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Temporal trends and outcomes of percutaneous coronary intervention in young patients (aged ≤40 years)

Evolução temporal e resultados de intervenção coronária percutânea em pacientes jovens (≤40 anos)

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ABSTRACT – Background: The prevalence of coronary artery disease and percutaneous coronary intervention in young patients is not well established. The objective of this study was to investigate the profile of young patients undergoing percutaneous coronary intervention in Brazil. **Methods:** A cross-sectional study was performed with data from the *Central Nacional de Intervenções Cardiovasculares* (CENIC), collected between 2006 and 2016, for patients aged ≤40 years undergoing percutaneous coronary intervention. **Results:** We enrolled 2,806 patients, mean age of 35.3±3.9 years. Most lesions on angiography were single-vessel (66.6%), in the left anterior descending artery (50.8%), and complex (68%). In respect to procedures, there was a difference over the years in the use of drug-eluting stents (p<0.0001), vessel diameter (p=0.015), stent length (p<0.0001), type of intervention (p=0.036), use of glycoprotein IIb/IIIa inhibitors (p<0.0001), thromboaspiration (p=0.0003), post-procedural TIMI flow (p=0.007), and post-procedural stenosis (p<0.001). As for in-hospital clinical outcomes, there were no significant differences among the periods. In the multivariate analysis, female sex (OR: 3.45; 95%CI: 1.25-9.5; p=0.016), hypertension (OR: 4.84; 95%CI: 1.34-17.52; p=0.016), previous coronary artery bypass graft (OR: 16.42; 95%CI: 1.62-166.45; p=0.018), primary percutaneous coronary intervention (OR: 25.67; 95%CI: 5.19-126.99; p=0.0001) and rescue percutaneous coronary intervention (OR: 26.44; 95%CI: 2.11-330.82; p=0.011) were independent predictors of in-hospital mortality. **Conclusion:** Percutaneous coronary intervention in young patients, in the CENIC registry, shows cases of high angiographic complexity, high success rates and low in-hospital complication rates over a 10-year period.

Keywords: Coronary artery disease; Angioplasty; Myocardial ischemia; Treatment outcome; Young adult

RESUMO – Introdução: A prevalência de doença arterial coronária e da intervenção coronária percutânea em pacientes jovens não é muito bem estabelecida. O objetivo deste estudo foi analisar o perfil dos pacientes jovens submetidos à intervenção coronária percutânea no Brasil. **Métodos:** Estudo transversal realizado com dados do registro da Central Nacional de Intervenções Cardiovasculares (CENIC) coletados entre 2006 e 2016 de pacientes com idade ≤40 anos submetidos à intervenção coronária percutânea. **Resultados:** Foram incluídos 2.806 pacientes com média de idade de 35,3±3,9 anos. À angiografia, a maior parte foi de lesões uniarteriais (66,6%), localizadas na artéria descendente anterior (50,8%) e complexas (68%). Referente aos procedimentos, houve diferença ao longo dos anos na utilização dos stents farmacológicos (p<0,0001), no diâmetro do vaso (p=0,015), no comprimento dos stents (p<0,0001), no tipo de intervenção (p=0,036), no uso de inibidores de glicoproteína IIb/IIIa (p<0,0001), na tromboaspiração (p=0,0003), no fluxo TIMI pós-procedimento (p=0,007) e na estenose pós-procedimento (p<0,001). Em relação aos desfechos clínicos na fase hospitalar, não houve diferença significativa entre os períodos. Na análise multivariada, sexo feminino (RC: 3,45; IC95% 1,25-9,5; p=0,016), hipertensão arterial sistêmica (RC: 4,84; IC95% 1,34-17,52; p=0,016), revascularização miocárdica cirúrgica prévia (RC: 16,42; IC95% 1,62-166,45; p=0,018), intervenção coronária percutânea primária (RC: 25,67; IC95% 5,19-126,99; p=0,0001) e intervenção coronária percutânea de resgate (RC 26,44; IC95% 2,11-330,82; p=0,011) foram preditores independentes de mortalidade intra-hospitalar. **Conclusão:** A intervenção coronária percutânea em pacientes jovens, no registro CENIC, identificou casos com alto grau de complexidade angiográfica, altas taxas de sucesso e baixas taxas de complicações intra-hospitalares ao longo de 10 anos.

