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The Benefits Conferred by Radial Access for Cardiac Catheterization Are Offset by a Paradoxical Increase in the Rate of Vascular Access Site Complications With Femoral Access

The Campeau Radial Paradox

Lorenzo Azzalini, MD, PhD, MSc,* Kunle Tosin, MD,* Malorie Chabot-Blanchet, MSc,† Robert Avram, MD,* Hung Q. Ly, MD, MSc,* Benoit Gaudet, RN,* Richard Gallo, MD,* Serge Doucet, MD,* Jean-François Tanguay, MD,* Réda Ibrahim, MD,* Jean C. Grégoire, MD,* Jacques Crépeau, MD,* Raoul Bonan, MD,* Pierre de Guise, MD,* Mohamed Nosair, MD,* Jean-François Dorval, MD,* Gilbert Gosselin, MD,* Philippe L. L'Allier, MD,* Marie-Claude Guertin, PhD,† Anita W. Asgar, MD,* E. Marc Jolicœur, MD, MSc, MHS*

ABSTRACT

OBJECTIVES The purpose of this study was to assess whether the benefits conferred by radial access (RA) at an individual level are offset by a proportionally greater incidence of vascular access site complications (VASC) at a population level when femoral access (FA) is performed.

BACKGROUND The recent widespread adoption of RA for cardiac catheterization has been associated with increased rates of VASCs when FA is attempted.

METHODS Logistic regression was used to calculate the adjusted VASC rate in a contemporary cohort of consecutive patients (2006 to 2008) where both RA and FA were used, and compared it with the adjusted VASC rate observed in a historical control cohort (1996 to 1998) where only FA was used. We calculated the adjusted attributable risk to estimate the proportion of VASC attributable to the introduction of RA in FA patients of the contemporary cohort.

RESULTS A total of 17,059 patients were included. At a population level, the VASC rate was higher in the overall contemporary cohort compared with the historical cohort (adjusted rates: 2.91% vs. 1.98%; odds ratio [OR]: 1.48, 95% confidence interval [CI]: 1.17 to 1.89; $p = 0.001$). In the contemporary cohort, RA patients experienced fewer VASC than FA patients (adjusted rates: 1.44% vs. 4.19%; OR: 0.33, 95% CI: 0.23 to 0.48; $p < 0.001$). We observed a higher VASC rate in FA patients in the contemporary cohort compared with the historical cohort (adjusted rates: 4.19% vs. 1.98%; OR: 2.16, 95% CI: 1.67 to 2.81; $p < 0.001$). This finding was consistent for both diagnostic and therapeutic catheterizations separately. The proportion of VASCs attributable to RA in the contemporary FA patients was estimated at 52.7%.

CONCLUSIONS In a contemporary population where both RA and FA were used, the safety benefit associated with RA is offset by a paradoxical increase in VASCs among FA patients. The existence of this radial paradox should be taken into consideration, especially among trainees and default radial operators. (J Am Coll Cardiol Intv 2015;8:1854–64)

Radial access (RA) for coronary angiography and percutaneous coronary intervention (PCI) reduces bleeding complications related to cardiac catheterization, and hence mortality, and increases patient comfort (1–4). First described by Canadian cardiologist Lucien Campeau in 1989 (5), RA has modernized the field of interventional cardiology and has become a popular approach for both trainees and experienced operators.

SEE PAGE 1865

Historically, cardiac catheterizations have been performed via femoral access (FA). Although FA remains necessary in multiple diagnostic and interventional settings, this technique has been associated with vascular access site complication (VASC) rates ranging from 2% to 6%, prolonged hospital stay, and even deaths (6–10). A safe access to the femoral artery can be jeopardized by obesity, severe atherosclerosis, and anticoagulation. For these reasons, the femoral puncture requires specific training and constant practice.

Recently, an unusually high rate of VASC (12.5%) has been observed in patients accessed via the femoral artery by default radial operators (11). Thus, although RA may reduce VASC rates at an individual level, we hypothesized that RA can paradoxically be associated with increased rates of complications at a population level due to a greater number of VASCs in FA patients (12). To address this important question, we sought to calculate the proportion of VASCs attributable to RA in a contemporary cohort of FA patients.

METHODS

Our evaluation covered 2 separate 2-year periods and included consecutive patients admitted to our tertiary-care teaching hospital who were referred for either diagnostic or therapeutic cardiac catheterization. Patients in the first period (April 1996 to March 1998) represented the historical control cohort, as only FA was used (7). The contemporary cohort comprised patients from the second period (April 2006 to March 2008), when our group transitioned from FA to RA and both approaches were used equally. Ethics approval was obtained by the local institutional review board. As this was a retrospective analysis conducted per institutional guidelines for data security and privacy, a waiver of consent was granted.

PATIENT POPULATION AND DATA COLLECTION. Patients possibly had multiple catheterizations over the course of the study, but only 1 catheterization per patient was kept for the analysis. For patients with repeated catheterizations over the course of the study, we classified patient-catheterization pairs according to the following hierarchy: catheterization complicated by a VASC > first catheterization. Moreover, diagnostic catheterizations followed by a therapeutic catheterization within 30 days were considered as staged and classified as therapeutic. When both RA and FA were used during a single catheterization (either because of a complex catheterization [e.g., high-risk PCI performed through the RA, assisted by intra-aortic balloon pump through the FA] or because of access crossover), the access was either classified according to the site through which the largest sheath was used (in case of complex catheterization) or according to the site through which the catheterization was finalized (in case of crossover). In particular, in case of radial-to-femoral crossover, access site was classified as femoral.

