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Analysis of patients submitted to percutaneous coronary intervention via radial artery access. The SAFIRA Registry database

Análise dos pacientes submetidos à intervenção coronária
percutânea por via radial. Dados do Registro SAFIRA

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ABSTRACT – Background: The choice of the radial access for performing percutaneous coronary interventions has grown due to evidence of the greater benefits of the technique, such as reduced vascular complications, lower bleeding rates, early ambulation, shorter hospital stay and lower costs. The present study aimed to analyze patients submitted to percutaneous coronary intervention using the radial access in comparison to the femoral artery access in elective cases or in acute coronary syndromes. **Methods:** An observational, single center study based on the SAFIRA registry database, which includes patients undergoing percutaneous coronary intervention with drug-eluting stents. The primary endpoint was the incidence of cardiovascular mortality in a 3-year follow-up. **Results:** A total of 2,453 patients were included, 1,237 of which allocated to the radial group and 1,216 to the femoral group. The prevalence of vascular complications was higher in the femoral group (OR: 15.4; $p=0.008$), as was the contrast volume used (OR: 1.001; $p=0.02$). The primary endpoint of cardiovascular mortality in the femoral group was 4.5% vs. 2.3% in the radial group (RR: 1.77; $p<0.01$). All-cause mortality rates (10.2% vs. 7.4%, RR: 1.37; $p=0.03$) and major adverse cardiac event rates (12.2% vs. 8.9%, RR: 1; 36; $p<0.01$) were also higher in the femoral group. When adjusted for relevant clinical variables, the femoral access remained as an independent predictor of cardiovascular mortality. **Conclusions:** Radial access was effective in reducing mortality, major adverse cardiac events and vascular complications among patients undergoing percutaneous coronary intervention.

Descriptors: Percutaneous coronary intervention; Radial artery; Femoral artery.

RESUMO – Introdução: A escolha da via radial para realização de intervenções coronárias percutâneas vem crescendo devido a evidências de maior benefício desta técnica, como redução de complicações vasculares, menores taxas de sangramento, deambulação precoce, menor tempo de internação hospitalar e custos mais baixos. O presente estudo objetivou analisar pacientes submetidos à intervenção coronária percutânea pela via radial, em comparação com a via femoral, em casos eletivos ou no cenário das síndromes coronárias agudas. **Métodos:** Trata-se de estudo observacional, unicêntrico, baseado no banco de dados do registro SAFIRA, que compreende pacientes submetidos à intervenção coronária percutânea com uso de stents farmacológicos. O desfecho primário analisado foi a incidência de mortalidade cardiovascular em 3 anos de seguimento. **Resultados:** Foram incluídos 2.453 pacientes, sendo 1.237 no grupo radial e 1.216 no grupo femoral. A prevalência de complicações vasculares foi maior no grupo femoral (RC: 15,4; $p=0,008$), assim como o volume de contraste utilizado (RC: 1,001; $p=0,02$). O desfecho primário de mortalidade cardiovascular no grupo femoral foi de 4,5% vs. 2,3% no grupo radial (RR: 1,77; $p<0,01$). As taxas de mortalidade geral (10,2% vs. 7,4%; RR: 1,37; $p=0,03$) e de eventos cardíacos adversos maiores (12,2% vs. 8,9%; RR: 1,36; $p<0,01$) também foram maiores no grupo femoral. Quando ajustado para variáveis clínicas relevantes, o acesso femoral se manteve como preditor independente de mortalidade cardiovascular. **Conclusões:** O acesso radial mostrou-se eficaz na redução de mortalidade, eventos cardíacos adversos maiores e complicações vasculares entre pacientes submetidos à intervenção coronária percutânea.

Palavras-chave: Intervenção coronária percutânea; Artéria radial; Artéria femoral.

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INTRODUCTION

The radial artery access for percutaneous coronary intervention (PCI) began to be used in 1992.^{1,2} Among its advantages are the anatomical location for puncture, easy compression, early removal of the introducer, lower risk of vascular complications and earlier ambulation.^{3,4} Recent studies have shown reduction in mortality with the use of the radial artery access in patients presenting acute coronary syndrome.^{5,6} The benefit is due to the reduction in hemorrhagic complications, since the need for effective antithrombotic therapy is greater in the acute scenario, increasing the risk of bleeding, which impacts the mortality of this population directly.⁷⁻⁹

The aim of the present study was to analyze patients submitted to PCI via radial access and compare it to femoral access patients, regarding all clinical presentations of coronary atherosclerotic disease.

