ORIGINAL RESEARCH

Predictors of common femoral artery access site complications in patients on oral anticoagulants and undergoing a coronary procedure

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Background: It is unclear whether patients on oral anticoagulants (OAC) undergoing a procedure using common femoral artery access have higher adverse events when compared to patients who are not anticoagulated at the time of the procedure.

Methods: We retrospectively reviewed data from consecutive patients who underwent a cardiac procedure at a tertiary medical center. Patients were considered (group A) fully or partially anticoagulated if they had an international normalized ratio (INR) $\geq$1.6 on the day of the procedure or were on warfarin or new OAC within 48 h and 24 h of the procedure, respectively. The nonanticoagulated group (group B) had an INR <1.6 or had stopped their warfarin and new OAC >48 h and >24 h preprocedure, respectively. The index primary end point of the study was defined as the composite end point of major bleeding, vascular complications, or cardiovascular-related death during index hospitalization. The 30-day primary end point was defined as the occurrence of the index primary end point and up to 30 days postprocedure.

Results: A total of 779 patients were included in this study. Of these patients, 27 (3.5%) patients were in group A. The index primary end point was met in 11/779 (1.4%) patients. The 30-day primary composite end point was met in 18/779 (2.3%) patients. There was no difference in the primary end point at index between group A (1/27 [3.7%]) and group B (10/752 [1.3%]; P=0.3155) and no difference in the 30-day primary composite end point between group A (2/27 [7.4%]) and group B (16/752 [2.1%]; P=0.1313). Multivariable analysis showed that a low creatinine clearance (odds ratio [OR] =0.56; P=0.0200) and underweight patients (<60 kg; OR =3.94; P=0.0300) were independent predictors of the 30-day primary composite end point but not oral anticoagulation (P=0.1500).

Conclusion: Patients on OAC did not have higher 30-day major adverse events than those who were not anticoagulated at index procedure.

Keywords: access site, common femoral artery, complications, oral anticoagulant

Introduction

Femoral artery access remains the most commonly used arterial access during coronary angiography and intervention despite an increase in radial procedures.[1,2] Femoral access complications remain infrequent, ranging from <1% to 17% of procedures.[3–7] It is not uncommon to see patients presenting to the cardiac catheterization laboratory on oral anticoagulant (OAC) fully or partially anticoagulated and undergoing common femoral artery (CFA) access.[8] Several new OAC (NOACs; oral Xa and thrombin inhibitors) have emerged within the past 3–6 years and are now an alternative to warfarin in treating patients with nonvalvular atrial fibrillation or venous thromboembolic

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disease.[9] Some data suggest that coronary procedures can be performed safely with uninterrupted OAC at the time of the index procedure.[10]

In this study, we investigated whether orally anticoagulated patients have a higher risk of femoral access site complications when compared to patients who are not anticoagulated with OAC during coronary procedures.

Methods

We retrospectively reviewed data from 779 consecutive patients who underwent a cardiac procedure (diagnostic or interventional) at a tertiary medical center. Patients were identified from the cardiac catheterization procedural log. Medical records were reviewed by dedicated research assistants, and data entry was audited by a Clinical Research Associate. The study was approved by the Genesis Health System Institutional Review Board at the medical center. Informed consent by patients to review their medical records was waived by the same institutional review board due to the retrospective nature of the study and the large number of patients included that made it impractical or impossible to obtain informed consent from patients. All investigators signed a patient confidentiality agreement with the medical center.

Patients were considered (group A) fully or partially anticoagulated if they had an international normalized ratio (INR) $\geq$1.6 on the day of the procedure or were on warfarin or NOAC within 48 h and 24 h of the procedure, respectively. The nonanticoagulated group (group B) had an INR <1.6 or have stopped their warfarin and NOAC >48 h and >24 h preprocedure, respectively. Non-CFA and bilateral CFA accesses were excluded. Radial procedures were excluded as they are performed infrequently in our medical center.