Patient-specific baseline characteristics, hospital data, comorbid conditions, and complications were obtained from the discharge summary database, including the diagnostic and intervention codes from hospital discharge claims as provided to the

ABBREVIATIONS AND ACRONYMS

CDCI = Charlson-Deyo comorbidity index

CI = confidence interval

ECI = Elixhauser comorbidity index

FA = femoral access

OR = odds ratio

PCI = percutaneous coronary intervention

RA = radial access

VASC = vascular access site complication

From the *Montreal Heart Institute, Université de Montréal, Montréal, Québec, Canada; and the †Montreal Health Innovations Coordinating Center, Montréal, Québec, Canada. Dr. Azzalini was funded by a grant from the Spanish Society of Cardiology. Dr. Avram received a CCS Bayer Resident Award 2014. Dr. Ly receives funding from La Fondation de l'Institut de Cardiologie de Montréal and the Des Groseillers et Bérard Chair in Interventional Cardiology from Université de Montréal. Dr. Tanguay has received research grant support from Abbott Vascular, Ikeria, and GlaxoSmithKline; and has served as a consultant/speaker for AstraZeneca, Eli Lilly, Abbott Vascular, Actelion, and Bayer. Dr. Bonan has served as a consultant and received honoraria from Medtronic. Dr. L'Allier is supported by La Fondation de l'Institut de Cardiologie de Montréal; holds the Des Groseillers et Bérard Chair in Interventional Cardiology from Université de Montréal; has served as a consultant to Abbott Vascular and St. Jude Medical; has received institutional educational grants from Medtronic, Abbott Vascular, Eli Lilly, and AstraZeneca; and has received research grants from St. Jude Medical, Volcano/Philips, and AstraZeneca. Dr. Jolicoeur is supported by research grants from the Fonds de Recherche du Québec en Santé, The Canadian Institutes for Health Research (CIHR), and by La Fondation de l'Institut de Cardiologie de Montréal. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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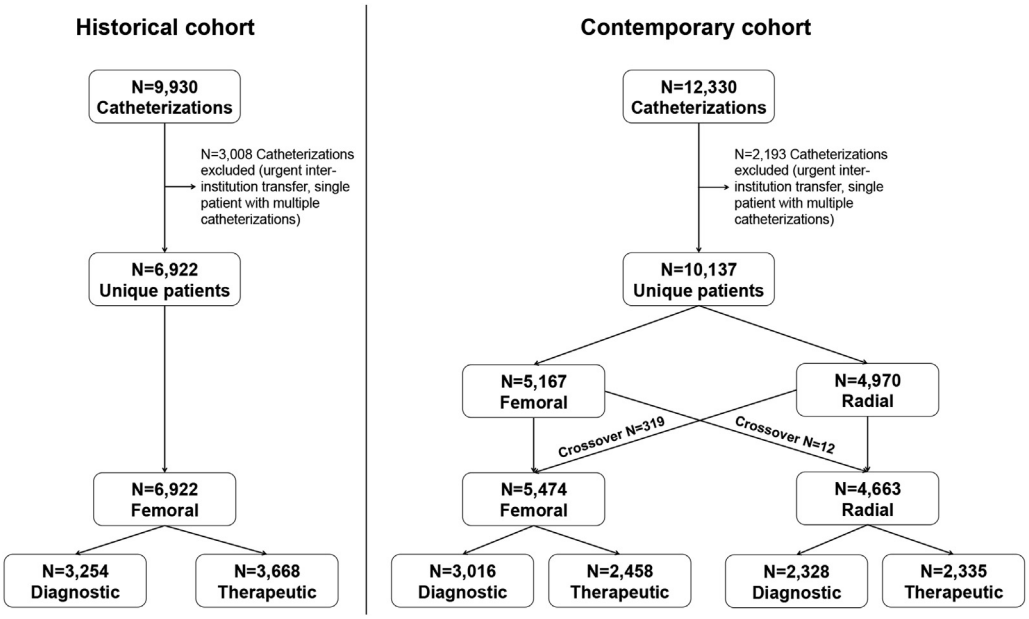
FIGURE 1 Study Population



Régie de l'Assurance Maladie du Québec, our provincial health administrative database. The discharge summary database was populated by professional medical archivists following a comprehensive review of the medical charts of patients using the International Classification of Diseases, 9th Revision for patients in the historical cohort and the 10th Revision for those in the contemporary cohort. The reliability and predictive capability of this approach in cardiology has previously been validated (13-16). Procedural details related to the cardiac catheterization for the contemporary cohort were abstracted from the Mac-Lab catheterization laboratory software (GE Healthcare, Little Chalfont, United Kingdom), using MySQL (Oracle Corp., Redwood Shores, California). Cross-tabulation of the different databases was performed with SAS version 9.3 (SAS Institute, Cary, North Carolina) using specifically written code. Deterministic medical record linkage was performed with the use of an encrypted unique personal provincial health insurance number. Data quality was ensured by verification by three independent investigators (L.A., K.T., and B.G.), as detailed in the Online Appendix.

DEFINITION OF VASCULAR ACCESS SITE COMPLICATIONS. As per standard institutional policies, all patients are systematically followed-up for 30 days after hospital discharge by a specialized nurse, who prospectively monitors and documents the occurrence of all VASCs including: major hematoma, pseudoaneurysm, arteriovenous fistula, retroperitoneal hematoma, arterial thrombosis, dissection and perforation, distal embolization, femoral nerve injury, local infection, and arterial avulsion, as previously reported (7). Detailed VASC definitions are provided in the Online Appendix. VASCs were individually recorded and were classified by their highest level of severity.

STATISTICAL ANALYSIS. Baseline characteristics, clinical presentation, procedural data, and VASCs are presented by cohort and vascular access site. Continuous variables are presented as mean ± SD and compared with the Student *t* test. Categorical variables are presented as frequency (percentages) and compared using the chi-square test. For all tests, $p < 0.05$ was considered significant. Basic assumptions were verified before analysis. Analyses were performed with SAS version 9.4 (SAS Institute, Cary, North Carolina).

