Rev Bras Cardiol Invasiva.
2014;22(4):353-8

Original Article

Percutaneous Coronary Intervention in Young Patients

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ABSTRACT

Background: Cardiovascular disease has shown increasing occurrence rates among young people and data of percutaneous coronary intervention (PCI) in this group are scarce. Our objective was to perform a retrospective evaluation of the profile and in-hospital clinical outcomes of young patients in this PCI registry. **Methods:** From 2006 to 2012, 6,288 patients were consecutively submitted to PCI, of whom 151 were < 40 years of age (Group 1) and 6,127 were ≥ 40 years of age (Group 2). Logistic regression models were applied to identify the predictors of cardiac events and major adverse cardiac and cerebrovascular events (MACCE) in the study population. **Results**: In Group 1, there was a prevalence of smoking, myocardial infection as a clinical presentation, single vessel disease (left anterior descending artery as the culprit vessel), thrombotic lesions, and TIMI flow 0/1. The clinical success of PCI (96.0 % vs. 95.5 %; p = 0.89), and the occurrence of MACCE (3.3% vs. 3.3%; p = 0.82), death (0.0% vs. 1.0%; p = 0.39, stroke (0.0% vs. 0.1%; p > 0.99), myocardial infarction (3.3% vs. 2.3%; p = 0.41) or emergency revascularization (0.6% vs. 0.03%; p = 0.56) were similar between groups. In the multivariate analysis, age and presence of functional class Killip III and IV were the variables that best explained the occurrence of MACCE. **Conclusions**: Patients with age < 40 years represented a small fraction of the cases in this series and had a clinical and angiographic profile different from the older patients, suggesting the need to establish primary prevention measures earlier in individuals with the observed profile.

DESCRIPTORS: Coronary artery disease. Percutaneous coronary intervention. Young adult. Treatment outcome. Age factors.

RESUMO

Intervenção Coronária Percutânea em Pacientes Jovens

Introdução: A doença cardiovascular tem apresentado ocorrência crescente na população jovem e dados da intervenção coronária percutânea (ICP) nesse grupo são escassos. Nosso objetivo foi avaliar retrospectivamente o perfil e os resultados clínicos hospitalares de pacientes jovens do nosso registro de ICP. **Métodos**: No período de 2006 a 2012, 6.288 pacientes foram submetidos consecutivamente à ICP, sendo 151 com idade < 40 anos (Grupo 1) e 6.137 ≥ 40 anos (Grupo 2). Modelos de regressão logística foram aplicados para identificar os preditores de eventos cardíacos e cerebrovasculares adversos maiores (ECCAM) na população estudada. **Resultados**: No Grupo 1, prevaleceram o tabagismo, o infarto agudo do miocárdio como apresentação clínica, lesões em um único vaso (sendo a artéria descendente anterior o vaso mais tratado), lesões com trombos e o fluxo TIMI 0/1. O sucesso clínico da ICP (96,0% vs. 95,5%; p = 0,89) e a ocorrência de ECCAM (3,3% vs. 3,3%; p = 0,82), de óbito (0,0% vs. 1,0%; p = 0,39), acidente vascular cerebral (0,0% vs. 0,1%; p > 0,99), infarto agudo do miocárdio (3,3% vs. 2,3%; p = 0,41) ou revascularização de emergência (0,6% vs. 0,03%; p = 0,56) foram semelhantes entre os grupos. Na análise multivariada, a idade e a presença das classes funcionais Killip III e IV foram as variáveis que melhor explicaram a ocorrência de ECCAM. **Conclusões**: Pacientes com idade < 40 anos representaram uma fração menor dos casos dessa casuística, e apresentaram perfil clínico e angiográfico distinto dos mais velhos, o que sugere a necessidade de instituir medidas de prevenção primária mais precoce nos que se enquadram no perfil observado.

DESCRITORES: Doença da artéria coronariana. Intervenção coronária percutânea. Adulto jovem. Resultado do tratamento. Fatores etários.