Descritores: Doença da artéria coronariana; Angioplastia; Isquemia miocárdica; Resultado do tratamento; Adulto jovem

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INTRODUCTION

The main cause of death in the world is coronary artery disease (CAD).¹ Although there is much data on the subject, the prevalence of premature CAD, myocardial infarction (MI) and percutaneous coronary intervention (PCI) in young patients has not been well established.^{2,3} Genetic mutations associated with familial hypercholesterolemia⁴ and hyperhomocysteinemia,⁵ in addition to classic risk factors, such as smoking, hypertension, insulin resistance, obesity and family history of premature CAD, show a correlation with early atherosclerotic events.⁶

The *Central Nacional de Intervenções Cardiovasculares* (CENIC; <http://www.corehemo.net/>) is an online registry maintained by the *Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista* (SBHCI). In this registry, patient and procedural characteristics are voluntarily submitted by members of the SBHCI as per an established protocol. Detailed information is collected about PCI procedures conducted at approximately 200 interventional cardiology centers in the country.

This study aimed to outline the national scenario of PCI in young patients (aged ≤ 40 years), as recorded in the CENIC database, looking at different periods and regions of Brazil, regarding patient profile, procedural characteristics, and in-hospital outcomes.

METHODS

Patient selection

In this analysis, we included all patients ≤ 40 years of age undergoing PCI in the period from June 2006 to March 2016. This is a retrospective cross-sectional study based on the CENIC registry. The data were collected on standardized forms and stored in an electronic database.

The temporal analysis of the 2006-2016 period was conducted by breaking down the sample into three groups: Group A (2006-2008), Group B (2009-2011) and Group C (2012-2016).

For analysis of clinical variables, the individual patient was considered as the sample unit. Some patients underwent to more than one procedure. In these cases, the procedure to be considered was randomly selected.

Our work was submitted to the Research Ethics Committee of the Hospital Leforte (5485) and was approved, under the CAEE 90669518.6.0000.5485.

Clinical characteristics

With respect to clinical presentation, patients were divided into asymptomatic (those with positive functional tests for myocardial ischemia), stable angina, non-ST-segment elevation acute coronary syndrome (NSTEMI) (comprising patients with unstable angina, and non-ST-segment elevation myocardial infarction - NSTEMI), as well as ST-segment elevation myocardial infarction (STEMI). The myocardial infarction (MI) classification and diag-

nostic criteria were defined according to a pre-established protocol.⁷ Left ventricular dysfunction was defined as left ventricular ejection fraction $< 50\%$ on echocardiography. To define the functional class, we used the Killip/Kimball classification.⁸

Angiographic and procedural characteristics

Multivessel coronary artery disease was defined as the presence of $\geq 50\%$ stenosis in more than one coronary artery. The coronary flow pre and post-procedure was assessed and described as per the Thrombolysis in Myocardial Infarction (TIMI) grade flow.⁹ CAD complexity was determined according to the American Heart Association/American College of Cardiology (AHA/ACC) classification.^{10,11}

Procedural success was visually defined, encompassing the achievement of residual stenosis $< 20\%$ and absence of death, periprocedural MI, or the need for emergency heart surgery, defined as major adverse cardiovascular events (MACE).

Statistical analysis

Continuous variables with normal distribution were described as mean and standard deviation. Categorical variables were described as absolute numbers and percentages. For comparison of continuous variables in relation to the 2006-2016 groups, the Chi-square test was employed. When required, we used the likelihood ratio test. For comparison of categorical variables in relation to the 2006-2016 groups, we used the analysis of variance (ANOVA). For multiple comparisons, the Bonferroni correction was used. To assess the influence of variables of interest regarding mortality, we used the simple logistic regression model. Also, multiple logistic regression was performed by forward selection to determine the independent variables that better explained the occurrence of death. Variables with many missing data were not considered in the multiple logistic regression analysis (e.g.: left ventricular dysfunction and collateral circulation). When looking at mortality-related variables, if the patient had been submitted to more than one procedure, we used random selection to narrow down to one procedure per patient. P-values ≤ 0.05 were considered statistically significant. We used the software Statistical Package for Social Science (SPSS), version 20.0.