MODELING OF OUTCOMES. To estimate the proportion of VASC attributable to RA in the contemporary cohort of FA patients, we used the concept of attributable risk (17): $100 \times (I_e - I_u)/I_e$; where I_e represents the risk in those exposed ([number of events in exposed patients]/[number of exposed patients]) and

TABLE 1 Baseline Characteristics and Comorbid Conditions

	Historical Cohort	Contemporary Cohort			
	Femoral (n = 6,922)	Femoral (n = 5,474)	Radial (n = 4,663)	Overall (n = 10,137)	p Value
Age, yrs	61.5 ± 11.1	64.9 ± 12.7	62.7 ± 11.0	63.9 ± 12.0	<0.001* <0.001† <0.001‡
Female	2,192 (31.7)	2,173 (39.7)	996 (21.4)	3,169 (31.3)	0.58* <0.001† <0.001‡
Body mass index, kg/m^2	N/A	27.8 ± 5.0	29.2 ± 5.3	28.4 ± 5.2	N/A* N/A† <0.001‡
Diabetes mellitus	1,082 (15.6)	1,350 (24.7)	1,169 (25.1)	2,519 (24.8)	<0.001* <0.001† 0.64‡
Dyslipidemia	2,103 (30.4)	3,232 (59.0)	3,231 (69.3)	6,463 (63.8)	<0.001* <0.001† <0.001‡
Hypertension	1,900 (27.4)	2,902 (53.0)	2,679 (57.4)	5,581 (55.1)	<0.001* <0.001† <0.001‡
Active smoking	893 (12.9)	991 (18.1)	1,228 (26.3)	2,219 (21.9)	<0.001* <0.001† <0.001‡
Coronary artery disease	4,296 (62.1)	2,516 (46.0)	3,203 (68.7)	5,719 (56.4)	<0.001* <0.001† <0.001‡
Peripheral artery disease	154 (2.2)	682 (12.5)	433 (9.3)	1,115 (11.0)	<0.001* <0.001† <0.001‡
Stroke	233 (3.4)	183 (3.3)	102 (2.2)	285 (2.8)	0.04* 0.94† <0.001‡
Heart failure	303 (4.4)	502 (9.2)	286 (6.1)	788 (7.8)	<0.001* <0.001† <0.001‡
Chronic kidney disease	350 (5.1)	612 (11.2)	344 (7.4)	956 (9.4)	<0.001* <0.001† <0.001‡
Elixhauser comorbidity index					
0	2,764 (39.9)	861 (15.7)	908 (19.5)	1,769 (17.5)	<0.001*
1	2,167 (31.3)	1,359 (24.8)	1,363 (29.2)	2,722 (26.9)	<0.001†
2	1,169 (16.9)	1,296 (23.7)	1,109 (23.8)	2,405 (23.7)	<0.001‡
3 or higher	822 (11.9)	1,958 (35.8)	1,283 (27.5)	3,241 (32.0)	
Charlson-Deyo comorbidity index					
0	3,038 (43.9)	1,762 (32.2)	1,387 (29.7)	3,149 (31.1)	<0.001*
1	2,587 (37.4)	1,986 (36.3)	1,964 (42.1)	3,950 (39.0)	<0.001†
2	824 (11.9)	894 (16.3)	792 (17.0)	1,686 (16.6)	<0.001‡
3 or higher	473 (6.8)	832 (15.2)	520 (11.2)	1,352 (13.3)	

Values are mean ± SD or n (%), as appropriate. The p value comparisons: *historical vs. overall contemporary cohort; †historical vs. femoral contemporary cohort; ‡radial vs. femoral contemporary cohort.

N/A = not available.

I_u represents the risk in those unexposed ([number of events in unexposed patients]/[number of unexposed patients]). Operationally, the risk attributable to RA was estimated from the difference between the proportion of VASCs in FA subjects of the contemporary cohort (exposed to introduction of RA, I_e) and the proportion of VASC in the historical (unexposed) cohort (I_u), expressed as a fraction of the proportion of VASCs in FA subjects of the contemporary cohort (I_e). Additional information is available in the Online Appendix.

To control for confounding variables between cohorts, VASC rates were adjusted using logistic regression analysis with block entry of variables. The principal model was built using the following candidate independent variables: age, sex, period of

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TABLE 2 Clinical Presentation and Procedural Data

	Historical Cohort	Contemporary Cohort			
	Femoral (n = 6,922)	Femoral (n = 5,474)	Radial (n = 4,663)	Overall (n = 10,137)	p Value
Clinical presentation					
ST-segment elevation myocardial infarction (primary and rescue PCI)	683 (9.9)	517 (9.4)	501 (10.7)	1,018 (10.0)	0.71* 0.43† 0.03‡
Cardiogenic shock	92 (1.3)	112 (2.0)	4 (0.1)	116 (1.1)	0.28* 0.002† <0.001‡
Type of procedure					
Diagnostic	3,254 (47.0)	3,016 (55.1)	2,328 (49.9)	5,344 (52.7)	<0.001* <0.001† <0.001‡
Therapeutic	3,668 (53.0)	2,458 (44.9)	2,335 (50.1)	4,793 (47.3)	
Procedural data					
Access site crossover§	0	319 (6.1)	12 (0.3)	331 (3.4)	N/A* N/A† <0.001‡
Concomitant femoral vein puncture	N/A	1,217 (23.2)	38 (0.8)	1,255 (12.8)	N/A* N/A† <0.001‡
Sheath size					
5-F or lower	N/A	188 (3.6)	137 (3.0)	325 (3.4)	N/A*
6-F	N/A	4,791 (92.5)	4,392 (97.0)	9,183 (94.6)	N/A†
7-F or higher	N/A	198 (3.8)	1 (0.02)	199 (2.1)	<0.001‡
Vascular closure device	0	1,632 (31.1)	4 (0.1)	1,636 (16.6)	N/A* N/A† <0.001‡
Need for intra-aortic balloon pump	114 (1.6)	238 (4.3)	29 (0.6)	267 (2.6)	<0.001* <0.001† <0.001‡
Anticoagulant agent					
Heparin	N/A	4,164 (79.4)	4,457 (96.9)	8,621 (87.6)	N/A*
Bivalirudin	N/A	39 (0.7)	42 (0.9)	81 (0.8)	N/A†
None	N/A	1,039 (19.8)	101 (2.2)	1,140 (11.6)	<0.001‡
Glycoprotein IIb/IIIa inhibitors	N/A	629 (12.0)	886 (19.3)	1,515 (15.4)	N/A* N/A† <0.001‡

Values are n (%). The p value comparisons: *historical vs. overall contemporary cohort; †historical vs. femoral contemporary cohort; ‡radial vs. femoral contemporary cohort.
§Data presented in relation to the classification used in the final statistical model.