The index primary end point of the study was defined as the composite end point of major bleeding, vascular complications (arteriovenous (AV) fistula or pseudoaneurysm), or cardiovascular death during index hospitalization. The 30-day primary end point was defined as the occurrence of the index primary end point and up to 30 days postprocedure. Other secondary end points included the following major adverse events: major bleeding, total death, cardiac death, vascular complications, including AV fistula and pseudoaneurysm, stroke (hemorrhagic or embolic), and myocardial infarction. Demographic, clinical, and procedural angiographic variables were collected (Table 1).

Major bleeding was defined as a drop of 3 units of hemoglobin or transfusion of 2 units of blood with a clear

Table 1 Descriptive analysis

Baseline variables	n	Mean ± SD
Age (years)	779	65.6±12.2
Body mass index (kg/m²)		
Male	486	31.2±6.5
Female	293	31.3±7.7
Creatinine clearance (mL/min)		
Male	486	105.1±48.7
Female	293	82.8±42.6
International normalized ratio	51	1.7±1.2
Activated clotting times (s)	193	259.8±65.7
Procedure time (min)	778	52.1±49.7
Fluoroscopy time (min)	776	15.2±17.9
Contrast used (mL)	777	180.4±111.5
Systolic blood pressure when sheath removed (mmHg)	767	130.5±22.3
Intraprocedural heparin (units per kg)	296	94.1±47

	n	n'	%
Male	779	486	62.4
Age >75 (years)	779	184	23.6
Weight <60 kg	779	50	6.4
Hyperlipidemia	779	590	75.7
Hypertension	779	593	76.1
Diabetes mellitus	779	282	36.2
History of smoking	779	445	57.1
History of heart failure	779	68	8.7
History of atrial fibrillation	779	83	10.7
History of myocardial infarction	779	145	18.6
Systolic blood pressure (>140/90 mmHg) after sheath is removed	779	85	10.9
Sheath size	802		
6 French		428	53.4
8 French		363	45.3
Others		11	1.3
Method of hemostasis	802		
Closure device		567	70.7
Closure device and manual hemostasis		219	27.3
Manual hemostasis		12	1.5
Others		4	0.5
Type of closure device	802		
Perclose		557	69.4
Angioseal		221	27.6
Others		13	2.3
Not applicable		11	1.6
Antiplatelet therapy during procedure	779		
None		19	2.4
Mono antiplatelet		202	25.9
Dual antiplatelet		554	71.1
Others		4	0.5
Oral anticoagulation during procedure	779		
Anticoagulated (group A)		27	3.5
Not anticoagulated (group B)		752	96.5
Intraprocedural parenteral anticoagulation	779		
None		315	40.4

(*Continued*)

Table 1 (*Continued*)

Baseline variables	n	n′	%
Bivalirudin		165	21.2
Heparin		273	35.0
Heparin and bivalirudin		19	2.4
GpIIb/IIIa inhibitors and heparin		6	0.8
GpIIb/IIIa inhibitors and heparin and bivalirudin	779	1	0.1
Procedure urgency	779		
Elective		479	61.5
Urgent		233	29.9
Emergent		67	8.6
Prolonged procedure time (>90 min)	779	98	12.6
Low hemoglobin <10 g per dL preprocedure	779	27	3.5

Abbreviation: SD, standard deviation.

source of bleed: intracranial bleed or retroperitoneal bleed. Myocardial infarction was defined as the presence of 2 of the following: rise in troponin and presence of chest pain or ST segment elevation. Clinically relevant nonmajor bleed was defined as the occurrence of a bleed that required an intervention (stopping the OAC or extending hospital stay or admission) without meeting the definition of a major bleed.

