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Cerebrovascular event after cardiac catheterization in the modern era: prevalence, in-hospital clinical course, and 30-day follow-up

Evento cerebrovascular após cateterismo cardíaco na era moderna: prevalência, evolução intra-hospitalar e seguimento em 30 dias

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ABSTRACT – **Background:** Stroke is a potentially serious complication that can occur after cardiac catheterization. However, there is no data in the contemporary literature about the prevalence or clinical course of this complication in a Brazilian population. The objective of this study was to evaluate the prevalence and clinical course of patients with a cerebrovascular event, considering a primary composite outcome (cardiovascular death, cerebrovascular reischemia, and severe sequelae) within 30 days of follow-up. **Methods:** A single-center study in which patients aged 40 years or older undergoing coronary angiography or percutaneous coronary intervention from March 2013 to February 2014 were retrospectively analyzed. Patients who presented cerebrovascular events were compared with the control group. **Results:** A total of 7,980 procedures were performed in the period, and cerebrovascular events occurred in 12 individuals (0.15%); in that, 5 (41.7%) transient ischemic attacks and 7 (58.3%) ischemic strokes. Among the patients with a cerebrovascular event, there was a predominance of males (66.7%) and mean age of 64.9±9.3 years; atrial fibrillation, chronic renal failure, coronary artery bypass graft, and left ventricular dysfunction were identified in 25% of sample. The clinical and procedural characteristics were similar in both groups, with a lower number of diabetics in the control group (p=0.05). No complications related to primary outcome were identified. **Conclusion:** In this contemporary series, the prevalence of cerebrovascular events after interventional cardiology procedures was low, in a high volume tertiary center. The patients presented a satisfactory clinical course, potentially due to early diagnosis and treatment.

Keywords: Stroke; Coronary angiography; Percutaneous coronary intervention

RESUMO – **Introdução:** O acidente vascular cerebral é uma complicação potencialmente grave, que pode ocorrer após o cateterismo cardíaco. Entretanto, não há dados na literatura contemporânea sobre a prevalência e nem sobre a evolução clínica desta complicação em uma população brasileira. O objetivo deste estudo foi aferir a prevalência e a evolução clínica dos pacientes com evento cerebrovascular, considerando um desfecho primário composto (óbito cardiovascular, reisquemia cerebrovascular e sequela grave) em 30 dias de seguimento. **Métodos:** Estudo unicêntrico, no qual foram analisados retrospectivamente os pacientes com 40 anos ou mais de idade submetidos à cinecoronariografia ou intervenção coronária percutânea entre março de 2013 e fevereiro de 2014. Pacientes que apresentaram evento cerebrovascular foram comparados com grupo controle. **Resultados:** Foram realizados 7.980 procedimentos no período, com ocorrência de evento cerebrovascular em 12 indivíduos (0,15%), sendo 5 (41,7%) ataques isquêmicos transitórios e 7 (58,3%) acidentes vasculares cerebrais isquêmicos. Dentre os pacientes com evento cerebrovascular, houve predomínio do sexo masculino (66,7%) e média de idade de 64,9±9,3 anos; fibrilação atrial, insuficiência renal crônica, revascularização cirúrgica do miocárdio e disfunção ventricular esquerda foram identificados em 25% da amostra. As características clínicas e do procedimento foram semelhantes entre os grupos, com menor número de diabéticos no grupo controle (p=0,05). Não foram identificadas complicações relacionadas ao desfecho primário. **Conclusão:** Nesta série contemporânea, a prevalência de evento

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cerebrovascular após procedimento em cardiologia intervencionista foi baixa, no contexto de um centro terciário de alto volume. Os pacientes apresentaram evolução clínica satisfatória, potencialmente devido ao diagnóstico e ao tratamento precoces.