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Received on: 09/01/2014 • Accepted on: 11/10/2014

Rev Bras Cardiol Invasiva.
2014;22(4):353-8

Coronary artery disease (CAD) manifestations have been increasingly more frequent among young people. Currently, it is estimated that about 10% of individuals with CAD are under the age of 45 years.[1] The French registry FAST AMI revealed a significant increase in acute myocardial infarction (AMI), the main clinical manifestation of CAD among young subjects, in patients under the age of 60 years in the last 15 years. Obesity and smoking are the main risk factors related to this increase.[2] Brazilian data also indicate an increase of AMI in younger, tobacco-consumer patients.[3] It is critical to understand the nature of CAD in young people, due to the clinical and socioeconomic impact of this disease.

Percutaneous coronary intervention (PCI) has been the invasive treatment modality most often used in the treatment of CAD in its different forms of presentation. In an earlier published analysis of the multicenter registry Angiocardio, when comparing with the population of the registry's initial period (2006-2008), the population in its most recent period (2009-2012) was younger, with a higher prevalence of smoking and diabetes.[4]

In Brazil, publications on PCI in young subjects are scarce.[5,6] Thus, the authors analyzed the in-hospital results of most recent PCIs from the Angiocardio registry in patients under 40 years, retrospectively assessing their profile and in-hospital clinical outcomes. The predictors of major cardiac and cerebrovascular events (MACCE) of the entire study population were also evaluated.

METHODS

Population

From August of 2006 to October of 2012, 6,288 consecutive patients underwent PCI at the centers that participate in the Angiocardio Registry (Hospital Bandeirantes, Hospital Rede D'Or São Luiz Analia Franco, and Hospital Leforte Hospital, in the city of São Paulo; Hospital Vera Cruz, in Campinas; and Hospital Regional do Vale do Paraíba, in Taubaté, all in the state of São Paulo, Brazil). Data were prospectively collected and stored in a computer database available via Internet to all centers participating in the registry. For this analysis, the population was divided into two groups: Group 1 comprised patients aged < 40 years (151 patients) and Group 2 comprised patients aged ≥ 40 years (6,137 patients).

The clinical events studied were: in-hospital death, periprocedural infarction, stroke, and emergency coronary artery bypass graft surgery (CABG) at hospital discharge.

Procedure

Almost all interventions were performed using the transfemoral route; the transradial route was the option chosen in only in a few cases. During the procedure, the technique and choice of material were left to the operating physician's discretion, as well as the decision regarding the need of glycoprotein IIb/IIIa use. Unfractionated heparin was used at the beginning of the procedure (70-100 U/kg), except in patients who were already being treated with low molecular weight heparin.

All patients received antiplatelet therapy in combination with acetylsalicylic acid (ASA), at loading doses of 300 mg and maintenance doses of 100-200 mg/day; and clopidogrel at loading doses of 300-600 mg and maintenance doses of 75 mg/day. Four hours after starting heparin, the femoral sheaths were removed. The radial sheaths were removed immediately after the procedure.

Angiographic analysis and definitions

The analyzes were performed by experienced operating physicians, based on at least two orthogonal projections, and using digital quantitative angiography. In this study, the same angiographic criteria stated in the database of the Centro Nacional de Intervenções Cardiovasculares (CENIC) of Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista (SBHCI) were used. The type of injury was classified according to the American College of Cardiology and American Heart Association (ACC/AHA) criteria.[7] In determining the pre- and postprocedural coronary flow, the Thrombolysis in Myocardial Infarction (TIMI) grading system was used.[8] Procedural success was defined as angiographic success (residual stenosis < 30%, with TIMI 3 flow) and no occurrence of MACCE, comprising death, periprocedural myocardial infarction, stroke, and emergency CABG.[9]

Deaths from any cause were recorded, and periprocedural infarction was defined by the reappearance of a typical chest pain and by the presence of electrocardiographic changes (a new ST-segment elevation or new Q waves) and/or angiographic evidence of target-vessel occlusion. An emergency CABG was defined as that performed immediately after PCI.