RESULTS

The sample in this study had a total of 2,806 patients, with a mean age of 35.3 ± 3.9 years, and a higher prevalence of males in all groups (74.4% on average), with no difference between the groups over the years. Hypertension, dyslipidemia, acute coronary syndrome (ACS) and Killip 1 class were very prevalent in the three groups (58.2%, 44.1%, 62.2% and 81.7%, respectively), unlike type 2 diabetes mellitus, with a small prevalence in the groups (15% on average). It is worth noting that there was signi-

ficant and progressive reduction of smoking over the years ($p<0.0001$) (Table 1).

With regard to angiographic characteristics, presented in table 2, a total of 3,680 vessels were treated, and most

PCI were in patients with single-vessel lesions (66.6%), in the left anterior descending artery (50.8%), and 68% were classified as AHA/ACC type B₂/C, denoting more complex lesions. Over the years, there was a difference regarding

Table 1. Clinical characteristics

Characteristic	Group A (n=827 patients)	Group B (n=970 patients)	Group C (n=1,009 patients)	p-value
Age	35.5±3.7	35.3±4.0	35.1±4.1	0.056
Male sex	620 (75.0)	713 (73.5)	756 (74.9)	0.707
Smoking	353 (42.7)	368 (37.9)	290 (28.7)	<0.0001
Hypertension	497 (60.1)	567 (58.5)	568 (56.4)	0.273
Dyslipidemia	371 (44.9)	415 (43.5)	442 (44.1)	0.855
Type 2 DM	112 (13.5)	140 (16.4)	127 (14.9)	0.270
Prior MI	157 (19.0)	136 (15.9)	164 (19.3)	0.132
Prior PCI	104 (12.8)	121 (12.8)	148 (14.9)	0.300
Prior CABG	20 (2.4)	17 (1.8)	28 (2.8)	0.308
Clinical presentation				<0.0001
Stable angina	264 (31.9)	260 (26.8)	286 (28.3)	
Asymptomatic	53 (6.4)	110 (11.3)	87 (8.6)	
STEMI	317 (38.3)	349 (36.0)	324 (32.1)	
NSTE-ACS	193 (23.3)	251 (25.9)	312 (30.9)	
Killip, n (%)				<0.0001
1	259 (82.7)	268 (77.0)	275 (85.7)	
2	31 (9.9)	54 (15.5)	33 (10.3)	
3	10 (3.2)	12 (3.4)	4 (1.2)	
4	13 (4.2)	14 (4.0)	9 (2.8)	

Results expressed as mean±standard deviation, or n (%). DM: diabetes mellitus; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery; STEMI: ST-segment elevation myocardial infarction; NSTE-ACS: non-ST segment elevation acute coronary syndrome.

Table 2. Angiographic characteristics

Characteristic	Group A (n=883 procedures/ n=1,087 vessels)	Group B (n=1,032 procedures/ n=1,289 vessels)	Group C (n=1,059 procedures/ n=1,304 vessels)	p-value
Coronary disease extension				0.056
Single vessel	564 (65.4)	628 (64.4)	687 (69.7)	
Two-vessel	232 (26.9)	254 (26.1)	207 (21.0)	
Three-vessel	66 (7.6)	92 (9.4)	90 (9.1)	
LMCA	1 (0.1)	1 (0.1)	1 (0.1)	
Treated vessels				0.017
RCA	295 (27.1)	308 (23.9)	397 (30.4)	
LCx	208 (19.1)	277 (21.5)	264 (20.2)	
LAD	567 (52.2)	686 (53.2)	617 (47.3)	
Venous graft	10 (0.9)	11 (0.9)	14 (1.1)	
LMCA	7 (0.6)	7 (0.5)	12 (0.9)	
Type B2/C lesions	657 (67.5)	47 (77.0)	7 (63.6)	0.287
Calcified lesions	149 (13.7)	178 (14.0)	118 (9.6)	0.001
Thrombotic lesions	258 (23.7)	317 (24.6)	252 (19.3)	0.003
Lesions >20mm	268 (24.7)	312 (24.2)	311 (23.8)	0.900
Bifurcations	294 (27.0)	307 (23.8)	261 (20.0)	0.0003
Total occlusion	250 (23.2)	329 (25.5)	345 (26.5)	0.172
TIMI flow pre				0.657
0/1	316 (29.1)	366 (28.4)	357 (27.4)	
2/3	771 (70.9)	923 (71.6)	946 (72.6)	
Left ventricular dysfunction	393 (55.8)	412 (61.8)	398 (57.1)	0.065
Collateral circulation	140 (16.7)	97 (17.3)	95 (14.9)	0.491

