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Temporal investigation of percutaneous coronary intervention for non-ST segment elevation acute coronary syndrome

Investigação temporal da intervenção coronária percutânea nas síndromes coronárias agudas sem supradesnívelamento do segmento ST

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ABSTRACT – Background: Percutaneous coronary intervention is the most recommended method of myocardial revascularization in acute coronary syndrome patients. The objective of this study was to analyze the clinical profiles and outcomes of patients with non-ST segment elevation acute coronary syndrome undergoing percutaneous coronary intervention. **Methods:** We retrospectively analyzed 53,889 patients with non-ST segment elevation acute coronary syndrome, who underwent percutaneous coronary intervention between June 2006 and March 2016. A database was used to define the patients' clinical and angiographic characteristics, procedures and clinical outcomes. The patients were grouped into different chronological periods, and variables were analyzed to determine their influence over death outcomes. **Results:** Factors such as advanced age, female sex, history of infarction or coronary artery bypass surgery, diabetes, multivessel disease, left ventricular dysfunction, and collateral circulation were associated to a higher risk of in-hospital death for these patients. The success rate of the procedures increased along time and the risk of death decreased. **Conclusion:** Advances in the available medical technology have changed the profile of percutaneous coronary intervention, which has led to a higher rate of procedure success and a lower risk of death and complications.

Keywords: Percutaneous coronary intervention; Myocardial revascularization; Non-ST elevated myocardial infarction

RESUMO – Introdução: A intervenção coronária percutânea é o método preferencial de revascularização miocárdica nos pacientes com síndrome coronária aguda. No presente estudo, objetivamos analisar o perfil e os desfechos clínicos de pacientes com síndrome coronária aguda sem supradesnívelamento do segmento ST submetidos à intervenção coronária percutânea. **Métodos:** Um total de 53.889 pacientes com síndrome coronária aguda sem supradesnívelamento do segmento ST, submetidos à intervenção coronária percutânea no período entre junho de 2006 e março de 2016, foi avaliado retrospectivamente a partir de um banco de dados, com o objetivo de se definirem suas características clínicas, angiográficas, dos procedimentos e seus desfechos clínicos. As variáveis foram comparadas agrupando-se os pacientes em períodos cronológicos distintos, avaliando-se a influência de cada uma delas para ocorrência de óbito. **Resultados:** Idade avançada, sexo feminino, história de infarto ou cirurgia de revascularização miocárdica, diabetes, doença multiarterial, disfunção ventricular esquerda e circulação colateral foram fatores relacionados ao maior risco de óbito hospitalar nesses pacientes. A taxa de sucesso dos procedimentos aumentou ao longo dos anos, enquanto o risco de óbito diminuiu. **Conclusão:** O avanço das tecnologias médicas disponíveis tem alterado o perfil da intervenção coronária percutânea, levando ao maior sucesso do procedimento e ao menor risco de óbito e complicações.

Descritores: Intervenção coronária percutânea; Revascularização miocárdica; Infarto do miocárdio sem supradesnível do segmento ST

INTRODUCTION

Percutaneous coronary intervention (PCI) is the most frequently used method of coronary revascularization in patients with non ST-elevation acute coronary syndrome

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(NST-ACS). After the initial risk stratification, most NST-ACS patients undergo coronary angiography (early or selective invasive strategy). Depending on the clinical, angiographic and anatomic criteria, the next step is PCI.^{1,2} Data from North America show an increase by 54% in the use of PCI and a reduction by 14% in coronary artery bypass grafting (CABG) for NST-ACS patients between 2001 and 2011.³ Only approximately 10% of NST-ACS patients will require CABG during their hospital stay.⁴

For high-risk patients who require the invasive technique, PCI improves their prognosis and reduces the risk of death and non-fatal acute myocardial infarction (AMI).⁵⁻⁸ Records from different countries have shown a reduction in the incidence of heart failure and mortality after acute coronary syndromes (ACS).⁹⁻¹¹ In-hospital mortality of NST-ACS patients in the United States also decreased between 2001 and 2011, regardless of the treatment proposed: clinical (reduction by 29%; $p < 0.001$), surgical (reduction by 41%; $p < 0.001$) or percutaneous (reduction by 16%; $p = 0.29$).

Our objective for this study was to analyze the clinical outcomes and profiles of NST-ACS patients undergoing PCI.