Statistical analysis

The data, stored in an Oracle-based database, were plotted in Excel spreadsheets and analyzed using SPSS, version 15.0. Continuous variables were expressed as means ± standard deviations, and categorical variables as absolute numbers and percentages. Associations between continuous variables were analyzed using Student's *t*-test. Associations between categorical variables were evaluated using the chi-squared test, Fisher's exact test, or likelihood ratio, as appropriate. A significance level of $p < 0.05$ was

adopted. Regression and multiple logistic models were used to identify predictors of MACCE.

RESULTS

Table 1 lists the clinical characteristics of patients. Patients aged < 40 years accounted for 2.4% of all subjects treated in this series. Group 1 was found to be, on average, 30 years younger, with higher prevalence of smokers and patients with clinical picture of AMI with ST-segment elevation. Group 2 had higher prevalence of hypertension, diabetes, and previous AMI, stroke, CABG, and PCI.

From an angiographic point of view, patients in Group 1 presented higher single-vessel involvement, with predominance of the anterior descending artery; thrombotic lesions; and TIMI flow grade 0 and 1 before the procedure. Calcified lesions and total occlusions were more frequent in Group 2 (Table 2).

Regarding the characteristics of the procedure (Table 3), the number of treated vessels per patient was higher in Group 2 (1.2 ± 0.5 vs. 1.4 ± 0.6; $p < 0.01$), as well as the number of stents per patient (1.1 ± 0.7 vs. 1.3 ± 0.6; $p < 0.01$). Primary and rescue coronary interventions in the acute phase of infarction were more frequent in Group 1.

Procedural success was similar between groups. Table 4 shows the clinical outcomes during hospitalization. There was no difference between groups regarding MACCE (3.3% vs. 3.3%; $p = 0.82$), death (0.0% vs. 1.0%; $p = 0.39$), stroke (0.0% vs. 0.1%, $p > 0.99$), AMI (3.3% vs. 2.3%, $p = 0.41$), or emergency CABG (0.6% vs. 0, 03%; $p = 0.56$).

In the univariate analysis, the variables age; Killip III/IV functional group; multivessel involvement, B2/C lesions; long, calcified or thrombotic lesions; occlusive lesions; pre-PCI TIMI flow grade 0/1; presence of collateral circulation; primary PCI; use of glycoprotein IIb/IIIa inhibitors; and thromboaspiration showed a significant relationship with MACCE occurrence. In the multivariate analysis, age (odds ratio [OR]: 1.02; 95% confidence interval [95% CI]: 1.00-1.05; $p = 0.03$) and Killip III/IV (OR: 6.0; 95% CI: 3.3-10.9; $p < 0.01$) were the variables that better explained the occurrence of in-hospital MACCEs.

TABLE 1
Clinical characteristics

Characteristic	Group 1 (n = 151)	Group 2 (n = 6,137)	*P-value*
Age, years	34.9 ± 4.2	62.5 ± 11.2	< 0.01
Male gender, n (%)	113 (74.8)	4,185 (68.2)	0.10
Smoking, n (%)	65 (43.0)	1,498 (24.4)	< 0.01
Hypertension, n (%)	76 (50.3)	4,590 (74.8)	< 0.01
Dyslipidemia, n (%)	43 (28.5)	2,198 (35.8)	0.08
Diabetes, n (%)	21 (13.9)	1,875 (30.6)	< 0.01
Previous myocardial infarction, n (%)	15 (9.9)	1,004 (16.4)	0.04
Previous coronary artery bypass graft surgery, n (%)	6 (4.0)	659 (10.7)	0.01
Previous percutaneous coronary intervention, n (%)	15 (9.9)	1,287 (21.0)	< 0.01
Chronic renal failure, n (%)	1 (0.7)	161 (2.6)	0.21
Previous stroke, n (%)	0 (0.0)	191 (3.1)	0.05
Clinical picture, n (%)			< 0.01
Asymptomatic	52 (34.4)	1,741 (28.4)	
Stable angina	16 (10.5)	1,547 (25.2)	
Ischemic equivalent	5 (3.3)	407 (6.7)	
Acute coronary syndrome	17 (11.3)	921 (15.0)	
Acute myocardial infarction	61 (40.0)	1,521(24.8)	
Killip, n (%)			0.13
I	27 (79.4)	595 (74.7)	
II	3 (8.8)	113 (14.2)	
III	3 (8.8)	21 (2.6)	
IV	1 (2.9)	67 (8.4)	

