

Peripheral arterial disease as a risk factor for atrial fibrillation in the postoperative period of myocardial revascularization: a retrospective cohort study

Doença arterial periférica como fator de risco para fibrilação atrial no período pós-operatório de cirurgia de revascularização do miocárdio: um estudo de coorte retrospectivo

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ABSTRACT

Introduction: Postoperative atrial fibrillation (POAF) is the most common complication of myocardial revascularization surgery, associated with predisposing factors and outcomes such as increased hospital stay, higher stroke and mortality rates. The objective of this study is to estimate the incidence of POAF and associated factors and outcomes, with emphasis on peripheral arterial disease. **Methods:** A retrospective cohort study was carried out involving adult patients admitted to the intensive care unit in the immediate postoperative period of myocardial revascularization surgery in a private hospital in South Brazil. Sociodemographic data, comorbidities, hospital and intensive care unit stay, occurrence of stroke and death were collected. Multivariate analyses were performed to identify independent relationships between variables using Poisson Regression with a robust estimator. Relative risks and 95% confidence intervals were estimated. **Results:** A total of 421 patients were included. The incidence of POAF was 23.8% (100 patients), statistically and independently associated with patient's older age ($p < 0.001$), with systemic arterial hypertension ($p < 0.001$) and with peripheral arterial disease ($p < 0.001$). Increased incidence of POAF was also associated with increased hospital and intensive care unit length of stay. **Conclusion:** A higher incidence of POAF after myocardial revascularization was associated with peripheral arterial disease, older age, and systemic arterial hypertension.

Keywords: Atrial Fibrillation. Arrhythmias, Cardiac. Myocardial Revascularization. Perioperative Care.

INTRODUCTION

Postoperative atrial fibrillation (POAF) represents the most common complication of coronary artery bypass (CABG) with incidence rates ranging from 10 to 47%¹⁻⁸. It is a relevant condition as it is associated with increased mortality and hospital length of stay and costs^{2,9-12}. Previously considered benign and self-limiting^{3,13,14}, growing evidence indicates that POAF is associated with unfavorable clinical outcomes^{1,3,5,6,15,16} and higher rates of long-term complications, such as late recurrence events related to atrial fibrillation (AF), heart failure hospitalization and mortality^{17,18}.

In general, AF is the arrhythmia with the highest incidence and prevalence in clinical practice

worldwide and it is estimated that its prevalence will continue to grow in the coming decades^{19,20}.

Potential risk factors and their impact on hospital stay, costs and clinical complications have been addressed with CABG. Older age, male gender, use and duration of cardiopulmonary bypass, previous suspension of adrenergic beta-blockers and other drugs are normally pointed out as indicators of increased risk^{1,10,11,21-26}, some (such as age and gender) coinciding with those of AF unrelated to CABG^{19,20}. In this context, peripheral arterial disease (PAD) was evaluated as a potential risk factor for POAF in this cohort.

Furthermore, pharmacological and non-pharmacological measures that can reduce the incidence of POAF have been investigated²⁵⁻²⁸. Antiarrhythmic

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drugs, such as amiodarone and beta-blockers, administered prior to the procedure showed promising results^{25,27,28} and other measures such as atrial artificial stimulation in the immediate postoperative period were tested, showing a reduction in AF^{28,29}. However, there is still no consensus and medical societies present different recommendations regarding prophylactic measures^{4,30}.

Likewise, recommendations related to the prevention and treatment of POAF are also not consistent, neither are those regarding anticoagulants used to prevent embolic events^{4,30,31}. Furthermore, even though the use of anticoagulants is included in the American Guidelines, for example, it is not yet systematically applied³².

Prophylaxis and treatment recommendations differ from each other. In addition, they are not stratified and individualized according to disease severity or other criteria; in theory they should be consistently applied to all patients^{4,30}.

The objective of this study was to estimate the incidence of POAF after CABG, associated factors and its impact in relation to the length of stay in the intensive care unit (ICU) and in the hospital, besides hospital mortality and incidence of ischemic stroke

METHODS

This study was a retrospective longitudinal cohort investigation. The study period ranged from January 2017 to June 2023. The investigation was conducted in a reference hospital for cardiovascular diseases in Florianópolis, Santa Catarina, Brazil. The study population consisted of all patients of both sexes admitted to the ICU after CABG during the study period, totaling 421 individuals. Because the study adopted a census approach, including all eligible patients with available medical records within the defined time frame, no a priori sample size calculation was performed. Those undergoing combined surgeries (CABG with repair or valve replacement, with correction of aortic aneurysm, with left ventricular aneurysmectomy and correction of ventricular septal defect) and patients with a previous record of AF (medical record or use of anticoagulants without another reason) were excluded

The data were obtained through the review of the digital medical records in use at the hospital

(Phillips Tasy health management system™, Delphi version 3.07.1820.04) and entered into an entered into a Microsoft Excel™ spreadsheet using a research instrument designed for this study. Data were collected by a single investigator.