METHODS

The present study was evaluated by the Research Ethics Committee of *Hospital Leforte*, and was registered on *Plataforma Brasil*, receiving its approval by CAAE 14465319.0.0000.5485.

We retrospectively analyzed clinical and angiographic data about the in-hospital outcomes and procedures of 53,889 NST-ACS patients, who underwent PCI in Brazil, between 2006 and 2016. Data were obtained from *Central Nacional de Intervenções Cardiovasculares* (CENIC; <http://www.corehemo.net/>). This is an official agency of the *Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista* (SBHCI) and operates as a database. It is fed voluntarily by full and probationary members of SBHCI and compiles information on therapeutic procedures performed by interventional cardiologists in Brazil. Data from CENIC can show us Brazilian interventional cardiology activities, classify patient profiles, evaluate clinical results and the quality of catheterization laboratories services, and demonstrate trends throughout time.

In our study, we analyzed the total sample of patients registered between June 2006 and March 2016. The studied decade was divided into the following periods: 2006-2008; 2009-2011; and 2012-2016. We compared the results and profiles of patients who underwent PCI for NST-ACS throughout the studied period (2006-2016) and checked the influence of distinct variables on in-hospital mortality.

Statistical analysis

To compare categorical variables in relation to the periods between 2006-2016, we used the Chi-square test. Whenever necessary, we also used the likelihood ratio test. To compare continuous variable, we used the analysis

of variance (ANOVA). For multiple comparisons, we used Bonferroni's correction. To check the influence of variables of interest regarding mortality, we used the simple logistic regression model. For all analyses, significance level was set at 5% ($p < 0.05$).

RESULTS

Between June 2006 and March 2016, 53,889 patients and 56,151 procedures (mean of 1.04 procedures per patients) were retrospectively analyzed. A total of 76,392 vessels were treated, and 74,249 (97.2%) of them were treated with stents, totaling up 74,889 stents. The patients' clinical characteristics are shown in table 1. During the second period (2009-2011), the mean age of patients was higher than in the other periods. In the last period (2012-2016), there was an increase in the proportion of male ($p < 0.0001$) and diabetic ($p < 0.0001$) patients, and a reduction of patients who were smokers ($p < 0.0001$), hypertensive ($p < 0.0001$), with dyslipidemia ($p < 0.0001$), history of acute MI ($p < 0.0001$), PCI ($p < 0.0001$) and CABG ($p < 0.0001$).

Angiographic characteristics are presented in table 2. In the last period (2012-2016), there were more single-vessel patients treated, and in the first period (2006-2008), the number of two-vessels and three-vessels was higher than in the other periods. Moreover, between 2012 and 2016, a higher proportion of left circumflex (LCx) treatments and a lower proportion of venous and arterial bypass graft were observed as compared to previous periods. On the other hand, there was a reduction, throughout time, in the total number of treatments for calcified lesions, thrombotic lesions, long lesions and interventions in bifurcations. The presence of collateral circulation was more frequent in the last period, as were treatments for occlusions and lesions with more severe flow reductions (Thrombolysis in Myocardial Infarction – TIMI 0 and 1). In the period between 2009 and 2011, there was a higher proportion of patients with left ventricular dysfunction (LVD).

Table 1. Clinical characteristics

Characteristics	2006-2008 (n=15,084 patients)	2009-2011 (n=19,518 patients)	2012-2016 (n=19,287 patients)	p-value
Age, years	63.6 (11.6)	63.8 (11.6)	63.4 (11.6)	0.0006
Male sex	9,575 (63.5)	12,533 (64.2)	12,746 (66.1)	<0.0001
Smoking	3,982 (26.4)	4,315 (22.1)	4,108 (21.3)	<0.0001
Hypertension	12,467 (82.7)	16,183 (83.0)	15,474 (80.3)	<0.0001
Dyslipidemia	9,76 (60.8)	11,073 (57.5)	10,959 (57.2)	<0.0001
Diabetes mellitus	3,893 (25.8)	4,377 (24.3)	4,747 (28.3)	<0.0001
Previous myocardial infarction	2,861 (19.0)	3,399 (18.9)	2,470 (14.8)	<0.0001
Prior PCI	2,969 (20.0)	3,443 (18.1)	3,299 (17.4)	<0.0001
Prior coronary artery bypass grafting	1,695 (11.2)	1,890 (9.7)	1,374 (7.1)	<0.0001

Results expressed by mean $\pm$ standard deviation or n (%). PCI: Percutaneous coronary intervention.