Rev Bras Cardiol Invasiva.
2014;22(4):353-8

TABLE 2
Angiographic characteristics

Characteristic	Group 1 (n = 151/179 vessels/189 injuries)	Group 2 (n = 6,137/8,174 vessels/9,012 injuries)	*P-value*
Extent of coronary disease, n (%)			< 0.01
One-artery	131 (86.8)	4,362 (71.1)	
Two-artery	16 (10.6)	1,453 (23.7)	
Three-artery	4 (2.6)	322 (5.2)	
Vessels treated, n (%)			< 0.01
Anterior descending	98 (54.7)	3,283 (40.2)	
Circumflex	37 (20.7)	2,105 (25.8)	
Right coronary	41 (22.9)	2,433 (29.8)	
Venous or arterial grafts	3 (1.7)	298 (3.6)	
Left main coronary artery	0 (0.0)	55 (0.7)	
Injury type B2/C, n (%)	109 (62.6)	4,495 (56.4)	0.12
Calcified lesions, n (%)	56 (29.6)	4,061 (45.2)	< 0.01
Thrombotic lesions, n (%)	35 (18.5)	791 (8.8)	< 0.01
Lesions > 20 mm, n (%)	17 (9.0)	1,116 (12.4)	0.19
Bifurcation injuries, n (%)	19 (10.1)	751 (8.4)	0.49
Total occlusions, n (%)	54 (28.6)	1,169 (13.0)	< 0.01
Left ventricular dysfunction, n (%)	10 (50.0)	392 (41.6)	0.60
Pre-procedure Thrombosis in Myocardial Infarction flow grade, n (%)			< 0.01
0/1	62 (32.8)	1,350 (15.0)	
2/3	127 (67.2)	7,632 (85.0)	
Collateral circulation, n (%)	33 (17.5)	1,263 (14.0)	0.21

TABLE 3
Procedure characteristics

Characteristics	Group 1 (n = 151/179 vessels/189 injuries)	Group 2 (n = 6,137/8,174 vessels/9,012 injuries)	*P-value*
Treated vessels/patient	1.2 ± 0.5	1.4 ± 0.6	< 0.01
Stent/patient relationship	1.1 ± 0.7	1.3 ± 0.6	< 0.01
Stenting, n (%)	158 (88.3)	7,446 (91.1)	0.24
Drug-eluting stents, n (%)	30 (19.0)	1,582 (21.3)	0.55
Stent size, mm	3.00 ± 0.41	2.97 ± 0.49	0.30
Stent length, mm	19.1 ± 6.8	18.6 ± 7.0	0.43
Types of intervention, n (%)			< 0.01
Primary PCI	25 (16.6)	574 (9.4)	
Rescue PCI	10 (6.6)	192 (3.1)	
Glycoprotein IIb/IIIa inhibitors, n (%)	16 (10.6)	437 (7.1)	0.14
Thromboaspiration, n (%)	4 (3.0)	164 (2.8)	0.80
Post-procedure TIMI flow grade, n (%)			
0/1	9 (4.8)	169 (2.0)	0.01
2/3	177 (95.2)	8,333 (98.0)	< 0.01
Stenosis degree, %			0.22
Pre-	88.0 ± 12.6	83.0 ± 12.9	
Post-	5.5 ± 21.1	3.5 ± 15.7	
Procedural success, n (%)	145 (96.0)	5,858 (95.5)	0.89

PCI, percutaneous coronary intervention; TIMI, Thrombosis in Myocardial Infarction.