Sociodemographic, anthropometric information, comorbidities, length of stay in hospital and ICU, postoperative stroke, death, as well as information on the occurrence of POAF were collected.

Recording the occurrence of AF in patients was the dependent variable when analyzing potential factors associated with its incidence. Otherwise, in case of death, stroke and length of hospital and ICU stay were reviewed and AF was considered as an independent variable.

To collect data for the detection of AF, medical records were initially evaluated in search of information about their occurrence. If AF had been entered in the medical records, the variable was considered to exist. In the hypothesis of this first assessment of the medical records failure, a second way of detecting arrhythmia was used: the indication to control the rhythm with intravenous amiodarone, which is routine in the service in cases of AF in the postoperative period. This information was obtained by surveying patients who used the medication during the period of hospitalization with the date of prescription and dispensation. With these data in hand, we checked whether the information about arrhythmia occurrence had already been detected in the first evaluation of the medical records. In the case of patients who had a record of intravenous amiodarone use and there was no such indication in the first evaluation, the medical record was reevaluated focusing on the date of prescription and use of the medication for a new search for the AF record, since the drug could have been used possibly for another indication.

Missing data were handled using complete-case analysis for each model; denominators are provided in the tables. Missingness was minimal.

To reduce selection bias, we included all consecutive eligible patients undergoing isolated CABG during the study period. To minimize outcome misclassification, POAF was ascertained using a two-step strategy (medical record documentation and, when absent, verification through intravenous amiodarone

use followed by targeted record review). Potential confounding was addressed using multivariable modeling as described below.

Age and gender were recorded in the electronic medical records for all participants. The body mass index (BMI) was calculated using data reported in the medical records. Previous systemic arterial hypertension (SAH) was identified based on two possible sources of information (or both): if a record of comorbidity was available upon admission on medical evolution; and/or if the patient had a record of antihypertensive medications use. Previous diabetes mellitus (DM) diagnosis was confirmed when these same criteria were met. Heart failure was considered existing if recorded in the medical records. Smoking was considered if the patients maintained the habit in the 90 days prior to surgery. Previous stroke was considered if recorded in the medical records. Peripheral arterial disease (PAD) was acknowledged if there was a record of previous vascular surgery (lower limb revascularization) or if there was an examination with ultrasound Doppler confirming an atherosclerotic lesion with stenosis >50% in lower limb arteries. The cardiopulmonary bypass time (in minutes) was also collected from the records, this being the surgical description. Lengths of stay were obtained using the Tasy system™. The occurrence of stroke in the postoperative period was obtained from the medical evolution from hospitalization to the final outcome including hospital death.

Descriptive statistics were performed for the variables studied using frequency distribution tables and measures of central tendency and dispersion for quantitative variables. Bivariate analysis was performed using the chi-square test to assess the association between categorical variables and the occurrence of POAF. The significance level was set at $p < 0.05$. Variables presenting p -values ≤ 0.20 in the bivariate analysis

were included in the multivariable model. Multivariate analysis was performed using Poisson regression with robust variance to estimate adjusted relative risks and their respective 95% confidence intervals (95% CI). This modeling strategy allowed the identification of independent associations between the variables studied and the occurrence of POAF, as well as adjustment for potential confounding factors.

All statistical analyses were performed using SPSS Statistics for Windows™, version 18.0 (SPSS Inc., Chicago, IL, USA).

The present study was submitted and approved by the Human Research Ethics Committee of the Universidade do Sul de Santa Catarina (UNISUL) under number 6,266,496 (CAEE: 71168823.5.0000.0261).

RESULTS

The investigation included adult patients admitted to the ICU of a private hospital after CABG. A total of 421 patients who had undergone the procedure between January 2017 and the end of June 2023 were included. Out of this sample, 80.8% were men aged 64.1 years (SD=9.6), while women's mean age was 67.0 years (SD=8.8) ($p=0.014$). The population median age was 65 years.