Table 2. Angiographic characteristics

Characteristics	2006-2008 (n=15,725 procedures/ n=21,670 vessels)	2009-2011 (n=20,318 procedures/ n=27,792 vessels)	2012-2016 (n=20,108 procedures/ n=26,930 vessels)	p-value
Coronary disease extension				<0.0001
Single vessel	6,811 (44.3)	9,469 (48.1)	10,794 (55.3)	
Two-vessel	5,165 (33.6)	6,264 (31.9)	5,636 (28.9)	
Three-vessel	3,308 (21.5)	3,891 (19.8)	3,030 (15.5)	
Multi-vessel + LMCA	0 (0.0)	4 (0.02)	23 (0.12)	
LMCA	78 (0.5)	38 (0.2)	26 (0.1)	
Treated vessels				<0.0001
RCA	6,001 (27.7)	7,858 (28.3)	7,612 (28.3)	
LCx	5,300 (24.5)	6,879 (24.8)	6,862 (25.5)	
LAD	9,319 (43.0)	11,836 (42.6)	11,426 (42.4)	
Venous graft	813 (3.8)	934 (3.4)	660 (2.5)	
LMCA	237 (1.1)	285 (1.0)	370 (1.4)	
Type B ₂ /C lesions	13,365 (67.9)	852 (76.1)	377 (90.2)	<0.0001
Calcified lesions	6,002 (27.7)	7,054 (25.4)	5,790 (22.0)	<0.0001
Thrombotic lesions	2,204 (10.2)	2,648 (9.5)	2,210 (8.2)	<0.0001
Lesions >20 mm	5,623 (25.9)	6,776 (24.4)	6,495 (24.1)	<0.0001
Bifurcations	6,289 (29.0)	6,611 (23.8)	5,516 (20.5)	<0.0001
Occlusions	1,416 (6.6)	1,794 (6.5)	2,352 (8.7)	<0.0001
TIMI flow pre				
0/1	2,070 (9.6)	3,182 (11.5)	3,286 (12.2)	<0.0001
2/3	19,596 (90.4)	24,606 (88.5)	23,639 (87.8)	
Left ventricular dysfunction	6,732 (51.7)	7,608 (57.1)	7,001 (53.4)	<0.0001
Collateral circulation	1,641 (10.9)	1,347 (12.0)	1,542 (12.6)	<0.0001

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

Table 3. Characteristics of procedures

Characteristics	2006-2008 (n=15,084 patients/ n=15,725 procedures/ n=20,969 stents)	2009-2011 (n=19,518 patients/ n=20,318 procedures/ n=27,345 stents)	2012-2016 (n=19,287 patients/ n=20,108 procedures/ n=26,575 stents)	p-value
Treated vessels/patient	1.43 (0.7)	1.43 (0.71)	1.40 (0.72)	<0.0001
Use of stent	14,553 (96.5)	18,935 (97.0)	18,652 (96.7)	0.019
Stent/patient ratio	1.44 (0.71)	1.45 (0.72)	1.43 (0.72)	0.016
Drug-eluting stents	4,718 (22.5)	8,059 (29.5)	8,048 (30.3)	<0.0001
Stent diameter, mm	3.03 (0.48)	3.00 (0.48)	2.97 (0.5)	<0.0001
Stent length, mm	18.8 (6.8)	19.5 (7.6)	19.9 (8.1)	<0.0001
Glycoprotein IIb/IIIa inhibitors	897 (5.7)	603 (3.0)	223 (1.1)	<0.0001
Thromboaspiration	11 (0.1)	58 (0.2)	82 (0.3)	<0.0001
TIMI flow post				
0/1	157 (0.7)	598 (2.2)	246 (0.9)	<0.0001
2/3	20,792 (99.3)	26,724 (97.8)	26,312 (99.1)	<0.0001
Stenosis grade				
Pre	85.5 (12.2)	85.5 (14.4)	86.1 (14.6)	<0.0001
Post	2.1 (8.5)	2.4 (7.1)	4.9 (4.3)	<0.0001
Success of procedure	15,261 (97.0)	19,913 (98.0)	19,722 (98.1)	<0.0001

Results expressed by mean ± standard deviation or n (%). TIMI: Thrombolysis in Myocardial Infarction.

