door-to-balloon time, minutes	64.9 ± 34.9	63.6 ± 46.5	65.3 ± 29.9	0.71
Manual aspiration thrombectomy, n (%)	281 (57.5)	34 (63.0)	247 (56.8)	0.47
Direct stent implantation, n (%)	238 (58.9)	33 (61.1)	205 (47.1)	0.06
Post-dilation, n (%)	278 (56.9)	27 (50.0)	251 (57.7)	0.31
Access route, n (%)				0.16
Radial	461 (94.3)	54 (100.0)	407 (93.6)	
Femoral	23 (4.7)	0 (0.0)	23 (5.3)	
Ulnar	5 (1.0)	0 (0.0)	5 (1.1)	
Culprit lesion, n (%)				0.51
Left anterior descending artery	247 (50.6)	30 (55.6)	217 (49.9)	
Right coronary artery	185 (37.8)	21 (38.9)	164 (37.7)	
Left circumflex artery	55 (11.2)	3 (5.5)	52 (12.0)	
Left main coronary artery	2 (0.4)	0 (0.0)	2 (0.4)	
Glycoprotein IIb/IIIa inhibitor, n (%)	230 (47.0)	31 (57.4)	199 (45.7)	0.11
Number of catheters	1.3 ± 0.6	1.1 ± 0.4	1.3 ± 0.6	0.018
Diameter of the catheter, n (%)				> 0.99
5 F	1 (0.2)	0 (0.0)	1 (0.2)	
6 F	487 (99.6)	54 (100.0)	433 (99.6)	
7 F	1 (0.2)	0 (0.0)	1 (0.2)	
PCI type, n (%)				0.81
Balloon angioplasty	47 (9.6)	4 (7.4)	43 (9.9)	
Stenting	442 (90.4)	50 (92.6)	392 (90.1)	
Number of stents	1.1 ± 0.5	1.1 ± 0.6	1.1 ± 0.5	> 0.99
Stent type, n (%)				> 0.99
Drug-eluting stent	6 (1.4)	2 (4.0)	4 (1.0)	
Bare-metal stent	436 (98.6)	48 (96.0)	388 (99.0)	
Intra-aortic balloon, n (%)	2 (0.4)	0 (0.0)	2 (0.5)	> 0.99

PCI: percutaneous coronary intervention.

**Table 3**  
In-hospital efficacy and safety outcomes.

Variable	General (n = 489)	Age ≤ 45 years (n = 54)	Age > 45 years (n = 435)	p-value
Angiographic success, n (%)	451 (92.2)	51 (94.4)	400 (92.0)	0.79
MACE, n (%)	42 (8.6)	2 (3.7)	40 (9.2)	0.30
Death, n (%)	30 (6.1)	1 (1.9)	29 (6.7)	0.23
Reinfarction, n (%)	9 (1.8)	1 (1.9)	8 (1.8)	> 0.99
Stroke, n (%)	1 (0.2)	0 (0.0)	1 (0.2)	> 0.99
In-hospital stent thrombosis, n (%)	9 (1.8)	0 (0.0)	9 (2.1)	0.61
Acute	2 (0.4)	0 (0.0)	2 (0.5)	
Subacute	7 (1.4)	0 (0.0)	7 (1.6)	
Major bleeding, n (%)	4 (0.8)	0 (0.0)	4 (0.9)	> 0.99

MACE: major adverse cardiac events (death, reinfarction, stroke, stent thrombosis, or major bleeding).

Data from registries such as FAST-MI (French Registry of Acute ST-Elevation or non-ST-elevation Myocardial Infarction) still show increased prevalence of smoking (from 32.0% to 40.9%) and obesity (from 14.3% to 20.1%) in the population of myocardial infarction patients over the past 15 years.<sup>2</sup> In the USA, among young individuals aged 18-44 years, 22.9% of men and 16.6% of women are smokers, and 69% of the general population is classified as obese or overweight.<sup>1</sup>

In assessing the population of young patients with an acute myocardial infarction diagnosis, the percentage of smokers can reach up to 74%, as in the CRAGS (Coronary Artery Disease in Young Adults) study.<sup>14</sup> It is known that smoking contributes negatively in the regulation cascades engaged in preventing coronary occlusion, besides promoting changes in tissue plasminogen activator response to bradykinin. Furthermore, the hypercoagulability state and endothelial dysfunction present in smokers predispose to the formation of intracoronary thrombi.<sup>15</sup>

In the present study, patients aged ≤ 45 years represented 11% of all STEMI cases (37% female), with high prevalence of modifiable risk factors such as obesity (35.2%) and smoking (72.2%), and lower percentages of hypertension, dyslipidemia, diabetes mellitus, and previous myocardial infarction. The characteristics of procedures – for instance, a lower mean number of catheters used, shorter fluoroscopy time, and higher percentage of direct stent implantation – suggest less angiographic complexity in this subgroup, as well as a low rate of major adverse cardiac events during hospitalization, exemplified by mortality rates of 1.9% vs. 6.7% in patients > 45 years. Similar findings were reported by the London Chest Hospital, a reference center for chest pain, which, from 2004 to 2012, registered 3,618 primary PCIs. Patients aged ≤ 45 years constituted 10.1% of the sample, and smoking had a prevalence of 62.7%, with a 30-day mortality of 1.6%.<sup>16</sup>

Together, these data reflect the importance of instituting health policies that address young people and target primary or secondary prevention, with emphasis on changes in lifestyle, particularly smoking cessation, regular physical activity, and a balanced diet to maintain proper weight. These are low-cost actions with great potential for reducing the incidence of new cases of myocardial infarction in this population.