Statistical analysis

Descriptive analysis of all variables was performed using mean ± standard deviation for continuous variables and percentages for dichotomous variables. Independent samples *t*-test was used for continuous variables and Fisher's exact testing for dichotomous variables. Bivariate analysis was used to compare Group A (anticoagulated) and Group B (not anticoagulated) and the unadjusted differences between subjects who met the 30-day primary composite endpoint versus subject who did not. Binary logistic regression analysis with backward elimination was performed with modeling for gender, low body weight (<60 kg), preprocedural hemoglobin, creatinine clearance (CrCl), activated clotting time, fluoroscopy time, body mass index (BMI), heparin dose/weight (kg), prolonged procedure time (>90 min), urgency of procedure, group A (vs B), heparin, and bivalirudin. Collinearity existed between prolonged procedure time and fluoroscopy time; prolonged procedure time was selected for modeling. CrCl, activated clotting time, and BMI were transformed using Johnson transformation due to nonnormality. Interactions between variables were explored with no significance. Hosmer–Lemeshow goodness of fit test was used for model determination (*P*-value >0.05). Minitab 17 and Cytel Studio 11 were used to conduct the analysis.

Results

Demographic and clinical characteristics

A total of 779 patients were included in this study (mean age 65.6±12.2 years, males 62.4%). Of these patients, 27 (3.5%) patients were in group A. Table 1 describes patients' demographic and clinical characteristics. Notably, 464/779 (59.6%) underwent an interventional procedure and received intraprocedural anticoagulation with either bivalirudin (21.2%) or heparin (35.0%) or both (2.4%). GpIIb/IIIa inhibitors were rarely used (0.9%). Closure devices were used in most patients (98.0%), predominantly Perclose (69.0%) followed by Angioseal (27.3%).

Outcomes

The index primary end point was met in 11/779 (1.4%) patients. All adverse events at index procedure were seen in 25/779 (3.2%) patients. These were adjudicated to be definitely or maybe related to access site in 7/25 (28.0%) and procedure related in 12/25 (48.0%). There was no difference in the primary composite end point at index between group A (1/27 [3.7%]) and group B (10/752 [1.3%]; *P*=0.3155). There was also no difference in the total adverse events at index between group A (3/27 [3.7%]) and group B (22/752 [2.9%]; *P*=0.6391).

The 30-day primary composite end point (Table 2) was met in 18/779 (2.3%) patients. All adverse events at the 30-day postprocedure were seen in 43/779 (5.5%) patients. These were adjudicated to be definitely or maybe related to access site in 7/42 (17.9%) and procedure related in 14/42 (48.3%). There was no difference in the 30-day primary composite end point between group A (2/27 [7.4%]) and group B (16/752 [2.1%]; *P*=0.1313). There was also no difference in the total adverse events at 30 days between group A (4/27 [14.8%]) and group B (39/752 [5.2%]; *P*=1.000).

In bivariate analysis (Table 3), the 30-day primary end point was significantly associated with female gender (*P*=0.0481), weight <60 kg (*P*=0.0040), low hemoglobin at baseline (*P*=0.0410), reduced CrCl (*P*=0.0001), high activated clotting time (ACT) (*P*=0.0150), high intraprocedural heparin dose (units per kg; *P*=0.0110), and high BMI (*P*=0.0040) but not group A versus group B. There was also no association between the type of coronary procedure done (cardiac catheterization vs intervention) and the primary adverse event at the time of the procedure (0.95% and 1.72%, respectively, *P*=0.5393) or at 1 month (*P*=1.000). However, patients who underwent an intervention in group B had a higher primary adverse event at 1 month when compared to cardiac catheterization patients in group B.