METHODS

This is an observational, single center study, based on data from the Safety and Efficacy of Pharmacological Stents in a Real World Population registry (SAFIRA, <http://www.scielo.br/pdf/rbci/v22n1/0104-1843-rbci-22-01-0023.pdf>), which included consecutive patients that underwent PCI with drug-eluting stents, from July 2002 to August 2016. PCIs were performed according to the current recommendations and the vascular access was defined according to the clinical characteristics of patients, operator preference and arterial pulse amplitude.

The primary endpoint was cardiovascular mortality during a 3-year follow-up. Secondary endpoints analyzed were the following: all-cause mortality, acute myocardial infarction (MI), major adverse cardiac events (MACE), vascular complications, and volume of contrast. MACE comprised cardiovascular mortality, non-fatal acute MI or target vessel revascularization. Vascular complications included dissection, limb ischemia, compartment syndrome, pseudoaneurysm, arteriovenous fistula, or retroperitoneal hematoma. All deaths were considered cardiac, unless a non-cardiac cause could be clearly established. Acute MI was diagnosed by proven abnormal blood levels of myocardial necrosis markers (creatinine kinase - CKMB or troponin).

Data collection was performed using the SAFIRA Registry database, at the *Hospital Beneficência Portuguesa de São Paulo*, after approval by the Research Ethics Committee (protocol 778-12; CAEE: 00771112.9.0000.5483). All patients included in the study signed the Informed Consent Form. Clinical follow-up was performed by office consultation or telephone calls at 30 days, 6 and 12 months, and thereafter annually.

Statistical analysis

Categorical variables were expressed as absolute frequency and percentages, and compared using the Chi-square test.

Continuous variables were presented as mean and standard deviation and compared with Student's *t* test. Cumulative event-free survival curves were estimated by the Kaplan-Meier method and compared by the log-rank test.

The multivariate Cox regression model included clinical variables that reached statistical significance in the univariate analysis ($p < 0.05$). Interaction testing was used to investigate the potential impact of the clinical presentation (chronic vs. acute) at the primary endpoint. The proportional hazard hypothesis was tested using the Schoenfeld residuals test. A p -value < 0.05 was considered significant. Statistical analysis was performed using the STATA 14 software package (StataCorp LP, USA).

RESULTS

A total of 2,453 patients were included, 1,237 in the radial group and 1,216 in the femoral group. The femoral group had a higher percentage of female patients (34.0% vs. 23.0%; $p < 0.001$), a higher prevalence of chronic renal failure (9.9% vs. 6.7%; $p < 0.01$), and of previous percutaneous or surgical coronary artery bypass graft (CABG) (20.0% vs. 16.0%, $p = 0.01$, and 22.0% vs. 10.0%; $p < 0.01$, respectively). A higher prevalence of patients with ST-elevation myocardial infarction (STEMI) in the group of patients treated through radial access (3.5% vs. 1.9%) was observed. Since the radial technique was introduced more recently, there was a higher rate of use of second-generation drug-eluting stents and new antiplatelet agents, such as prasugrel and ticagrelor (90.1% vs. 55.4%; $p < 0.01$, and 10.8% vs. 6.7%; $p < 0.01$, respectively) in this group. Baseline clinical characteristics and procedures are shown in Tables 1 and 2.

The crossover rate between vascular accesses was 4.0% in the radial group and 0.5% in the femoral group. Vascular complications were more frequent (1.2% vs. 0.1%; OR: 15.4; $p = 0.008$) and the contrast volume was higher (136.0 ± 2.4 mL vs. 129.0 ± 1.2 mL; OR: 1.001; 95%CI, 1.001-1.003; $p = 0.02$) in the femoral group. The incidence of the primary endpoint, cardiovascular mortality, at 3 years was higher in the femoral group (4.5% vs. 2.3%; RR: 1.77; $p < 0.01$), as well as all-cause mortality (10.2% vs. 7.4%; RR: 1.37; $p = 0.03$) (Figures 1 and 2). There was also a higher incidence of MACE in the femoral group (12.2% vs. 8.9%; RR: 1.36; $p < 0.01$) (Figure 3). There was no difference between the groups regarding acute MI rates (3.2% vs. 2.5%; RR: 0.91; $p = 0.65$) (Table 3).

When adjusted for clinical variables that showed statistical significance in the univariate analysis (Table 4), femoral access remained an independent predictor of cardiovascular mortality, but it was no longer a predictor for all-cause mortality and MACE (Table 5). The clinical presentation did not alter the relation between type of vascular access and cardiovascular mortality (interaction $p = 0.94$), indicating a significant benefit for using the radial access, both for stable clinical presentation and ACS.