The incidence of POAF was 23.8% (95% CI 19.8; 27.8), that is, 100 cases (Table 1). Previous SAH was reported in 74.2% of patients, while PAD in 17.6%; DM was reported in 38.7% of patients, and previous insulin use in 9.5%. The average BMI of the sample was 28.9 kg/m² (SD=4.2) and the median was 27.6. The mean cardiopulmonary bypass time was 77 minutes (SD=24) and the median 76 minutes. The incidence of POAF was statistically associated with age over 65 years ($p < 0.001$), SAH ($p < 0.001$), PAD ($p < 0.001$) and previous insulin use ($p=0.032$) (Table 1).

Table 1 - Association between preoperative and perioperative variables and incidence of AF (n=421).

Variables	Atrial Fibrillation			p-value
	Yes n (%)	No n (%)	Total n (%)	
Gender				0,609
Male	79 (23.2)	261 (76.8)	340 (80.8)	
Female	21 (25.9)	60 (74.1)	81 (19.2)	

Variables	No			p-value
	Yes n (%)	No n (%)	Total n (%)	
Age in years (median)				<0.001
Up to 65	33 (16.2)	171 (83.8)	204 (48.4)	
Over 65	67 (30.9)	150 (69.1)	217 (51.6)	
Nutritional status				0.785
Eutrophic	19 (22.6)	65 (77.4)	84 (19.5)	
Overweight	81 (24.0)	256 (76.0)	337 (80.5)	
Active smoking				0.511
No	85 (23.2)	281 (76.8)	366 (86.9)	
Yes	15 (27.3)	40 (72.2)	55 (13.1)	
Systemic arterial hypertension				<0.001
No	12 (11.1)	96 (88.9)	108 (25.7)	
Yes	88 (28.1)	225 (71.9)	313 (74.3)	
Diabetes mellitus				0.440
No	58 (22.5)	200 (77.5)	258 (61.3)	
Yes	42 (25.8)	121 (74.2)	163 (38.7)	
Previous acute myocardial infarction				0.905
No	77 (23.6)	249 (76.4)	326 (77.4)	
Yes	23 (24.2)	72 (75.8)	95 (22.6)	
Previous stroke				0.375
No	95 (23.4)	311 (76.6)	406 (96.4)	
Yes	5 (33.3)	10 (66.7)	15 (3.6)	
Peripheral arterial disease				<0.001
No	70 (20.2)	277 (79.8)	347 (82.4)	
Yes	30 (40.5)	44 (59.4)	74 (17.6)	
Beta-blocker use				0.874
No	52 (24.1)	164 (75.9)	216 (51.3)	
Yes	48 (23.4)	157 (76.6)	205 (48.7)	
Insulin use (n=420)				0.032
No	85 (22.4)	295 (72.6)	380 (90.5)	
Yes	15 (37.5)	25 (62.5)	40 (9.5)	
Extracorporeal circulation time in minutes (median) (n=417)				0.547
Up to 76	52 (25.0)	156 (75.0)	208 (49.9)	
Over 76	47 (22.5)	162 (77.5)	209 (50.1)	

The results of the multivariate analysis showed that age, SAH and PAD were independently statistically associated with a higher incidence of AF. Patients over 65 years of age (sample median) showed a 7% higher incidence of AF [RR= 1.07 (95% CI 1.02; 1.12) p=0.005] compared to patients up to 65 years of age. Patients with a previous diagnosis of SAH had an 8% higher incidence of AF [RR= 1.08 (95% CI 1.03; 1.13) p<0.001] compared to those without, while patients with PAD

revealed a 10% higher AF incidence [RR= 1.10 (95% CI 1.02; 1.18) p=0.003] compared to those without. Previous insulin use was not independently associated with AF (Table 2).

It was also observed that the occurrence of AF increased 20% the risk of a longer hospital stay (>8 days) [RR= 1.20 (95% CI 1.11; 1.30) p<0.001] and 35% longer ICU stay (>4 days) [RR= 1.35 (95% CI 1.26; 1.46) p<0.001] (Table 3).

Table 2 - Results of multivariate analysis. Preoperative variables and incidence of AF.