Descritores: Acidente vascular cerebral; Angiografia coronária; Intervenção coronária percutânea

INTRODUCTION

Since its introduction, cardiac catheterization has been a method of central relevance in cardiological practice, both as a diagnostic tool and as a therapeutic modality. More recently, a progressive increase in the complexity of the population served and the procedures performed in catheterization laboratories (cath lab) in Brazil and worldwide has been observed. However, few studies have evaluated whether the increased risk profile has been accompanied by a change in the rate of complications related to percutaneous procedures in modern times.

Previous studies showed that cerebrovascular events can occur as a consequence of endovascular manipulation during cardiac catheterization.[1-6] However, this type of complication, with potentially great deleterious effects, has been little studied. Its prevalence and clinical course are poorly understood, especially in our population.

The present study aimed to evaluate the occurrence and early prognosis of cerebrovascular complications after diagnostic or therapeutic interventional cardiology procedures performed at a high-volume Brazilian tertiary center.

METHODS

We retrospectively analyzed all patients aged 40 years or older undergoing coronary angiography or percutaneous coronary intervention (PCI) at a tertiary hospital, from March 2013 to February 2014. Clinical information was obtained from the analysis of the organization database, and the 30-day follow-up was performed by the medical team, by telephone and review of electronic medical records. From the universe of patients seen in the period, we identified all those with a diagnosis of a cerebrovascular event (Cerebrovascular Event Group) on the first day after the percutaneous procedure, who were classified as stroke, defined as the onset of a new symptom and/or a change in the neurological examination, with persistence for a period of 24 hours or more, or as transient ischemic attack (TIA), defined by reversal of the neurological deficit in the first 24 hours. All patients who presented a cerebrovascular event were evaluated by cranial computed tomography (CT).

To identify the clinical variables predicting cerebrovascular events, a 1:2 paired Control Group was obtained, homogenized as to age, sex, date and characteristics of the procedure (diagnostic or therapeutic). We compared the clinical characteristics and the primary outcome of both groups.

The primary outcome was defined as the prevalence of cardiovascular death events (any death, excluding those attributable to non-cardiovascular causes) and cerebrovascular reischemia or severe sequelae (permanent limiting motor deficit, aphasia, reduced cognitive function and functional dependence, defined as a modified Rankin scale ≥3) in the first 30 days.

Diagnostic procedures performed through the radial artery received unfractionated heparin at a dose of 5,000IU as routine. In cases performed via the femoral artery we did not use heparin. For PCI, unfractionated heparin at a dose of 100IU/kg was administered, with an activated clotting time (ACT) target between 250 and 350 seconds.

Statistical analysis was done using Statistics Package for the Social Sciences (SPSS), version 19.0 (IBM, New York, USA). Continuous variables were expressed as mean and standard deviation, and categorical variables as frequency in percentage. Clinical and procedural characteristics were compared in both groups using the Pearson Chi-squared test and Student's t-test. Values of $p<0.05$ were considered statistically significant.

This study was evaluated and approved by the Research Ethics Committee of the Hospital das Clínicas of the Faculdade de Medicina of the Universidade de São Paulo (CAAE: 24258819.3.0000.0068), under protocol 3.687.257.

RESULTS

Among the 7,980 procedures performed during the study period, 12 (0.15%) patients presented a cerebrovascular event within the first 24 hours. Of these, five (41.7%) patients presented TIA, and seven (58.3%) presented stroke. All events were ischemic, and no hemorrhagic stroke was observed. The diagnoses of ischemic stroke were confirmed by the identification of hypodensity areas in the cerebral parenchyma of these patients, compatible with recent ischemia, in the cranial CT. Among the patients who presented TIA, three underwent cranial magnetic resonance and two underwent cranial CT after 48 hours of the event, and no areas suggestive of recent ischemia were identified.