Table 1. Baseline clinical characteristics

Parameter	Radial (n=1,237)	Femoral (n=1,216)	p-value
Age, years	63.6±11.2	64.2±11.6	0.19
Male	954 (77.1)	805 (66.2)	<0.001
Diabetes mellitus	422 (34.1)	409 (33.6)	0.80
Chronic renal failure	83 (6.7)	120 (9.9)	0.005
Smoking	207 (16.7)	181 (14.9)	0.21
Hypertension	977 (79.0)	987 (81.2)	0.18
Dyslipidemia	804 (65.0)	805 (66.2)	0.53
COPD	20 (1.6)	15 (1.2)	0.42
Previous stroke	33 (2.7)	23 (1.9)	0.20
Peripheral arterial disease	18 (1.5)	29 (2.4)	0.09
Previous PCI	197 (15.9)	242 (19.9)	0.01
Previous CABG	128 (10.3)	264 (21.7)	<0.001
Clinical presentation			0.02
Stable angina	958 (77.4)	931 (76.6)	
NSTE-ACS	236 (19.1)	262 (21.5)	
STEMI	43 (3.5)	23 (1.9)	

Results expressed by mean ± standard deviation and n (%). COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft surgery; NSTE-ACS: non-ST elevation acute coronary syndrome; STEMI: ST-elevation myocardial infarction.

Table 2. Clinical presentation and procedure characteristics

Clinical presentation and procedure characteristics	Radial (n=1,237)	Femoral (n=1,216)	p-value
Lesion classification (AHA/ACC)			
Type A/B ₁	567 (45.8)	534 (43.9)	0.34
Type B ₂	318 (25.7)	380 (31.2)	0.002
Type C	572 (46.2)	561 (46.1)	0.96
In-stent restenosis	59 (4.8)	75 (6.2)	0.13
Bifurcation lesions	122 (9.9)	136 (11.2)	0.29
Stent diameter, mm			
<3.0	580 (38.7)	533 (36.1)	0.13
3.0	575 (38.3)	652 (44.1)	<0.001
3.5	299 (20.0)	264 (17.9)	0.15
>3.5	44 (3.0)	28 (1.9)	0.66
Vessels with ≥50% stenosis			
Left main coronary artery	30 (2.4)	39 (3.2)	0.24
Left anterior descending artery	854 (52.7)	420 (50.5)	0.32
Right coronary artery	382 (30.9)	382 (31.4)	0.78
Left circumflex artery	422 (34.1)	393 (32.3)	0.35
Diagonal branch	70 (5.7)	72 (5.9)	0.78
First generation DES	122 (9.9)	542 (44.6)	<0.001
Second generation DES	1,115 (90.1)	674 (55.4)	<0.001
ASA	1,219 (98.5)	1,198 (98.5)	0.96
Clopidogrel	1,104 (89.2)	1,135 (93.3)	<0.001
Prasugrel or ticagrelor	133 (10.8)	81 (6.7)	<0.001
GP IIb/IIIa inhibitors	13 (1.1)	24 (2.0)	0.61

Results expressed by n (%). AHA/ACC: American Heart Association/American College of Cardiology; DES: drug-eluting stents; ASA: acetylsalicylic acid; GP: glycoprotein.

Figure 1. Kaplan-Meier curve for cardiovascular death stratified by vascular access. **Figure 2.** Kaplan-Meier curve for all-cause death stratified by vascular access. **Figure 3.** Kaplan-Meier curve for major adverse cardiac events stratified by vascular access.

Table 3. Clinical endpoints according to vascular access after 3 years

Endpoint	Femoral	Radial	RR	95%CI	p-value
Cardiovascular deaths	4.5	2.3	1.77	1.39-2.90	<0.01
MI	3.2	2.5	0.91	0.62-1.35	0.65
MACE	12.2	8.9	1.36	1.17-2.66	<0.01
All-cause deaths	10.2	7.4	1.37	1.02-1.58	0.03

Results expressed as %. RR: relative risk; 95%CI: 95% confidence interval; MI: myocardial infarction; MACE: major adverse cardiac events.