Results expressed as mean±standard deviation, or n (%). LMCA: left main coronary artery; RCA: right coronary artery; LCx: left circumflex artery; LAD: left anterior descending artery; TIMI: Thrombolysis in Myocardial Infarction.

the treated vessel ($p=0.017$), calcified lesions ($p=0.001$), thrombotic lesions ($p=0.003$) and lesions involving bifurcations ($p=0.0003$).

Table 3 presents procedural data with 2,974 PCI conducted and 3,552 stents placed (1.19 stent per patient). There was a statistically significant difference over the years regarding use of drug-eluting stents ($p<0.0001$), vessel diameter ($p=0.015$), stent length ($p<0.0001$), type of intervention ($p=0.036$), use of glycoprotein IIb/IIIa inhibitors ($p<0.0001$), thromboaspiration ($p=0.0003$), post-procedural TIMI flow ($p=0.007$), and post-procedural stenosis ($p<0.001$) among the three groups.

As for in-hospital clinical outcomes (death, emergency revascularization, periprocedural MI or MACE), there were no significant differences between the groups (Table 4). The univariate analysis of predictors of in-hospital mortality is shown in table 5. In the multivariate analysis, female sex (OR: 3.45; 95%CI 1.25-9.5; $p=0.016$), hypertension (OR: 4.84; 95%CI 1.34-17.52; $p=0.016$), previous coronary artery bypass graft (CABG) (OR: 16.42; 95%CI 1.62-166.45; $p=0.018$), primary PCI (OR: 25.67; 95%CI 5.19-126.99; $p=0.0001$) and rescue PCI (OR: 26.44; 95%CI 2.11-330.82; $p=0.011$) were independent predictors of in-hospital mortality (Table 6).

Table 3. Characteristics of procedures

Characteristic	Group A (n=827 patients/ n=883 procedures/ n=1,029 stents)	Group B (n=970 patients/ n=1,032 procedures/ n=1,247 stents)	Group C (n=1,009 patients/ n=1,059 procedures/ n=1,276 stents)	p-value
Treated vessels/patient	1.3±0.6	1.3±0.7	1.3±0.6	0.33
Use of stent	782 (94.6)	911 (93.9)	950 (94.2)	0.844
Stent/patient ratio	1.3±0.7	1.4±0.8	1.3±0.6	0.121
Drug-eluting stents	128 (12.5)	252 (20.2)	362 (28.4)	<0.0001
Stent diameter, mm	3.1±0.5	3.1±0.5	3.1±0.5	0.140
Stent length, mm	18.9±6.2	20.5±7.9	21±8.2	<0.0001
Types of intervention				0.036
Primary PCI	174 (19.7)	222 (21.5)	186 (17.6)	
Rescue PCI	19 (2.2)	10 (1.0)	13 (1.2)	
Glycoprotein IIb/IIIa inhibitors	85 (9.6)	80 (7.8)	40 (3.8)	<0.0001
Thromboaspiration	9 (0.9)	38 (8.0)	36 (2.8)	0.0003
TIMI flow post				0.007
0/1	49 (4.8)	29 (2.3)	46 (3.6)	
2/3	978 (95.2)	1,212 (97.7)	1,229 (96.4)	
Diameter stenosis				
Pre	87.7±11.8	87.6±12.3	87.8±13.1	0.899
Post	2.3±8.9	2.7±8.4	5.1±4.6	<0.0001
Success of procedure	848 (96.0)	1,003 (97.2)	1,027 (97.0)	0.324

Results expressed as mean±standard deviation, or n (%). PCI: percutaneous coronary intervention; TIMI: Thrombolysis in Myocardial Infarction.