N/A = not available; PCI = percutaneous coronary intervention.

the year (dichotomized as July to September vs. October to June), number of cardiac catheterizations during the index admission, ST-segment elevation myocardial infarction, type of catheterization (diagnostic vs. therapeutic), and a comorbidity index. For the latter predictor, we compared the discriminatory performance of 2 indexes: the Charlson-Deyo comorbidity index (CDCI) (18,19) and the Elixhauser comorbidity index (ECI) (20). Briefly, the CDCI and ECI infer clinical data from administrative coding of discharge diagnoses. Taking into account 17 and 30 comorbidities, respectively, the CDCI and ECI have been shown to correlate with in-hospital mortality, length of stay, health care-related costs, as well as medium- and long-term mortality (18-21). Moreover, both have been validated and shown to predict in-hospital mortality in PCI patients (22). Additional details are available in the Online Appendix. The comorbidity index providing the greater discrimination was selected in the final model. Model discrimination was evaluated with the C-statistic. The ECI provided a greater discrimination in the femoral cohorts subgroups and was therefore selected in the final model.

This model was used separately on 8 subgroups of patients (historical cohort, contemporary FA cohort, contemporary RA cohort, overall contemporary cohort, diagnostic catheterizations in historical cohort, therapeutic catheterization in historical cohort, diagnostic catheterizations in contemporary FA cohort, and therapeutic catheterizations in contemporary FA cohort), and the probability of VASCs

was estimated for an "average" patient from the historical cohort. For each subgroup, the estimated probability was calculated using the beta coefficients provided by the logistic regression performed on this subgroup and the mean values (for continuous variables) and proportions (for categorical variables) observed in the historical cohort for the covariates. These estimated probabilities were then used in place of I_e and I_u to calculate the adjusted attributable risk. We performed several stratified analyses: according to ECI subcategories, baseline risk of VASCs, and propensity of undergoing FA in the contemporary cohort (additional details are provided in the Online Appendix). To allow pairwise-adjusted comparisons of subgroups, we also performed logistic regressions including the same covariates, as well as their interaction with the group variable (cohort or access site, depending on the subgroups compared). Odds ratios (ORs) along with 95% confidence intervals (CIs) and p values are presented.

RESULTS

BASELINE CHARACTERISTICS, CLINICAL PRESENTATION, AND PROCEDURAL DATA. Of the 17,059 patients included in the analysis, 6,922 belonged to the historical cohort, and 10,137 to the contemporary cohort (**Figure 1**). In the contemporary cohort, 5,474 patients (54.0%) underwent FA and 4,663 patients (46.0%) underwent RA. Patients in the contemporary cohort were older and presented with a higher burden of cardiovascular risk factors and comorbid conditions compared with patients in the historical cohort (**Table 1**). There were no differences in the incidence of ST-segment elevation myocardial infarction and cardiogenic shock between the 2 cohorts (**Table 2**). However, a greater proportion of patients underwent therapeutic catheterizations in the historical cohort. Demographic and procedural data for patients that experienced a VASC are available in Online Table 1.

VASC RATES. The rates of VASCs in the historical and overall contemporary cohorts were similar (unadjusted rates: 2.89% vs. 3.18%; p = 0.29) (**Table 3**, **Figure 2A**). After adjustment, the risk of VASCs for contemporary patients was higher than for historical patients (adjusted rates: 2.91% vs. 1.98%; adjusted OR: 1.48, 95% CI: 1.17 to 1.89; p = 0.001). In the contemporary cohort, RA patients experienced fewer VASCs compared with FA patients (unadjusted rates: 1.42% vs. 4.68%; p < 0.001; adjusted rates: 1.44% vs. 4.19%; adjusted OR: 0.33, 95% CI: 0.23 to 0.48; p < 0.001). FA patients in the contemporary cohort experienced more VASCs compared with patients in the historical cohort (unadjusted rates: 4.68% vs. 2.89%; p < 0.001; adjusted rates: 4.19% vs. 1.98%; adjusted OR: 2.16, 95% CI: 1.67 to 2.81; p < 0.001). This difference was driven by a higher incidence of major hematoma (3.80% vs. 1.24%; p < 0.001) and retroperitoneal hematoma (0.22% vs. 0.03%; p = 0.002). The difference in the overall incidence of VASCs among FA patients between the historical and contemporary cohorts persisted in the sensitivity analysis where diagnostic (adjusted OR: 2.30, 95% CI: 1.36 to 3.91; p = 0.002) and therapeutic (adjusted OR: 2.24, 95% CI: 1.64 to 3.06; p < 0.001) catheterizations among FA patients were analyzed separately (**Figure 2B**). Predictors of VASCs are presented in Online Table 2.

TABLE 3 Vascular Access Site Complications

	Historical Cohort	Contemporary Cohort			
	Femoral (n = 6,922)	Femoral (n = 5,474)	Radial (n = 4,663)	Overall (n = 10,137)	p Value
Major hematoma	86 (1.24%)	208 (3.80%)	61 (1.31%)	269 (2.65%)	<0.0001* <0.0001† <0.0001‡
Pseudoaneurysm	81 (1.17%)	16 (0.29%)	0	16 (0.16%)	<0.0001* <0.0001† 0.0002‡
Arterial thrombosis	12 (0.17%)	6 (0.11%)	1 (0.02%)	7 (0.07%)	0.04* 0.35† 0.09‡
Arterial dissection	3 (0.04%)	7 (0.13%)	0	7 (0.07%)	0.50* 0.10† 0.01‡
Arterial perforation	0	3 (0.05%)	1 (0.02%)	4 (0.04%)	0.10* 0.05† 0.40‡
Arteriovenous fistula	9 (0.13%)	2 (0.04%)	0	2 (0.02%)	0.005* 0.08† 0.19‡
Retroperitoneal hematoma	2 (0.03%)	12 (0.22%)	0	12 (0.12%)	0.05* 0.002† 0.001‡
Distal embolization	4 (0.06%)	1 (0.02%)	0	1 (0.01%)	0.07* 0.28† 0.36‡
Others§	3 (0.04%)	1 (0.02%)	3 (0.06%)	4 (0.04%)	0.90* 0.44† 0.24‡
Total	200 (2.89%)	256 (4.68%)	66 (1.42%)	322 (3.18%)	0.29* <0.0001† <0.0001‡

Values are n (%). The p value comparisons: *historical vs. overall contemporary cohort; †historical vs. femoral contemporary cohort; ‡radial vs. femoral contemporary cohort. §"Others" indicates arterial avulsion, femoral nerve injury, and local infection.