In the Cerebrovascular Event Group there was a predominance of males (66.7%), with mean age of 64.9±9.3 years. In 50% of cases (n=6), the diagnosis of cerebrovascular event was made within the cath lab. In four cases (33.3%), the percutaneous procedure was performed urgently. Of these, three patients presented ST segment elevation myocardial infarction (MI). In only one case, a manual thrombus aspiration with a thrombectomy catheter was performed. Most cerebrovascular events occurred after diagnostic procedures (n=7; 58.3%). Permanent atrial fibrillation (AF), chronic renal failure (CRF), previous coronary artery bypass grafting (CABG), and left ventricular dysfunction were identified in 25% of sample. We found a lower prevalence of diabetic patients in the control group (66.6% vs. 33.3%), but with no statistical significance (p=0.05). The other characteristics were similar in both groups (Tables 1 and 2). Of the patients diagnosed with stroke, one of them

Table 1. Clinical characteristics

Variable	Cerebrovascular Event Group (n=12)	Control Group (n=24)	p-value
Age, years	64.9±9.3	64.7±8.7	1.00
Male sex	8 (66.7)	16 (66.7)	1.00
Hypertension	9 (75.0)	16 (66.7)	0.60
Diabetes mellitus	8 (66.7)	8 (33.3)	0.05
Smoking	5 (41.7)	8 (33.3)	0.63
Dyslipidemia	8 (66.7)	14 (58.3)	0.62
Chronic renal failure	3 (25.0)	7 (29.2)	0.79
Atrial fibrillation	3 (25.0)	2 (8.3)	0.17
Previous stroke	0	0	1.00
Prior CABG	3 (25.0)	2 (8.3)	0.17
LVEF <45%	3 (25.0)	5 (20.8)	0.77
Carotid stenosis	1 (8.3)	0	0.15

Results expressed as mean±standard deviation or n (%). CABG: coronary artery bypass grafting; LVEF: left ventricular ejection fraction.

Table 2. Characteristics of procedures

Variable	Cerebrovascular Event Group (n=12)	Control Group (n=24)	p-value
Coronary angiography	7 (58.3)	14 (58.3)	1.00
PCI	5 (41.7)	10 (41.7)	1.00
Type of the procedure			0.59
Elective	8 (66.7)	18 (75.0)	
Urgency	4 (33.3)	6 (25.0)	
Access			0.30
Radial	5 (41.7)	6 (25.0)	
Femoral	7 (58.3)	18 (75.0)	
Manual thrombus aspiration	1 (8.3)	1(4.2)	0.60
Fluoroscopy time			
Coronary angiography	9.4±3.8	8.0±3.9	0.54
PCI	16.0±8.1	13.6±6.3	0.62

Results expressed as n (%) or mean±standard deviation. PCI: percutaneous coronary intervention.

underwent thrombolysis with intravenous alteplase 90 minutes after onset of symptoms, with a good clinical course and complete reversal of the motor deficit (Table 3). The other cases of stroke were treated conservatively, because, in the neurologist's evaluation, they had a National Institutes of Health (NIH) stroke score below 4.

In the first 30 days after the adverse event, there was a death due to cancer. There were no outcomes related to the primary outcome (cardiovascular death, cerebrovascular reischemia, or severe sequelae) in both groups. One patient maintained a reduction in visual acuity identified as a sequela of stroke, but without impairment of functional capacity (modified Rankin scale =1). No patient had permanent motor sequelae (Table 4). There was also no re-hospitalization or MI in the follow-up period.

Table 3. In-hospital findings

Procedures	(n=7,980)
Total number of events	12 (0.15)
Ischemic stroke	7 (58.3)
Transient ischemic attack	5 (41.7)
Intravenous thrombolysis	1 (9.1)
In-hospital death	0
Diagnosis at cath lab	6 (50)

Results expressed as n (%).

Table 4. Results in the 30-day follow-up

Variable	Cerebrovascular Event Group (n=12)	Control Group (n=24)
Primary outcome	0	0
Death due to any cause	1 (8.3)	0
New stroke	0	0
Severe sequela	0	0
Myocardial infarction	0	0
Readmission	0	0
Motor sequela	0	0
Other sequelae	1 (8.3)	0

Results expressed as n (%).