Variables	RRc	95% CI	p-value	RRa	95% CI	p-value
Age in years (median)			<0.001			0.005
Up to 65	1.00			1.00		
Over 65	1.09	1.04; 1.14		1.07	1.02; 1.12	
Systemic arterial hypertension			<0.001			<0.001
No	1.00			1.00		
Yes	1.10	1.05; 1.15		1.08	1.03; 1.13	
Peripheral arterial disease			<0.001			0.003
No	1.00			1.00		
Yes	1.13	1.05; 1.21		1.10	1.02; 1.18	
Insulin use			0.032			0.192
No	1.00			1.00		
Yes	1.09	1.01; 1.20		1.06	0.97; 1.16	

RRc - crude relative risk; RRa - adjusted relative risk. Omnibus test: chi-square 3.496; degrees of freedom: 4; p=0.478.

Table 3 - Association between the occurrence of AF and different outcomes (n=421).

Variable	Length of hospital stay (> 8 days*)		ICU length of stay (> 4 days*)		Stroke		Death	
	RR (95% CI)	p	RR (95% CI)	p	RR (95% CI)	p	RR (95% CI)	p
Atrial fibrillation	1.20 1.11; 1.30	<0.001	1.35 1.26; 1.46	<0.001	1.01 0.99; 1.03	0.179	1.01 0.99; 1.03	0.179

*Median. RR - relative risk.

Five cases of postoperative ischemic stroke (1.2%) were reported. In the AF group, the incidence of this condition was 3%, compared to 0.6% in the group without AF (p=0.179). A total of five deaths occurred (1.2%). In the AF group of patients, mortality was 3%, compared to 0.6% in the group without AF (p=0.179).

DISCUSSION

Our study showed 23.8% POAF incidence, corroborating recent literature, although different incidences ranging between 10 and 47% have been observed¹⁻⁸. In order to determine the actual incidence of POAF and assuming that the data collection methodology used justifies the divergent results, a double checking

procedure was adopted consisting in evaluating the patient's electronic medical record and a second evaluation if the patient showed signs of translated rhythm control (intravenous amiodarone).

POAF incidence was similar in men (23.2%) and women (25.9%). In the literature, males are associated with significantly more cases of AF, which is considered a risk factor^{2,3,7,9,25,26,31,33}, as in non-surgery AF^{19,20}. In this study, this was not observed, which is consistent with findings reported in a systematic review and meta-analysis⁵ and by Veen et al³⁴. A possible reason may be associated with the fact that women in our study were on average older than men, with older age being another variable strongly associated with a higher AF incidence as shown in the literature and also in this study^{3,5-9,21,25,26,30,33}.

Previous suspension of beta-blocker administration was not associated with a higher incidence of AF, a factor mentioned in some papers^{4,25,26,35}. The practice adopted in the study center of always resuming beta-blocker use the soonest (often the day after surgery) may explain this finding. This also enhances the implementation of the prescription already suggested in some guidelines, but not systematically used^{4,25,30}.

In our study cardiopulmonary bypass time was very similar in the groups with and without AF. This information is not consistent in the literature though^{21,24-36,35}.

Previous SAH diagnosis was associated with a higher incidence of AF, in line with the findings in the literature^{2,5,8,23,25,26,33,37}. The prevalence was quite high, enhancing the relevance from a clinical standpoint and justifying further studies with greater stratification of patients in relation to severity and to the use of certain antihypertensive medications.

DM diagnosis was not associated with a higher incidence of AF, but previous insulin use showed an initial association, but lost statistical significance when subjected to multivariate analysis. The study of the relationship between DM and the use of insulin deserves further study on the stratification of severity and duration of the disease as it represents a correlation with systemic inflammation and unfavorable outcomes in different scenarios^{7,25,33,37}.

Active smoking in this study was not associated with AF, unlike evidence in the literature^{2,3,7,8,26}. Smoking is one of the main factors in the development of coronary disease and AF in general^{20,38}. The non-association found can be explained by the number of active smokers of only 13.1%, as well as by the adoption of the current prescription to suspend smoking in the preoperative period as a way of avoiding complications³⁹.

Previous diagnosis of PAD was strongly associated with the incidence of AF, corroborating the literature available^{2,8}. Furthermore, severe PAD may be directly associated with the higher incidence of AF⁴⁰. Therefore, one must consider the possibility that its presence reflects greater complexity and severity, and this hypothesis could be reinforced by the fact that in CABG prognostic, the prevalence of PAD correlates

with a higher risk of mortality³⁸⁻⁴⁰. There is also growing evidence that AF has an increased incidence prediction with higher scores in other conditions, also influenced by the PAD presence²³.

The duration of postoperative ICU and hospital stay until discharge was significantly increased in AF patients. This finding is similar to that of most studies and causes an increase in healthcare costs^{4-6,9-12,31}.