#### Study limitations

This analysis had the following limitations: its observational and unicentric nature, the limited sample size, lack of long-term clinical follow-up, as well as non-performance of routine diagnostic tests for illicit drugs such as cocaine, a known promoter of coronary spasm and hypercoagulability in an environment of sympathetic activity exacerbation, which represents a common cause of acute coronary syndrome in young people.

#### Conclusions

Patients aged ≤ 45 years represented approximately 10% of cases of ST-segment elevation acute myocardial infarction, showed high prevalence of modifiable risk factors, especially smoking, favorable in-hospital clinical outcome after primary percutaneous coronary intervention, and less technical complexity when compared to patients > 45 years. Health policies addressing changes in lifestyle are low-cost actions, with potential impact on reducing future events in this population.

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#### Conflicts of interest

The authors declare no conflicts of interest.

#### References

- Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al.; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2015 update: a report from the American Heart Association. *Circulation*. 2015;131(4):e29-e322.
- Puymirat E, Simon T, Steg PG, Schiele F, Guéret P, Blanchard D, et al.; USIK USIC 2000 Investigators; FAST MI Investigators. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. *JAMA*. 2012;308(10):998-1006.
- Matte BS, Bergoli LCC, Balvedi JA, Zago AC. Perfil da intervenção coronária percutânea no infarto agudo do miocárdio com supradesnivelamento do segmento ST no Brasil de 2006 a 2010 – Registro CENIC. *Rev Bras Cardiol Invasiva*. 2011;19(2):131-7.
- Bienert IRC, Ribeiro EE, Kajita LJ, Perin MA, Campos CAH, Trentin F, et al. Prognóstico tardio em jovens com coronariopatia estável: evolução em 10 anos após intervenção coronária percutânea. *Rev Bras Cardiol Invasiva*. 2012;20(4):161-5.
- Cantarelli MJ, Castello Jr. HJ, Gonçalves R, Gioppato S, Navarro E, Guimarães JBF, et al. Intervenção coronária percutânea em jovens. *Rev Bras Cardiol Invasiva*. 2014;22(4):355-8.
- Choudhury L, Marsh JD. Myocardial infarction in young patients. *Am J Med*. 1999;107(3):254-61.
- Hoit BD, Gilpin EA, Henning H, Maisel AA, Dittrich H, Carlisle J, et al. Myocardial infarction in young patients: an analysis by age subsets. *Circulation*. 1986;74(4):712-21.
- Conti RAS, Solimene MC, Luz PL, Benjô AL, Lemos Neto PA, Ramires JAF. Comparação entre homens e mulheres jovens com infarto agudo do miocárdio. *Arq Bras Cardiol*. 202;79(5):510-7.
- Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, Badano LP, Blömmström-Lundqvist C, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). *Eur Heart J*. 2012;33(20):2569-619.

10. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr., Chung MK, de Lemos JA, et al.; American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127(4):e362-e425.
11. Mehran R, Rao SV, Bhatt DL, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the Bleeding Academic Research Consortium. *Circulation*. 2011;123(23):2736-47.
12. Gupta A, Wang Y, Spertus JA, Geda M, Lorenze N, Nkonde-Price C, et al. Trends in acute myocardial infarction in young patients and differences by sex and race, 2001 to 2010. *J Am Coll Cardiol*. 2014;64(4):337-45.
13. Pedersen F, Butrymovich V, Kelbæk H, Wachtell K, Helqvist H, Kastrup J, et al. Short and long-term cause of death in patients treated with primary PCI for STEMI. *J Am Coll Cardiol*. 2014;64(20):2101-8.
14. Lautamaki A, Airaksinen KEJ, Kiviniemi T, Vinco G, Ribichini F, Gunn J, et al. Prognosis and disease progression in patients under 50 years old undergoing PCI: The CRAGS (Coronary aRtery diseAse in younG adultS) study. *Atherosclerosis*. 2014;235(2):483-7.
15. Davidson L, Wilcox J, Kim D, Benton S, Fredi J, Vaughan D. Clinical features of precocious acute coronary syndrome. *Am J Med*. 2014;127(2):140-4.
16. Rathod KS, Jones DA, Gallagher S, Rathod VS, Weerackody R, Jain AK, et al. Atypical risk factor profile and excellent long-term outcomes of young patients treated with primary percutaneous Coronary intervention for ST-elevation myocardial infarction. *Eur Heart J Acute Cardiovasc Care*. 2015; pii: 2048872614567453. Epub ahead of print.