TABLE 4
Clinical outcomes during hospitalization

Outcomes	Group 1 (n = 151)	Group 2 (n = 6,137)	*P-value*
MACCE, n (%)	5 (3.3)	200 (3.3)	0.82
Death n (%)	0 (0.0)	64 (1.0)	0.39
Emergency CABG, n (%)	1 (0.6)	2 (0.03)	0.56
Stroke, n (%)	0 (0.0)	6 (0.1)	> 0.99
Acute myocardial infarction, n (%)	5 (3.3)	143 (2.3)	0.41

MACCE, major adverse cardiac and cerebrovascular events; CABG, coronary artery bypass graft surgery

DISCUSSION

The frequency of younger patients (under 40 years) in PCI registries has ranged from 1% to 16%.[10-12] The increasingly earlier exposure to smoking, obesity, and stress have been listed as a cause of CVD in young people.[12-14] In the present study, smoking was the most common risk factor among young people, who were mostly males. Male smokers, obese, and with family history of CAD are the group most commonly found in the literature among young people undergoing PCI or admitted with an acute coronary syndrome or AMI picture.[12,13] Among those infarcted, 2% to 11% are aged under 40 years.[14] Conversely, high blood pressure, diabetes, and dyslipidemia were less commonly seen in the group of patients aged < 40 years in the present study, which agrees with previously published studies.[15,16]

The more frequent occurrence of AMI among young people undergoing PCI explains the angiographic findings with predominance of thrombotic lesions or occlusions with pre-procedural TIMI flow grade 0/1. Young patients presenting with AMI showed a less intense atherosclerotic burden with high propensity for thrombus formation. Recent studies have correlated genetic factors to the development of atherosclerosis and occurrence of AMI in young people, describing polymorphisms in genes such as that for methylene tetrahydrofolate reductase,[17] platelet receptors,[18] and plasminogen activator inhibitors,[1,19] which predispose patients to an acute coronary event.

The lower atherosclerotic burden among young people explains the higher number of single-vessel disease in those patients in the present study, which is consistent with findings of previous studies.[1,12,20] As a result, in the interventions in this young group, the numbers of vessels treated and of stents used per patient were low. The preferential involvement of the anterior descending branch was also observed in other studies.[1,16] Also in relation to angiographic characteristics, among young people there is a smaller number of calcified lesions. Age itself is a risk factor for the onset of coronary calcification, not only involving the intima (more related to atherosclerosis), but especially the middle layer.[21]

The high success rate of the procedure and the low occurrence of MACCE, similar in both groups, derive from the lower angiographic complexity of patients referred for PCI (a smaller number of vessels treated and of stents used per patient) and from the effectiveness of PCI, which presents great results also in the older population. Young patients undergoing PCI are usually considered of low risk for the procedure, but the potentially aggressive nature of the CAD and the long life expectancy may expose these subjects to a high risk of recurrent coronary events. In a five-year follow-up study, an angiographic multivessel pattern, diabetes, and hypertension were independent predictors of post-PCI disease progression. In that study, disease progression occurred in 13.5% of patients.[22]

In the present registry, age and presence of Killip III and IV functional classes were independent predictors of in-hospital MACCE. Chua et al.[18] reported only Killip III or IV class as a predictor of in-hospital morbidity and mortality in young patients with AMI. Active smoking, previous myocardial infarction, and low ejection fraction (< 50%) have also been described as MACCE predictors in patients with long-term follow-up.[12,14,21,22]

Study limitations

The limitations of this study were the retrospective data analysis and the absence of a longer follow-up.

CONCLUSIONS

Patients aged < 40 years represented a smaller fraction of the cases treated in this series. Smoking, AMI as clinical presentation, involvement of a single vessel and of anterior descending artery, lesions with thrombi, and TIMI flow grade 0/1 were the most observed characteristics among this group of young patients, which speaks in favor of the need to set earlier measures of primary prevention in patients matching the observed profile.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

FUNDING SOURCE

None.

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