DISCUSSION

Our study demonstrated a low rate of cerebrovascular events following cardiac catheterization, associated with a low risk of clinical events related to this complication. These results corroborate the current data available in the literature, which indicate a low occurrence of periprocedural cerebrovascular events, even in the context of an increase in the proportion of patients of higher complexity.[7-13] A study published by Werner et al. evaluated 46,888 patients who underwent PCI, and found an incidence of cerebrovascular events of 0.4%.[11] This slightly higher incidence is probably due to the fact that the study presented a significantly larger sample in relation to the number of patients evaluated in our study, besides having excluded all diagnostic procedures from their analysis. The KAMIR-NIH registry, recently published by Ahn et al., evaluated the clinical outcomes of 3,985 patients with type 2 diabetes with MI, and found a stroke incidence of 46 (1.5%) in patients receiving clopidogrel, and of 5 patients (0.5%), in the group receiving prasugrel or ticagrelor. This higher number of strokes when compared to those found in our study can be explained by the fact that the registry included a profile of more complex patients in their analysis, including diabetes mellitus patients with MI undergoing PCI.[12]

In our series, the most common comorbidities in the group of patients who presented cerebrovascular events were hypertension, diabetes mellitus, dyslipidemia, and

smoking habit, similar to the characteristics of the population of previous studies.[11,14] No clinical variable was associated with a higher event risk when we compared the sample of patients from the Cerebrovascular Event Group with those from the Control Group in our study.

In a National Cardiology Data Registry study with 706,782 patients, of which 1,540 were diagnosed with periprocedural stroke, the following predictors of complication were identified: acute coronary syndrome upon admission, advanced age, known cerebrovascular disease, and use of an intra-aortic balloon counterpulsation.[15] In another study, Popovic et al. found that chronic renal failure, diabetes mellitus, known cerebrovascular disease, heart failure, left ventriculography, and low-volume operators were independent predictors of cerebrovascular events after coronary angiography.[16]

It is important to emphasize that, although the main predictors of cerebrovascular event are related to the clinical condition of the patient, some factors associated with the procedure itself may be relevant, and they are important targets of preventive actions to minimize the risk of complications (e.g., use of smaller diameter material, appropriate aspiration of the catheters, careful handling of catheter and guidewire through the ascending aorta, especially in patients at higher risk, and adequate antithrombotic therapy during the procedure).[1,6]

In the TOTAL trial, Jolly et al. randomly evaluated 10,732 STEMI patients, and demonstrated a higher occurrence of stroke in patients undergoing PCI with manual aspiration thrombectomy: 60 patients (1.2%) as compared to 36 (0.7%) in the group undergoing PCI without thrombectomy (95%CI 1.10-2.51, p=0.015). In our study, due to the small sample of STEMI patients, it was not possible to evaluate this correlation.[17]

The procedure time is always a concern regarding prevention of thromboembolic complications. In the multicenter RAY'ACT-1 registry study, the researchers found significantly less fluoroscopy time than in our sample (3.5 minutes in the femoral access group, and 3.8 minutes in the radial access group), but, unlike our study, those centers were not linked to medical schools, and there is no description of relevant clinical features, such as percentage of patients with previous CABG, and clinical outcomes have not been evaluated. Therefore, it is not possible to correlate such finding with a reduction in cerebrovascular events.[18] On the other hand, a study published by Adachi et al. evaluated fluoroscopy time in coronary angiography procedures and demonstrated results that are similar to those found in our study (8.5±5.8 minutes).[19] Shoji et al. evaluated 13,909 patients undergoing PCI in a prospective Japanese multicenter registry in order to compare the incidence of stroke in relation to the vascular access route. The fluoroscopy mean time was higher than that observed in our study (34.8±22.3 minutes in the stroke group, and 30.3±23.6 minutes in the group that did not present stroke, p=0.250); with an incidence rate of stroke of 0.3%. In this study, the use of the radial access was a predictor of stroke risk reduction (p=0.014).[13] In our study, the vascular access route and the fluoroscopy time had no impact on the occurrence of cerebrovascular events.