THE FRACTION OF VASCS IN FA PATIENTS ATTRIBUTABLE TO RA. We estimated that 52.7% of VASCs in contemporary FA patients were attributable to the

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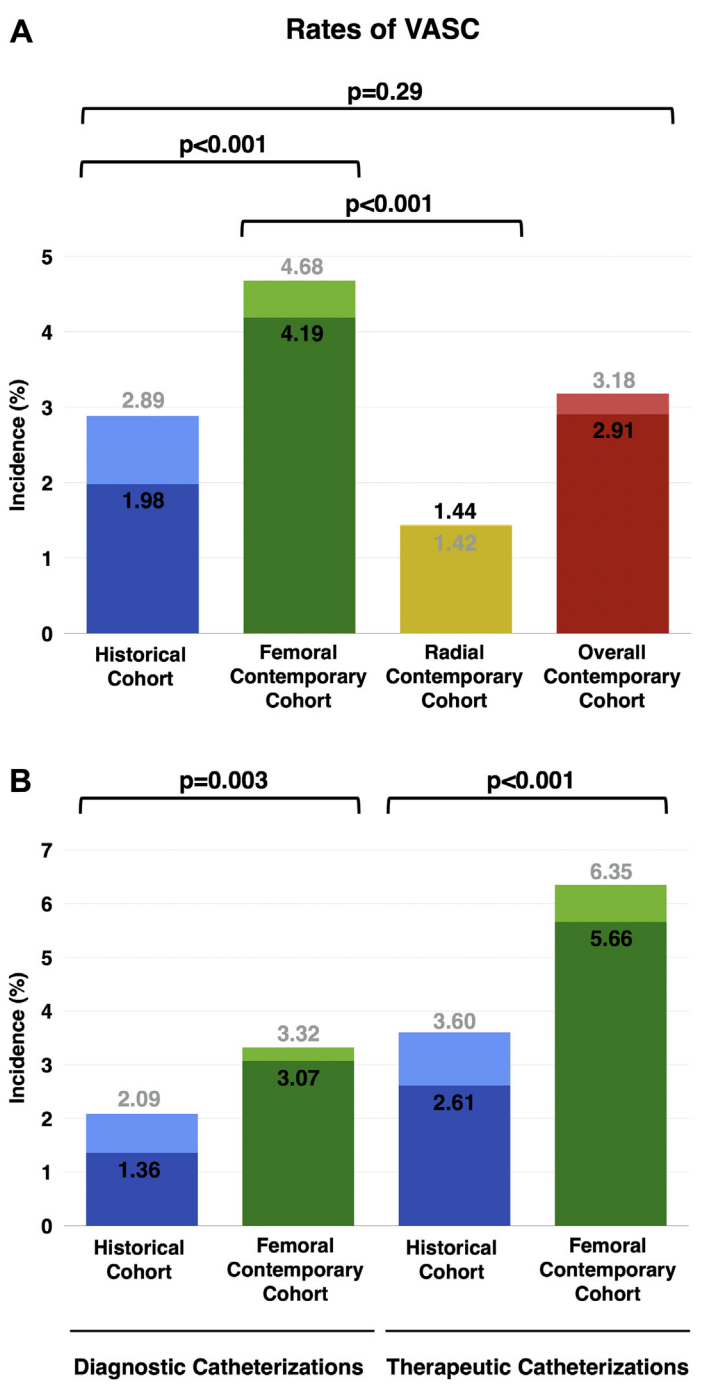
FIGURE 2 VASC Rates



(A) All catheterizations across historical versus contemporary (femoral, radial, and overall) cohorts. **(B)** Diagnostic and therapeutic catheterizations separately (historical vs. femoral contemporary cohorts). The p values refer to comparisons between unadjusted rates. Crude rates are displayed in **gray** and adjusted rates are shown in **black**. The highest predictive power among the 2 multivariate models tested for adjustment was obtained by the model including demographics and clinical variables, as well as the Elixhauser comorbidity index (C-statistic 0.74 in the historical cohort). VASC = vascular access site complication.

use of the RA. This means that, after multivariate adjustment, 52.7% of the VASCs experienced in FA patients of the contemporary cohort are attributable to the emphasis on RA. Similar attributable risks were obtained when analyzing diagnostic (55.8%) and therapeutic (53.9%) catheterizations separately. We further analyzed adjusted VASC rates and adjusted attributable risk of VASC across ECI categories (**Figure 3**). Although VASC rates increased in parallel with the ECI in the historical cohort, VASC rates did not show such a consistent pattern in the contemporary FA cohort. As a result, the attributable risk of a VASC decreased from a maximal value of 66.3% in patients with ECI = 0 (low comorbidity) to a minimum of 15.7% in ECI ≥3 (high comorbidity). Moreover, we performed a similar stratified analysis according to the quartiles of VASC risk score, using the model presented in Online Table 2B (**Figure 4**). Similar to the analysis stratified by ECI categories, the unadjusted attributable risk of VASCs decreased from a maximum of 38.2% for subjects in the first quartile to a minimum of 11.5% for patients in the fourth quartile. Finally, we stratified according to the propensity of undergoing FA in the contemporary cohort and compared the resulting VASC rates to the one of the historical cohort (**Figure 5**); similar to the 2 other stratified analyses, the unadjusted attributable risk of VASC was highest (51.0%) among subjects in the first quintile (i.e., with lowest propensity of receiving FA).