Table 2 Adverse events in orally anticoagulated (group A) versus nonanticoagulated (group B) patients

Adverse events	Group A	Group B	Total	*P*-value
Index adverse events	n=27	n=752	n=779	
Major bleeding	1	7	8	
Clinically relevant nonmajor bleed	0	3	3	
Noncardiovascular death	0	3	3	
Cardiac death	2	6	8	
Vascular complications	0	3	3	
Total adverse events, n (%)	3 (11.1%)	22 (2.9%)	25 (3.2%)	0.7500
Adverse events maybe or definitely related to access site			7/25 (28%)	
Adverse events maybe or definitely related to procedure			12/25 (48%)	
Primary composite endpoint at index, (major bleeding, vascular complications, and cardiac death), n (%)	1 (3.7%)	10 (1.3%)	11 (1.4%)	0.3200
30-day adverse events	n=27	n=752	n=779	
Major bleeding	2	10	12	
Clinically relevant nonmajor bleed	0	3	3	
Noncardiovascular death	0	3	3	
Cardiac death	2	7	9	
Stroke	0	3	3	
Myocardial infarction	0	7	7	
Vascular complications	0	6	6	
Total adverse events, n (%)	4 (14.8%)	39 (5.2%)	43 (5.5%)	0.6300
Adverse events maybe or definitely related to access site			9/43 (20.9%)	
Adverse events maybe or definitely related to procedure			15/43 (34.9%)	
30-day primary composite end point, (major bleeding, vascular complications, and cardiac death), n (%)	2 (7.4%)	16 (2.1%)	18 (2.3%)	0.1300

Multivariable analysis (Table 4) using various models showed that a low CrCl (odds ratio [OR] 0.56, *P*=0.0200) and underweight patients (<60 kg; OR 3.94, *P*=0.0300) were independent predictors of the 30-day primary composite end point but not oral anticoagulation (*P*=0.15). On the other hand, a low hemoglobin preprocedure (OR 0.65, *P*=0.0140), emergent/urgent procedure (OR 8.9, *P*<0.0000), a prolonged procedure time (OR 12.08, *P*=0.0010), and

Table 3 Unadjusted differences between subjects who met the 30-day primary composite endpoint versus subjects who did not

Variables	Total	No end point met	30-day primary end point met	*P*-value
Gender	n=779			
Female	293	282 (36.5%)	11 (61.1%)	0.0481
Male	486	479 (61.5%)	7 (38.9%)	
Weight	n=779			
<60 kg	729	716 (91.9%)	13 (72.2%)	0.0040
≥60 kg	50	45 (5.8%)	5 (27.8%)	
Access site-related complications	n=43			
Unrelated	34	24 (92.3%)	10 (58.8%)	0.0115
Maybe and definite	9	2 (7.7%)	7 (41.2%)	
Procedure-related complications	n=42			
Unrelated	26	20 (83.3%)	6 (33.3%)	0.0014
Maybe and definite	16	4 (16.7%)	12 (66.7%)	
Coronary procedure	n=779			
Cardiac catheterization	315	309 (40.6%)	6 (33.3%)	0.6318
Cardiac intervention	464	452 (59.4%)	12 (66.7%)	
Preprocedure hemoglobin (g/dL)	747	729	18	0.0410
Creatinine clearance (mL/min)	771	753	18	0.0001
Activated clotting time (s)	193	185	8	0.0150
Fluoroscopy time (min)	776	758	18	0.0230
Body mass index (kg/m²)	779	761	18	0.0040
Heparin/weight (units per kg)	296	285	11	0.0110

Table 4 Logistic regression analysis for predictors of adverse events

Variables	Odds ratio (OR)	95% OR confidence interval	P-value
Analysis for predictors of 30-day primary composite end point			
Transformed creatinine clearance	0.56	0.33, 0.92	0.0200
Weight <60 (vs >60) kg	3.94	1.26, 12.37	0.0300
Group A (vs B)	2.12	0.80, 17.93	0.1500
Analysis for predictors of 30-day composite primary and secondary events			
Transformed hemoglobin preprocedure	0.65	0.46, 0.92	0.0140
Group A (vs B)	3.82	1.15, 12.68	0.0500
Urgency of procedure (emergent/urgent vs elective)	8.9	3.61, 21.91	<0.0000
Procedure time	12.08	3.29, 44.30	0.0010

orally anticoagulated patients (OR 3.82, P=0.0500) were independent predictors of the 30-day composite primary and secondary end points.