Unlike other publications, we found no case of in-hospital death or within 30 days of follow-up. A plausible explanation for this may be the fact that a considerable number of patients presented TIA as an event, associated with a less complex profile of patients, when compared with other more robust studies, which included only patients with MI and/or diabetes in their samples.[7,8,11,12,20] As in the in-hospital period, the 30-day follow-up of our sample indicated an incidence of mortality, sequelae, and functional impairment lower than that found in the current literature.[7,8,11-15,20] It is possible that the relatively high proportion of TIA in our population (compared to stroke) contributed to a better prognosis in our series.

The present study is a retrospective analysis of a single center, with a small number of cerebrovascular events, which limits the wide application of the data found. Cases of later manifestation or with subtle or subclinical manifestations may have been underdiagnosed, underestimating the occurrence of cerebrovascular events. Also, our study was limited to a 30-day clinical follow-up, and it was not possible to infer the later clinical course of the patients included in the study.[14,21]

CONCLUSION

The results of the study corroborate the current data available in the literature and show a low prevalence of periprocedural cerebrovascular events. There was no death due to a cerebrovascular event. The patients maintained good quality of life in their daily activities after the complication. We believe that the favorable in-hospital and late clinical course of these patients occurred due to early diagnosis, evaluation and multidisciplinary care, with a close interaction among interventional cardiology, neurology, radiology, and intensive care teams.

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None.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

CONTRIBUTION OF AUTHORS

Conception and design of the study: PAL, PEH, EER, GMA; data collection: FRF, BLRF, GGM, SZ; data interpretation: GFAPJ, FAP, CMC, PRS, GMA; writing of the text: PAL, AEF, GMA; approval of the final version to be published: PAL, GMA.