Table 4. In-hospital clinical outcomes

Outcome	Group A (n=827 patients)	Group B (n=970 patients)	Group C (n=1,009 patients)	Total (n=2,806 patients)	p-value
Periprocedural MI	1 (0.1)	5 (0.6)	2 (0.2)	8 (0.3)	0.2088
Emergency CABG	0 (0)	1 (0.13)	0 (0)	1 (0.06)	0.5587
Death	5 (0.6)	7 (0.8)	5 (0.6)	17 (0.7)	0.7859
MACE	6 (0.7)	12 (1.2)	6 (0.6)	24 (0.9)	0.2671

Results expressed as n (%). MI: myocardial infarction; CABG: coronary artery bypass graft; MACE: major adverse cardiovascular events.

Table 5. Univariate analysis of predictors of in-hospital mortality

Predictors of mortality	Estimate	p-value	OR	95%CI
2009-2011 vs. 2006-2008	0.30	0.605	1.36	0.43-4.29
2012-2016 vs. 2006-2008	-0.07	0.916	0.94	0.27-3.24
Age	-0.06	0.231	0.94	0.85-1.04
Sex, female vs. male	0.96	0.049	2.61	1.0-6.8
Smoking, no vs. yes	0.37	0.493	1.44	0.51-4.11
Hypertension, no vs. yes	1.88	0.003	6.56	1.88-22.88
Dyslipidemia, no vs. yes	0.97	0.091	2.63	0.86-8.09
Diabetes mellitus, yes vs. no	0.20	0.755	1.22	0.35-4.27
Prior MI, yes vs. no	-16.41	0.993	0.03	0.0001-13.21
Previous PCI, no vs. yes	0.88	0.394	2.42	0.32-18.34
Previous CABG, no vs. yes	-0.99	0.342	0.37	0.05-2.86
Clinical presentation, angina vs. STEMI	-17.15	0.991	0.01	<0.00012-3.83
Clinical presentation, asymptomatic vs. STEMI	-17.15	0.995	0.03	<0.00016-14.6
Clinical presentation, NSTEMI vs. STEMI	-2.47	0.017	0.08	0.01-0.64
Killip, 1 vs. 4	-5.12	<0.0001	0.01	0.001-0.03
Killip, 2 vs. 4	-20.38	0.996	0.002	<0.000104-1.09
Killip, 3 vs. 4	-1.22	0.088	0.30	0.07-1.2
Extension of coronary disease, two-vessel vs. single-vessel	0.13	0.827	1.14	0.36-3.64
Extension of coronary disease, three-vessel vs. single-vessel	-0.21	0.839	0.81	0.1-6.34
Extension of coronary disease, LMCA vs. single-vessel	4.43	0.0005	83.95	7.03-1002.11
Left ventricular dysfunction, yes vs. no	15.82	0.991	37.65	0.072-19685.55
Collateral circulation, yes vs. no	-0.17	0.823	0.84	0.19-3.78
Types of intervention, primary vs. others	2.78	<0.0001	16.20	4.6-57.05
Types of intervention, rescue vs. others	2.83	0.015	16.93	1.72-166.41
Glycoprotein IIb/IIIa inhibitors, yes vs. no	-0.29	0.777	0.75	0.1-5.66

MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; STEMI: ST-segment elevation myocardial infarction; NSTEMI: non-ST segment elevation acute coronary syndrome; LMCA: left main coronary artery.

Table 6. Multivariate analysis of independent predictors of in-hospital mortality

Predictors of mortality	Estimate	p-value	OR	95%CI
Constant	-8.48	<0.0001		
Sex, female vs. male	1.24	0.0164	3.45	1.25-9.5
Hypertension, yes vs. no	1.58	0.0164	4.84	1.34-17.52
Prior CABG, yes vs. no	2.80	0.0179	16.42	1.62-166.45
Types of intervention, primary vs. others	3.25	0.0001	25.67	5.19-126.99
Types of intervention, rescue vs. others	3.27	0.0111	26.44	2.11-330.82

CABG: coronary artery bypass graft.