Discussion

Adverse events during index coronary angiography occurred in 3.7% of patients. This is within the reported range of access site complications. In multivariate analysis, irrespective of the intraprocedural anticoagulant, patients with uninterrupted anticoagulation with OAC did not have an increase in the composite primary end point of major bleeding, vascular complications (AV fistula or pseudoaneurysm), or cardiovascular death during their index hospitalization and up to 30 days when compared to patients who were not anticoagulated with OAC.

These data, however, do not apply to patients who receive lytic therapy (as none of our patients had received a thrombolytic) or GPIIb/IIIa inhibitors (<1% of patients in our cohort).[11] Furthermore, these data are in the setting of the majority of patients receiving a closure device and, therefore, cannot be extended to those who undergo hemostasis with manual compression. There are conflicting data on the value of vascular closure devices in reducing complications postfemoral arterial access in patients undergoing cardiac procedures.[12–15] Recent data, however, seem to favor closure devices in reducing complications postcardiac diagnostic or interventional procedures.[14,15] Finally, no radial approach patients were included in this study (limited use of radial in our laboratory). Recent studies have shown that both radial and femoral approaches were safe after percutaneous coronary intervention but a radial approach had less vascular complications.[2,16] On the other hand, a femoral approach with vascular closure device (Angioseal) was noninferior to

a radial approach in reducing postcardiac procedure complications.[17] However, studies have shown that patients with uninterrupted warfarin undergoing radial approach had less vascular complications.[18,19]

In this study, univariate analysis indicated that the higher the units per kilogram of unfractionated heparin administered intraprocedurally, the higher the primary composite adverse end points. Intraprocedural antithrombotic therapy has been shown to increase the risk of vascular complications in patients who are on warfarin irrespective of the degree of anticoagulation.[20] Multivariate analysis, however, showed that intraprocedural heparin, when adjusted for CrCl and underweight patients (<60 kg), did not predict adverse events. The presence of renal failure is a strong predictor of adverse events postcardiac intervention.[21,22] In a study of 8,521 patients evaluating the relationship between glomerular filtration rate (GFR) and all-cause mortality, there was a decline in survival postcatheterization that correlated with a decline in GFR. In this study, for every 10-unit decrease in GFR, there was ~17.2% relative increase in mortality risk. This is consistent with the findings in this study that showed that an increase in CrCl reduces the likelihood of occurrence of the 30-day composite end points of major bleeding, vascular complications, and cardiovascular death (OR 0.56). Also, several studies have shown that a high or low BMI correlate with vascular complications.[3–5,7] In our study, a low weight of <60 kg was an independent predictor of complications in orally anticoagulated patients.

A lower preprocedural hemoglobin, OAC, a longer procedure time, and an urgent/emergent procedure independently predicted the combined 30-day adverse events (major bleeding, cardiac and noncardiac death, stroke, myocardial infarction, and vascular complications). These events are driven by death, myocardial infarction, and stroke and likely reflect a high-risk patient population with more unstable symptoms and requiring prolonged procedures.[23,24]

Limitation of the study

This is a retrospective study and therefore selection bias cannot be ruled out. This, however, was addressed by including all consecutive patients with the exception of excluding those with bilateral CFA and non-CFA access sites (small number of patients in our center). Therefore, data in this study do not apply to radial procedures. Radial access appears to be safe in patients actively on anticoagulation and is now becoming more widely adopted in the US. Finally, this study needs to be verified in a larger registry of patients on anticoagulation as the overall number of anticoagulated patients in this study is relatively small and with low number of patients reaching end points.

Conclusion

Independent predictors of the combined end points of major bleeding, vascular complications, or cardiovascular death at index or up to 30 days in patients undergoing coronary procedures are low weight (<60 kg) and renal insufficiency but not OAC. These conclusions are limited to patients undergoing femoral vascular access and not receiving GPIIb/IIIa inhibitors or lytic therapy.

Disclosure

The authors report no conflicts of interest in this work.

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