In our study overall mortality was 1.2% (5 patients), the same as the occurrence of stroke in another group of patients. The literature, including meta-analyses, has shown that AF and stroke are associated with higher mortality^{2,5,6,15,16,30}, although in the present study this did not occur as both conditions occurred in 3% of the AF group vs. 0.6% in the control group. Hypothetically, we can assume that the low incidence of these outcomes is associated with an insufficient sample size for this specific assessment. Therefore, the continuation of the study and this specific evaluation are justified because POAF, previously interpreted as benign^{13,14}, has a different meaning. POAF already has an established association with a worse long-term prognosis (mortality and late stroke), as recent studies have pointed out^{1,3,6,8,15,16}.

Further discussion is needed to clarify the role of AF in this context to obtain a better clarification. It is debatable whether AF merely represents a marker of severity or whether it causes complications and unfavorable outcomes¹⁸.

Considering the relevance of SAH as a factor associated with AF higher incidence, this study has the limitation of not recording the severity and duration of the disease, medications and doses previously used, as well as whether the control was adequate. The drugs used were indicated, but the precise doses for each patient were only entered in the documents during the last two years and these data were not collected.

The diagnosis of SAH was considered assertive if a record was found and/or if a prescribed or in use antihypertensive drug was mentioned. The only class of antihypertensives that was specifically entered was beta-blockers, as this was one of the independent variables. These limitations justify improving the evaluation to clarify implications of the mechanisms in genesis of POAF, risk stratification according to the severity and

control of the disease, and also of its actual prognostic implications.

Another possible limitation is related to the collection of retrospective data, making it impossible to verify the duration of the arrhythmia. These data are difficult to obtain and would require prospective and continuous assessment with electrocardiographic recording of the entry and exit of the AF rhythm.

In addition, some methodological aspects should be considered when interpreting the findings. Although the study included all eligible patients undergoing isolated CABG during the study period, the relatively low frequency of certain outcomes, such as stroke and death, may have limited the statistical power to detect associations with these events. Furthermore, as the investigation was conducted in a single reference hospital, caution is warranted when

generalizing the results to other settings or populations. Despite these limitations, the study provides relevant evidence on the incidence of postoperative atrial fibrillation and its associated factors in patients undergoing CABG.

CONCLUSION

It can be concluded that the incidence of POAF after CABG was 23.8%, statistically independently associated with older age, SAH and PAD. The occurrence of AF was associated with increased hospital and ICU length of stay. The study offers additional information to clarify the role of this complication in CABG. The actual meaning of AF still remains to be clarified, whether it causes unfavorable outcomes or is a mere marker of severity.

R E S U M O

Introdução: A fibrilação atrial pós-operatória (FAPO) é a complicação mais comum da cirurgia de revascularização miocárdica, sendo associada a fatores predisponentes e a desfechos como aumento do tempo de internação hospitalar, maiores taxas de acidente vascular encefálico e mortalidade. O objetivo deste estudo é estimar a incidência de FAPO e os fatores e desfechos associados, com ênfase na doença arterial periférica. **Métodos:** Foi realizado um estudo de coorte retrospectivo, envolvendo pacientes adultos admitidos na unidade de terapia intensiva no período pós-operatório imediato de cirurgia de revascularização miocárdica em um hospital privado da região sul do Brasil. Foram coletados dados sociodemográficos, comorbidades, tempo de internação hospitalar e em unidade de terapia intensiva, ocorrência de acidente vascular encefálico e óbito. Análises multivariadas foram realizadas para identificar relações independentes entre as variáveis, utilizando regressão de Poisson com estimador robusto. Os riscos relativos e os intervalos de confiança de 95% foram estimados. **Resultados:** 421 pacientes foram incluídos. A incidência de FAPO foi de 23,8% (100 pacientes), associada de forma estatisticamente significativa e independente à maior idade do paciente ($p<0,001$), à hipertensão arterial sistêmica ($p<0,001$) e à doença arterial periférica ($p<0,001$). O aumento da incidência de FAPO também foi associado ao maior tempo de internação hospitalar e em unidade de terapia intensiva. **Conclusão:** A maior incidência de FAPO após revascularização miocárdica foi associada à doença arterial periférica, maior idade e hipertensão arterial sistêmica.

Palavras-chave: Fibrilação Atrial. Arritmias Cardíacas. Revascularização Miocárdica. Cuidados Perioperatórios.

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