DISCUSSION

In this study we describe the profile of PCI procedures in young patients in Brazil, recorded in the CENIC-SBHCI registry. The main findings of the study were low prevalence of type 2 diabetes (15%) and high smoking rates (35 to 40%), predominantly single-vessel, highly complex lesions, of which 68% were AHA/ACC type B₂/C, and a prevalence of up to 30% of bifurcation lesions.

Data about MI in young patients are still scarce in the literature when compared with data on CAD in general. Perhaps the most widely known of all epidemiological

studies in cardiovascular medicine is the Framingham Heart Study, which reported, over a 10-year period, an incidence of MI in young adults (defined in the study as <55 years) of 51.1/1,000 in men and 7.4/1,000 in women.¹² The literature diverges when it comes to the definition of young adults in the context of early CAD and AMI, ranging from <40 to <55 years of age.^{13,14} Other authors have suggested 45 years as a cutoff in MI cases.^{6,15,16}

Despite their young age, we observed more complex coronary lesions in approximately two thirds of patients in this study, and bifurcation lesions in approximately 20

to 30%, pointing to more advanced coronary artery disease regardless of age, unlike the majority of studies, which show prevalence of 15 to 20%.¹⁷⁻¹⁹

Aging appears to have deleterious effects both on endothelial function and vascular remodeling, including increased intima-media thickness and increased wall stiffness.^{20,21} Thus, younger age was implicitly considered a positive prognostic factor. However, with the growing prevalence of risk factors at younger ages, the age factor has been less associated with the absence of CAD or less complex lesions, and most patients have more than one conventional cardiovascular risk factor.²² In addition, young patients who do not control their risk factors have recurring disease over time, including the need for new CABG.²³

Young patients with ischemic heart disease have a higher probability of being smokers and having positive family history, but a lower rate of diabetes.²⁴⁻²⁶ The present study reports the prevalence of smoking at roughly 35 to 40%, with progressive reduction over the 10 year-period (2006-2016). In a population of young adults diagnosed with MI, the percentage of smokers can reach up to 74%, like in the CRAGS (Coronary Artery Disease in Young Adults) study.²³

With regard to angiographic characteristics, the lower atherosclerotic burden among young adults explains the higher prevalence of single-vessel coronary artery disease, as seen in the present study, which is consistent with previous publications.¹⁶ As a result, there was a smaller number of treated vessels and stents utilized per patient in younger patients, as well as greater involvement of the left anterior descending artery.^{23,27-29} We found a relatively low rate of in-hospital MACE (<1%), and our results are in line with previous studies.^{23,30-32}

Overall, younger patients are not different from older patients with regard to PCI procedures, and it is of utmost importance to encourage aggressive management of risk factors, medical treatment and careful follow-up, since these patients have high-complexity CAD.

Limitations of the study

This was a retrospective and observational analysis, based on a registry and, therefore, there are limitations inherent to the study model. Procedures were performed at several centers and by different interventional cardiologists with diverse levels of experience, which could influence results. There is also the issue of underreporting of PCI cases in Brazil (given the voluntary nature of contributions), some variables with incomplete data, the non-adjudication of the CENIC registry data, and the failure to compare characteristics and events with patients aged >40 years. In addition, we only used data corresponding to the in-hospital period, and we do not have 30-day or later follow-up (>1 year) data, which makes it impossible to conduct a long-term procedure-related survival analysis.

CONCLUSIONS

Percutaneous coronary intervention in young patients (aged ≤40 years) in the CENIC registry showed a high degree of complexity, with a high prevalence of bifurcation, single-vessel lesions, high success rates, and low rates of in-hospital complications. Hence, all patients warrant the same aggressive management, modification of risk factors, and close follow-up, regardless of age of presentation of coronary artery disease.

SOURCE OF FINANCING

None.

CONFLICT OF INTEREST

The authors declare there are no conflicts of interest.

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