DISCUSSION

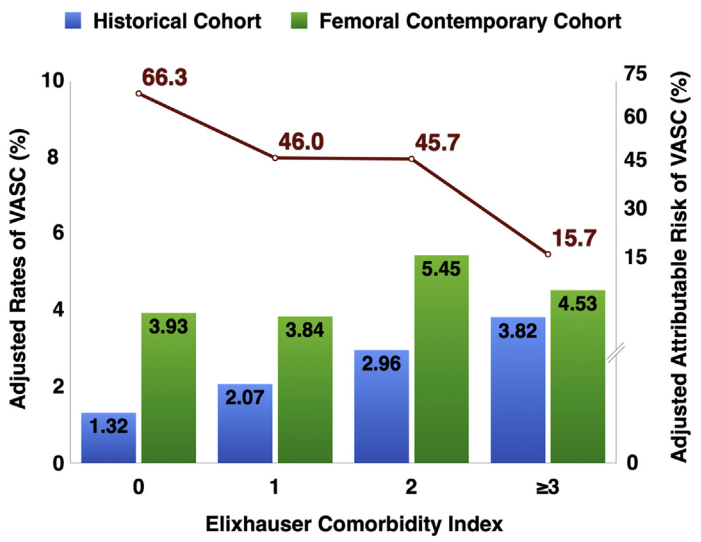
In this study, we investigated the effects of the introduction of RA on the occurrence of VASCs in a contemporary cohort of patients undergoing cardiac catheterization. We found that although RA reduced VASC rates at an individual level, it was paradoxically associated with increased rates of complications at a population level when compared to historical control subjects. The increased VASC rates at a population level were driven by complications in FA patients, which offset the benefit associated with RA. If indeed the RA is linked to an increase in femoral VASCs, eliminating the RA would potentially prevent up to 52.7% of VASCs in FA patients. This finding has important clinical and research implications, given the recent global shift toward RA by practitioners previously using FA (23,24).

The higher VASC rates seen with FA since the introduction of RA cannot be entirely explained by the case-mix unaccounted for between the historical and the contemporary cohorts. We believe that a

radial paradox does exist for several reasons. First, the higher VASC rates observed in contemporary FA patients remained clinically meaningful and statistically significant despite adjustment with an accurate multivariate model (C-statistic 0.74 in the historical cohort). Second, the attributable risk of VASCs showed an inverse relationship with the number of comorbid conditions (as quantified with the ECI), with the greatest attributable risk of VASC (66.3%) seen in patients with few comorbidities (ECI = 0), and the lowest attributable risk (15.7%) in patients with multiple comorbidities (ECI ≥3). This evidence suggests that the patients who most often experience the radial paradox are those with fewer comorbidities. Similar findings were observed when attributable risk was analyzed by stratum of VASC risk score and according to propensity of undergoing FA in the contemporary cohort: the risk of a femoral VASC attributable to RA was greatest in patients with the lowest baseline risk of a VASC and in patients with the lowest propensity of undergoing FA, that is, the patients with clinical characteristics for which the operator would usually favor using RA. Third, our findings were consistent in patients undergoing diagnostic catheterizations. Although it may be argued that therapeutic catheterization has markedly changed over the decade that separated the 2 cohorts, no such argument can be made for diagnostic catheterization, which has remained similar through the years. Moreover, because smaller sheath sizes were used in the contemporary cohort, the results would be more likely biased *against* the existence of a radial paradox. Finally, our findings have recently been alluded to by other groups who also observed unusually high rates of VASCs in FA patients. For example, Rafie et al. (11) reported VASC rates of 12.5% with FA among default radial operators in the United Kingdom, where FA is reserved for challenging clinical scenarios, in which both patient- and procedure-related risk factors for bleeding are highly prevalent. This phenomenon has also been hinted at by a recent analysis of the U.S. National Cardiovascular Data Registry, which reported that the risk of access site bleeding in FA patients increased after the adoption of RA by previously FA-only operators over a 3-year period (from 5.6% to 6.4%). Interestingly, the risk of FA site bleeding increased as a function of the relative increase in RA adoption: from 6.3% in the very-low adoption group (<2% of transradial PCIs), to 7.4% in the high adoption group (~45% transradial PCIs) ($p < 0.001$) (25).

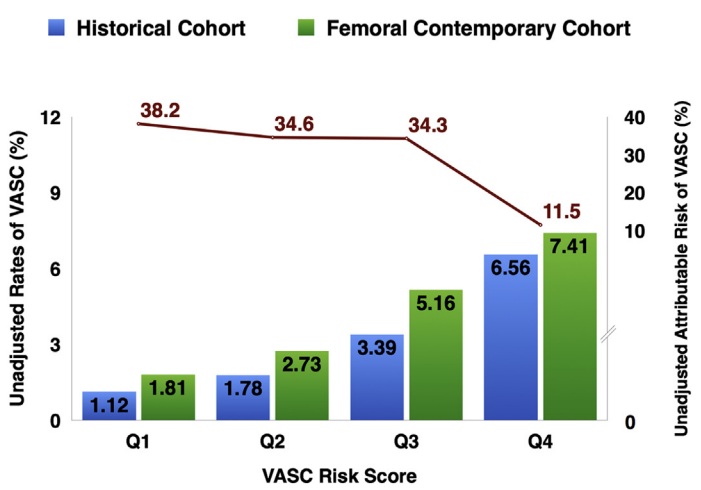
In many centers, the majority of cardiac catheterizations are performed through the RA (23). In such settings, trainees and less experienced operators have been trained to master the RA, but such operators are less accustomed to using the FA (12). Operator experience is a key determinant of outcomes for a wide range of medical procedures (26–28). We speculate that the radial paradox stems

FIGURE 3 VASC Stratified by Elixhauser Comorbidity Index



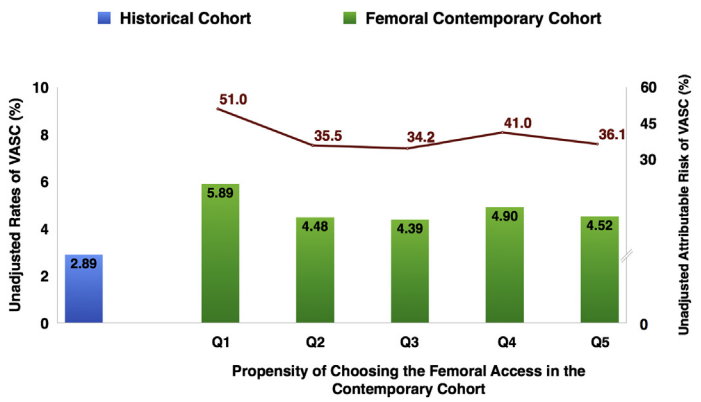
Adjusted rates and attributable risks of vascular access site complications (VASCs), across Elixhauser comorbidity index categories in the historical vs. femoral contemporary cohorts.