Table 3 summarizes procedure characteristics, including the number of stents used (74,889 stents). In the period between 2012 and 2016, there was a reduction in the number of treated vessels per patients ($p<0.001$), number of stents per patient ($p=0.016$), mean diameter of stents used ($p<0.001$) and use of glycoprotein IIb/IIIa inhibitors ($p<0.001$). On the other hand, we showed an increase in the use of drug-eluting stents ($p<0.001$), the length of stents used ($p<0.001$) and thromboaspiration ($p<0.001$). The degree of stenosis of the lesions was higher in the last period in relation to the other periods, as was the degree of residual stenosis ($p<0.001$). Procedure success increased gradually between the analyzed periods, reaching 98.1% ($p<0.001$) in the period 2012-2016.

Table 4 summarizes the clinical outcomes analyzed in the in-hospital phase. The occurrence of post-procedure acute MI, death, and adverse cardiac events was more frequent in the first period (2006-2008). The need for emergency CABG remained stable throughout the periods.

Table 4. In-hospital clinical outcomes

Outcome	2006-2008 (n=15,084 patients)	2009-2011 (n=19,518 patients)	2012-2016 (n=19,287 patients)	p-value
Acute MI	69 (0.5)	59 (0.3)	42 (0.3)	0.006
Emergency CABG	0 (0.0)	4 (0.02)	5 (0.03)	0.792
Death	120 (0.8)	97 (0.5)	114 (0.7)	0.015
MACE	173 (1.1)	155 (0.8)	154 (0.8)	0.0005

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

Table 5 evaluates the influence of independent variables on the occurrence of death. Patients treated between 2006 and 2008 had 1.48-fold higher risk of death than patients treated between 2009 and 2011. The comparison between the first and the last period did not show an increase in the risk of death (OR 0.83; 95%CI 0.64–1.07). For each extra year of age, the risk of death increased by 6%. Female patients (OR 1.34; 95%CI 1.07–1.67), diabetic patients (OR 1.64; 95%CI 1.3–2.08), those with a history of acute MI (OR 1.73; 95%CI 1.34–2.23) or a history of CABG (OR 1.59; 95%CI 1.16–2.18) showed a higher risk of death. The same happened with two-vessel disease patients (OR 2.48; 95%CI 1.81–3.39), three-vessel disease patients (OR 5.98; 95%CI 4.45–8.04) and isolated left main coronary artery (LMCA) disease (OR 71.74; 95%CI 40.45–127.24). Patients with LVD had a risk of death 4.93-fold higher. Presence of collateral circulation (OR 2.23; 95%CI 1.64–3.05) and patients requiring infusion of glycoprotein IIb/IIIa inhibitors (OR 5.07; 95%CI 3.71–6.93) also presented a higher risk of death after PCI.

DISCUSSION

Our study evaluated an expressive, heterogenous sample of patients from CENIC database, throughout a long period of time. During this period, several new technologies and drugs were introduced into medical practice. We observed changes in the patients' clinical characteristics from year to year, as well as changes in the procedures performed (number of stents per patient, longer stents, smaller diameter vessels, more frequent use of drug-eluting stents, and treatment of more complex lesions), success rate and risk of in-hospital death.

Table 5. Influence of independent variables in case of death

Variables	Estimate	p-value	OR	95%CI
2009-2011 vs. 2006-2008	-0.39	0.004	0.67	0.52-0.88
2012-2016 vs. 2006-2008	-0.19	0.148	0.83	0.64-1.07
Age, years	0.06	<0.0001	1.06	1.05-1.07
Sex, female vs. male	0.29	0.009	1.34	1.07-1.67
Smoking, no vs. yes	0.20	0.151	1.22	0.93-1.59
HTN, yes vs. no	-0.03	0.854	0.97	0.74-1.29
Dyslipidemia, no vs. yes	0.10	0.359	1.11	0.89-1.38
Diabetes mellitus, yes vs. no	0.50	<0.0001	1.64	1.30-2.08
Prior acute MI, yes vs. no	0.55	<0.0001	1.73	1.34-2.23
Previous PCI, no vs. yes	-0.25	0.081	0.78	0.59-1.03
Prior CABG, yes vs. no	0.46	0.004	1.59	1.16-2.18
Extension of coronary disease, two-vessel vs. single-vessel	0.91	<0.0001	2.48	1.81-3.39
Extension of coronary disease, three-vessel vs. single-vessel	1.79	<0.0001	5.98	4.45-8.04
Extension of coronary disease, multi-vessel + LMCA vs. single-vessel	1.69	0.999	5.40	0.01-2787.27
Extension of coronary disease, LMCA vs. single-vessel	4.27	<0.0001	71.74	40.45-127.24
Left ventricular dysfunction, yes vs. no	1.59	<0.0001	4.93	3.27-7.42
Collateral circulation, yes vs. no	0.80	<0.0001	2.23	1.64-3.05
Glycoprotein IIb/IIIa inhibitors, yes vs. no	1.62	<0.0001	5.07	3.71-6.93