REFERENCES

1. Eggebrecht H, Oldenburg O, Dirsch O, Haude M, Baumgart D, Welge D, et al. Potential embolization by atherosclerotic debris dislodged from aortic wall during cardiac catheterization: histological and clinical findings in 7,621 patients. Catheter Cardiovasc Interv. 2000;49(4):389-94.
2. Hamon M, Baron JC, Viader F, Hamon M. Periprocedural stroke and cardiac catheterization. Circulation. 2008;118(6):678-83.
3. Karalis DG, Quinn V, Victor MF, Ross JJ, Polansky M, Spratt KA, et al. Risk of catheter-related emboli in patients with atherosclerotic debris in the thoracic aorta. Am Heart J. 1996;131(6):1149-55.
4. Keeley EC, Grines CL. Scraping of aortic debris by coronary guiding catheters: a prospective evaluation of 1,000 cases. J Am Coll Cardiol 1998;32(7):1861-5.
5. Braekken SK, Endresen K, Russell D, Brucher R, Kjekshus J. Influence of guidewire and catheter type on the frequency of cerebral microembolic signals during left heart catheterization. Am J Cardiol 1998;82(5):632-7.
6. Hoffman SJ, Routledge HC, Lennon RJ, Mustafa MZ, Rihal CS, Gersh BJ, et al. Procedural factors associated with percutaneous coronary intervention-related ischemic stroke. JACC Cardiovasc Interv. 2012;5(2):200-6.
7. Dukkipati S, O'Neill WW, Harjai KJ, Sanders WP, Deo D, Boura JA, et al. Characteristics of cerebrovascular accidents after percutaneous coronary interventions. J Am Coll Cardiol. 2004; 43(7):1161-7.
8. Akkerhuis KM, Deckers JW, Lincoff AM, Tcheng JE, Boersma E, Anderson K, et al. Risk of stroke associated with abciximab among patients undergoing percutaneous coronary intervention. JAMA. 2001;286(1):78-82.
9. Weintraub WS, Mahoney EM, Ghazzal ZM, King SB 3rd, Culler SD, Morris DC, et al. Trends in outcome and costs of coronary intervention in the 1990s. Am J Cardiol. 2001;88(5):497-503.
10. Brown DL, Topol EJ. Stroke complicating percutaneous coronary revascularization. Am J Cardiol. 1993;72(15):1207-9.
11. Werner N, Bauer T, Hochadel M, Zahn R, Weidinger F, Marco J, et al. Incidence and clinical impact of stroke complicating percutaneous coronary intervention: results of the Euro heart survey percutaneous coronary interventions registry. Circ Cardiovasc Interv. 2013;6(4):362-9.
12. Ahn KT, Seong SW, Choi UL, Jin SA, Kim JH, Lee JH, Choi SW, Jeong MH, Chae SC, Kim YJ, Kim CJ, Kim HS, Cho MC, Gwon HC, Jeong JO, Seong IW; Korea Acute Myocardial Infarction Registry - National Institute of Health (KAMIR-NIH) Investigators. Comparison of 1-year clinical outcomes between prasugrel and ticagrelor versus clopidogrel in type 2 diabetes patients with acute myocardial infarction underwent successful percutaneous coronary intervention. Medicine (Baltimore). 2019; 98(11):e14833.
13. Shoji S, Kohsaka S, Kumamaru H, Sawano M, Shiraishi Y, Ueda I, et al. Stroke After Percutaneous Coronary Intervention in the Era of Transradial Intervention. Circ Cardiovasc Interv. 2018;11(12):e006761.
14. Fuchs S, Stabile E, Kinnaird TD, Mintz GS, Gruberg L, Canos DA, et al. Stroke complicating percutaneous coronary interventions: incidence, predictors, and prognostic implications. Circulation. 2002;106(1):86-91.
15. Aggarwal A, Dai D, Rumsfeld JS, Klein LW, Roe MT; American College of Cardiology National Cardiovascular Data Registry. Incidence and predictors of stroke associated with percutaneous coronary intervention. Am J Cardiol. 2009;104(3):349-53.
16. Popovic B, Carillo S, Agrinier N, Christophe C, Selton-Suty C, Juillière Y, et al. Ischemic stroke associated with left cardiac catheterization: the importance of modifiable and non-modifiable risk factors. Am Heart J 2013;165(3):421-6.
17. Jolly SS, Cairns JA, Yusuf S, Rokoss MJ, Gao P, Meeks B, Kedev S, Stankovic G, Moreno R, Gershlick A, Chowdhary S, Lavi S, Niemela K, Bernat I, Cantor WJ, Cheema AN, Steg PG, Welsh RC, Sheth T3, Bertrand OF, Avezum A, Bhindi R, Natarajan MK, Horak D, Leung RC, Kassam S, Rao SV, El-Omar M, Mehta SR, Velianou JL, Pancholy S, Džavík V; TOTAL Investigators. Outcomes after thrombus aspiration for ST elevation myocardial infarction: 1-year follow-up of the prospective randomised TOTAL trial. Lancet. 2016;387(10014):127-35.
18. Georges JL, Belle L, Meunier L, Dechery T, Khalifé K, Pecheux M, Elhaddad S, Amabile N, Pansieri M, Ballout J, Marchand X, Rouault G, Leddet P, Nugue O, Lucke N, Cattan S; RAY'ACT Investigators. Radial versus femoral access for coronary angiography and intervention is associated with lower patient radiation exposure in high-radial-volume centres: Insights from the RAY'ACT-1 study. Arch Cardiovasc Dis. 2017;110(3):179-87.
19. Adachi Y, Sakakura K, Wada H, Funayama H, Umemoto T, Momomura S, et al. Predictors of prolonged fluoroscopy time in diagnostic coronary angiography. J Cardiol. 2016;68(1):37-42.
20. Wong SC, Minutello R, Hong MK. Neurological complications following percutaneous coronary interventions (a report from the 2000-2001 New York State Angioplasty Registry). Am J Cardiol. 2005;96(9):1248-50.
21. Hoffman SJ, Holmes DR Jr, Rabinstein AA, Rihal CS, Gersh BJ, Lennon RJ, et al. Trends, predictors, and outcomes of cerebrovascular events related to percutaneous coronary intervention: A 16-year single-center experience. JACC Cardiovasc Interv. 2011;4(4): 415-22.