FIGURE 4 VASC Stratified by VASC Risk Score



Unadjusted rates and attributable risks of vascular access site complications (VASCs), across VASC risk score quartiles in the historical versus femoral contemporary cohorts.

FIGURE 5 VASC Stratified by Propensity of Undergoing FA



Unadjusted rates and attributable risks of vascular access site complications (VASCs), across quintiles of propensity score of undergoing femoral access in the contemporary cohort, compared with the historical cohort.

from operators' reduced expertise in safely accessing the femoral artery. We further speculate that modern radial operators reserve the FA for complex PCIs in critical clinical scenarios. The situation becomes synergistically problematic when poorly trained operators attempt challenging FAs. Although the radial paradox could possibly be explained by these hypotheses, they are not addressed by this analysis and need to be the focus of further research.

However, the topical debate on vascular access for cardiac catheterization is further compounded by the recent finding that the lowest rates of bleeding complications and mortality in patients undergoing FA are observed at high-volume radial centers compared with low-volume radial (i.e., mostly femoral) institutions (29,30). This is not surprising if we consider that high-volume radial centers are most frequently academic institutions, where expert interventionalists operate, new techniques are most likely to be quickly adopted and mastered, and state-of-the-art post-procedural care is provided. These findings, together with our data, indicate that, although the synergy between the loss of skills in securing FA and the selection of FA for challenging clinical scenarios has currently led to higher rates of VASCs, the widespread adoption of RA mitigated the adverse outcomes related to FA. These observations underscore the complexity of the issue and might contribute to the identification of adequate strategies to improve patient outcomes.

Indeed, actions are needed to reduce the rate of VASCs when FA is attempted. Fluoroscopy- (31) and ultrasound-guided (32) puncture, bivalirudin (33), and vascular closure devices (34) appear to be feasible and effective strategies. Additionally, systemic anticoagulation should only be administered once the ascending aorta has been successfully cannulated during an attempted radial catheterization to avoid puncturing the femoral artery in a fully anticoagulated patient, if crossover to FA is needed. We believe that educational programs for trainees and young interventional cardiologists should take into consideration this radial paradox in such a way to maximize exposure to optimal FA technique. Such programs could include formal teaching, focused workshops, and simulators, as is currently done for RA (35). Finally, maintaining a minimal FA volume could also be recommended.

STUDY LIMITATIONS. First, this is a retrospective study, with all the inherent bias ascribed to this type of design. However, we used multivariate analysis to minimize the effects of confounders, which showed good discriminatory performance. Second, some important potential sources of confounding were not recorded in our database (e.g., individual operator volume; patient creatinine and coagulation panel; sheath size, concomitant femoral vein puncture, anticoagulation, and glycoprotein IIb/IIIa inhibitors in the historical cohort, and so on). Nevertheless, the consistency of our findings in a sensitivity analysis and the use of a validated comorbidity index (20–22) should have minimized this issue. Finally, it could be argued that the contemporary (2006 to 2008) cohort does not represent more recent experience with RA/FA and current clinical practice. This cohort was selected in an effort to analyze the complex phenomenon of transitioning from a femoral to a radial program, which is now particularly relevant in many countries. In fact, in many centers (particularly those outside Europe and Canada) current experience with RA is moderate. For example, RA is used for >25% of PCIs at only ~20% of U.S. catheterization laboratories (25), for an overall use of just ~16% (36). Therefore, the use of RA in routine clinical practice most closely resembles the scenario described in our study.

CONCLUSIONS

We observed an increase in the rates of VASCs when FA is performed in a large, all-comer contemporary cohort of patients undergoing diagnostic or therapeutic cardiac catheterizations (where both RA

and FA are used) compared with historical control subjects. This increase of FA-related VASCs at a population level offset the benefit associated with RA at a patient level. The existence of a radial paradox should be taken into account, and appropriate actions should be taken to improve patient outcomes when FA is required.

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REPRINT REQUESTS AND CORRESPONDENCE: Dr. E. Marc Jolicoeur, Department of Medicine, Montreal Heart Institute, Université de Montréal, 5000 rue Bélanger Est, Montréal, Québec, H1T 1C8 Canada. E-mail: marc.jolicoeur@icm-mhi.org.

PERSPECTIVES

WHAT IS KNOWN? The femoral arterial puncture is a tactful intervention that requires knowledge, skills, and practice. After the relatively recent widespread adoption of RA, FA is used less often.

WHAT IS NEW? We found that the rate of vascular complications was higher in a contemporary cohort where both RA and FA was used compared with a historical cohort where only FA was utilized. This was driven by a higher rate of complications in femoral patients of the contemporary cohort. In the contemporary cohort, the safety benefit associated with RA was offset by a paradoxical increase in vascular complications among femoral patients. The existence of this radial paradox should be taken into consideration, especially among trainees and default radial operators.

WHAT IS NEXT? Additional studies should propose and test effective measures to improve FA techniques and minimize complication rates, thus improving patient clinical outcomes.

REFERENCES

1. Jolly SS, Amlani S, Hamon M, Yusuf S, Mehta SR. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. Am Heart J 2009;157:132–40.

2. Rao SV, Cohen MG, Kandzari DE, Bertrand OF, Gilchrist IC. The transradial approach to percutaneous coronary intervention: historical perspective, current concepts, and future directions. J Am Coll Cardiol 2010;55:2187–95.

3. Cooper CJ, El-Shiekh RA, Cohen DJ, et al. Effect of transradial access on quality of life and cost of cardiac catheterization: a randomized comparison. Am Heart J 1999;138:430–6.

4. Valgimigli M, Gagnor A, Calabró P, et al. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015; 385:2465–76.

5. Campeau L. Percutaneous radial artery approach for coronary angiography. Cathet Cardiovasc Diagn 1989;16:3–7.

6. Davis K, Kennedy JW, Kemp HGJ, Judkins MP, Gosselin AJ, Killip T. Complications of coronary arteriography from the Collaborative Study of Coronary Artery Surgery (CASS). Circulation 1979; 59:1105–12.