OR; odds ratio; 95%CI: 95% confidence interval; HTN: hypertension; MI: myocardial infarction; PCI: percutaneous coronary intervention; CABG: coronary artery bypass grafting; LMCA: left main coronary artery.

The mean age of patients evaluated in this study was 63.6 (± 11.6) years and most patients were male (64.7%). Female patients presented a higher risk of death. Women are often underdiagnosed (atypical symptoms, non-diagnostic electrocardiogram) and older, have more comorbidities, smaller vessels and receive less treatment than recommended in the guidelines.¹²⁻¹⁶ It is noteworthy mentioning the gradual decrease in number of patients who are smokers. The prevalence of smoking in the Brazilian population has systematically decreased in the last 25 years.¹⁷ On the other hand, we observed a higher number of diabetic patients, which points to an increased prevalence of diabetes in Brazil.¹⁸

Throughout the years, there was a reduction in the number of patients with a history of acute MI, PCI and CABG, which means a higher number of patients presenting their first coronary event. In the last period, we observe an increase in the proportion of single-vessel disease patients and a decrease of two- and three-vessel disease patients. It was to be expected that, year after year, we would see an increase in treatments of multivessel patients because of the development of technology and devices that can help interventional cardiologists during PCI. That was exactly what we observed, with a large proportion of complex lesions in the period 2012-2016. This higher angiographic complexity leads to a poorer clinical prognosis, even with the use of drug-eluting stents. However, our data show a higher success rate in the last period, even with more complex patients.^{19,20}

Our study also shows a small number of patients who underwent interventions for protected or unprotected LMCA lesions. Some authors suggest a trend of more frequent procedures for unprotected LMCA.²¹ On the other hand, the left anterior descending artery was the vessel most frequently submitted to PCI during the entire analyzed period. The higher prevalence of PCI for coronary chronic total occlusions in the last period (2012-2016) is justifiable, especially because specific techniques and materials become increasingly more available. The presence of collateral circulation was shown to be a predictor for mortality, which goes against the expectations that, in these patients, the collateral arteries would work as a protective network of muscle viability in ischemic territory.^{22,23}

It has been proven that stent implants reduce acute reocclusion of the vessel and restenosis, and are nowadays considered the best treatment, especially with the use of drug-eluting stents.²⁴ Data from the National (Nationwide) Inpatient Sample (NIS), from 1988-2004, and that include 1,747,736 PCI, also show a consistent increase in the use of PCI as a treatment option for myocardial revascularization.²⁵ A European registry published in 2006 that evaluated data from 32 countries of the European Society of Cardiology, between 1992 and 2003, had previously shown a gradual increase in the use of drug-eluting stents and in the number of ad-hoc procedures, and a decrease in the need for emergency CABG. That suggests the development of

new technologies increased the safety and the dissemination of PCI as the preferred revascularization therapy for coronary disease.²⁶ We have shown the increased use of drug-eluting stents in NST-ACS patients. In August 2014, an ordinance of the Brazilian Ministry of Health regulated the use of drug-eluting stents in the Brazilian Unified Health System (SUS).²⁷ Moreover, the most recent guidelines recommend the use of new-generation drug-eluting stents over bare metal stents in this clinical context.^{28,29}

Study limitations

Since it is a retrospective, non-randomized study, conducted using a database, there are limitations related to patient selection and procedure standardization. There was no systematic monitoring of patients. The registry is fed by volunteers, therefore, it does not represent the total number of procedures performed in all participating cath labs in Brazil, for several procedures are not registered in the system.

CONCLUSION

The percutaneous approach for coronary lesions that cause cardiac events and manifest as non ST-elevation acute coronary syndrome is becoming more and more frequent, and is now a routine procedure for interventional cardiologists. Even though several factors are associated to a poorer prognosis, advances in the available technologies have changed the profile of percutaneous coronary interventions, allowing a higher rate of success and a lower risk of death and complications.

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None.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

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