Table 4. Univariate analysis for cardiovascular mortality

Variable	RR	95%CI	p-value
Age	1.04	1.02-1.06	<0.001
Male	0.64	0.44-0.93	0.02
Diabetes mellitus	1.97	1.37-2.85	<0.001
Hypertension	1.77	1.02-3.05	0.04
Chronic renal failure	3.16	1.92-5.21	<0.001
NSTE-ACS	1.54	1.02-2.29	0.04
STEMI	1.60	0.51-5.07	0.42
COPD	1.00	0.25-4.03	0.99
Dyslipidemia	1.03	0.70-1.52	0.87
Previous stroke	2.15	0.79-5.85	0.13
Peripheral arterial disease	4.41	2.23-8.72	<0.001
Previous PCI	1.52	1.03-2.33	0.05
Previous CABG	2.01	1.33-3.02	0.001
First generation drug-eluting stents	1.15	0.76-1.72	0.50
Stent <3.0mm	1.14	0.76-1.61	0.57
Type C lesion	1.12	0.78-1.63	0.51

RR: relative risk; 95%CI: 95% confidence interval; NSTE-ACS: non-ST elevation acute coronary syndrome; STEMI: acute myocardial infarction with ST elevation; COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft surgery.

Table 5. Multivariate analysis for clinical events

Outcome	RR	95%CI	p-value
Cardiovascular death	1.52	1.01-2.29	0.05
Acute MI	0.83	0.56-1.24	0.38
MACE	1.22	0.98-1.53	0.07
All-cause death	1.15	1.92-1.44	0.21

RR: relative risk; 95%CI: 95% confidence interval; MI: myocardial infarction; MACE: major adverse cardiac events.

DISCUSSION

The present study has shown that the radial artery access reduced cardiovascular mortality rate, regardless of clinical presentation, showing a positive impact, both in the ACS scenario and for patients with stable coronary artery disease. We also observed the radial vascular access to be safer, with reduction in vascular complications and total contrast volume.

Radial artery access has been consolidated as the preferred option in patients submitted to PCI in recent years. Since the introduction of the technique, the development and improvement of materials, associated with the greater operator's experience, have made its results as effective as other vascular accesses (femoral puncture and brachial dissection).^{10,11}

The RIFLE (Radial Versus Femoral Randomized Investigation in ST-Elevation Acute Coronary Syndrome) study was conducted in four centers in Italy, comparing patients with STEMI.⁵ Similar to the findings observed in the present study, there was a lower rate of MACE and bleeding associated with the procedures performed via radial access. There was a reduction in cardiac mortality (9.2% in the femoral group vs. 5.2% in the radial group; $p=0.02$), and a 47% reduction in the rate of vascular complications related to the access route (6.8% femoral vs. 2.6% radial; $p=0.002$). The crossover rate of radial access to the femoral one was 4.7%, similar to the present registry.

The RIVAL (Radial Versus Femoral Access for Coronary Angiography and Intervention in Patients with Acute Coronary Syndromes) study, likewise, included only ACS patients and showed no difference in their primary MACE endpoint (3.7% in the radial vs. 4.0% in the femoral group; $p=0.50$).⁶ However, there was a significant reduction in the number of severe vascular complications (1.4% in the radial group vs. 3.7% in the femoral group; $p=0.0001$). On the other hand, the crossover rate of the radial to femoral access was 7.6%. Subgroup analysis showed a significant reduction in the primary endpoint in centers with greater expertise in performing procedures by the radial route (>142 procedures per operator/year), corroborating the data of the present study, which was performed in a center with vast experience in the technique.

MATRIX (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX), a randomized multicenter study, was published in 2015 and included 8,404 patients with ACS with and without ST segment elevation.¹² In the study, patients undergoing PCI via radial artery showed significantly lower rates in the endpoint that comprised death, acute MI, stroke and major bleeding, mainly due to the 33% relative reduction in the bleeding rate according to the Bleeding Academic Research Consortium (BARC) criteria. There was also a reduction by 28% in all-cause mortality rate (1.6% vs. 2.2%; RR: 0.72; 95%CI 0.53-0.99; $p=0.045$).

Unlike the studies cited, in the present registry the majority of patients had stable angina (77%) and since there was no interaction between the clinical presentation and the primary endpoint of cardiovascular mortality, it is possible to consider that the benefits of radial access are also evident in this scenario. A similar result was found in a single center study performed at the *Instituto Dante Pazzanese de Cardiologia*, in São Paulo, from 2007 to 2012, where 72.6% of patients had stable coronary artery disease and radial access was associated with a reduction in the risk of vascular complications when compared to the femoral access.¹³

CONCLUSION

The radial artery access was effective in reducing cardiovascular mortality, all-cause mortality, major adverse cardiac events and vascular complications in patients undergoing percutaneous coronary intervention with drug-eluting stents. After adjustment for relevant clinical factors, the femoral artery access remained as an independent predictor of cardiovascular mortality.

Funding source

None.

Conflict of Interest

The authors declare no conflicts of interest.

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