7. Chandrasekar B, Doucet S, Bilodeau L, et al. Complications of cardiac catheterization in the current era: a single-center experience. Catheter Cardiovasc Interv 2001;52:289–95.

8. Doyle BJ, Ting HH, Bell MR, et al. Major femoral bleeding complications after percutaneous coronary intervention: incidence, predictors, and impact on long-term survival among 17,901 patients treated at the Mayo Clinic from 1994 to 2005. J Am Coll Cardiol Intv 2008;1: 202–9.

9. Kennedy JW. Complications associated with cardiac catheterization and angiography. Cathet Cardiovasc Diagn 1982;8:5–11.

10. Johnson LW, Lozner EC, Johnson S, et al. Coronary arteriography 1984–1987: a report of the registry of the Society for Cardiac Angiography and Interventions. I. Results and complications. Cathet Cardiovasc Diagn 1989;17:5–10.

11. Rafie IM, Uddin MM, Ossei-Gerning N, Anderson RA, Kinnaird TD. Patients undergoing PCI from the femoral route by default radial operators are at high risk of vascular access-site complications. EuroIntervention 2014;9:1189–94.

12. Azzalini L, Jolicoeur EM. The use of radial access decreases the risk of vascular access-site-related complications at a patient level but is associated with an increased risk at a population level: the radial paradox. EuroIntervention 2014; 10:531–2.

13. Lambert L, Blais C, Hamel D, et al. Evaluation of care and surveillance of cardiovascular disease: can we trust medico-administrative hospital data? Can J Cardiol 2012;28:162–8.

14. Austin PC, Daly PA, Tu JV. A multicenter study of the coding accuracy of hospital discharge administrative data for patients admitted to cardiac care units in Ontario. Am Heart J 2002;144: 290–6.

15. Lee DS, Stitt A, Wang X, et al. Administrative hospitalization database validation of cardiac procedure codes. Med Care 2013;51:e22–6.

16. Levy AR, Tamblyn RM, Fitchett D, McLeod PJ, Hanley JA. Coding accuracy of hospital discharge data for elderly survivors of myocardial infarction. Can J Cardiol 1999;15:1277–82.

17. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. Am J Public Health 1998;88:15–9.

18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.

19. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992; 45:613–9.

20. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36:8–27.

21. Chu YT, Ng YY, Wu SC. Comparison of different comorbidity measures for use with administrative data in predicting short- and long-term mortality. BMC Health Serv Res 2010;10:140.

22. Kim KH, Ahn LS. [A comparative study on comorbidity measurements with lookback period using health insurance database: focused on patients who underwent percutaneous coronary intervention]. J Prev Med Pub Health 2009;42: 267–73.

23. Abdelaal E, Brousseau-Provencher C, Montminy S, et al. Risk score, causes, and clinical impact of failure of transradial approach for percutaneous coronary interventions. J Am Coll Cardiol Intv 2013;6:1129–37.

24. Bertrand OF, Rao SV, Pancholy S, et al. Transradial approach for coronary angiography and interventions: results of the first international transradial practice survey. J Am Coll Cardiol Intv 2010;3:1022–31.

25. Bradley SM, Rao SV, Curtis JP, et al. Change in hospital-level use of transradial percutaneous coronary intervention and periprocedural outcomes: insights from the National Cardiovascular

Data Registry. Circ Cardiovasc Qual Outcomes 2014;7:550–9.

26. Laffel GL, Barnett AI, Finkelstein S, Kaye MP. The relation between experience and outcome in heart transplantation. N Engl J Med 1992;327:1220–5.

27. Sanchez PL, Harrell LC, Salas RE, Palacios IF. Learning curve of the Inoue technique of percutaneous mitral balloon valvuloplasty. Am J Cardiol 2001;88:662–7.

28. Rosenthal GE, Vaughan-Sarrazin M. The July Phenomenon revisited: new insights on a lore of academic medicine. Circulation 2013;128:2729–31.

29. Jolly SS, Cairns J, Yusuf S, et al. Procedural volume and outcomes with radial or femoral access for coronary angiography and intervention. J Am Coll Cardiol 2014;63:954–63.

30. Nolan J. Radialists perform better femoral PCI. Paper presented at AimRADIAL2014; October 23–25, 2014; Chicago, IL.

31. Cilingiroglu M, Feldman T, Salinger MH, Levisay J, Turi ZG. Fluoroscopically-guided micropuncture femoral artery access for large-caliber sheath insertion. J Invasive Cardiol 2011;23:157–61.

32. Gedikoglu M, Oguzkurt L, Gur S, Andic C, Sariturk C, Ozkan U. Comparison of ultrasound guidance with the traditional palpation and fluoroscopy method for the common femoral artery puncture. Catheter Cardiovasc Interv 2013;82:1187–92.

33. Zeymer U, van't Hof A, Adgey J, et al. Bivalirudin is superior to heparins alone with bailout GP IIb/IIIa inhibitors in patients with ST-segment elevation myocardial infarction transported emergently for primary percutaneous coronary intervention: a prespecified analysis from the EUROMAX trial. Eur Heart J 2014;35:2460–7.

34. Kerré S, Kustermans L, Vandendriessche T, et al. Cost-effectiveness of contemporary vascular closure devices for the prevention of vascular complications after percutaneous coronary interventions in an all-comers PCI population. EuroIntervention 2014;10:191–7.

35. Mamas MA, Fraser DG, Ratib K, et al. Minimising radial injury: prevention is better than cure. EuroIntervention 2014;10:824–32.

36. Feldman DN, Swaminathan RV, Kaltenbach LA, et al. Adoption of radial access and comparison of outcomes to femoral access in percutaneous coronary intervention: an updated report from the National Cardiovascular Data Registry (2007–2012). Circulation 2013;127:2295–306.

KEY WORDS access site, cardiac catheterization, percutaneous coronary intervention, vascular complications

APPENDIX For an expanded Methods section and supplemental tables, please see the online version of this article.