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Risk Factors for Postoperative Puncture Site Bleeding after Interventional Treatment of Cerebrovascular Disease via Common Femoral Artery Puncture: A Retrospective Analysis of 710 Cases

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This study aimed to identify the risk factors associated with puncture site bleeding following percutaneous puncture of the common femoral artery during interventional treatment of cerebrovascular disease (CVD). A retrospective analysis was conducted on 710 patients who underwent interventional treatment for CVD via femoral artery puncture. Among them, 26 individuals (3.66%) experienced bleeding at the femoral artery puncture site. Binary logistic regression analysis was performed to identify risk factors for puncture site bleeding. The impact of salt bag compression on postoperative bleeding was evaluated in patients with intermediate to high bleeding risk scores. The bleeding group showed higher blood pressure, lower platelet counts, longer prothrombin time and activated partial thromboplastin time, as well as a higher prevalence of larger vascular sheath sizes and variations in the timing of anti-coagulant and anti-platelet therapy administration. The bleeding risk score was higher in the bleeding group, indicating its predictive value for bleeding risk. Higher bleeding risk score, unstable blood pressure, repeated puncture, and serious vascular conditions were significant risk factors for puncture site bleeding. Application of salt bag compression for a duration of 2 hours reduced postoperative puncture site bleeding in patients with intermediate to high bleeding risk scores. Our study identified several significant risk factors for puncture site bleeding after cerebral vascular intervention via femoral artery puncture, including the bleeding risk score, blood pressure, repeated puncture, and vascular conditions. Implementing salt bag compression as a preventive measure can help mitigate bleeding complications in these high-risk patients.

Keywords: femoral artery puncture; interventional surgery; pressure bag application; puncture site bleeding; risk factors
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Introduction

Cerebrovascular diseases (CVD) encompass a range of conditions affecting the blood vessels that supply the brain and are a leading cause of death and neurologic disability (Winkler et al. 2022). Ischemic stroke, hemorrhagic stroke, and transient ischemic attack (TIA) are common forms of CVD (Oliveira and Sampaio Rocha-Filho 2019; Johnston et al. 2021). CVD is a significant contributor to cognitive impairment and dementia, particularly among the elderly population (Koueik et al. 2023). Interventional treatments, such as thrombolysis (Faizy et al. 2023), angioplasty (Kellogg et al. 1998), stent implantation (Wang et al. 2020), embolization (Raymond et al. 2023), and aneurysm clipping (Eun and Park 2023), have emerged as essential options for managing CVD. These procedures, typically performed under local anesthesia, offer advantages over traditional surgical methods, including shorter hospital stays, faster recovery times, and reduced complications. Interventional treatment is often considered as a first-line approach for stroke patients who are ineligible for thrombolytic therapy or have failed other treatment modalities (Higashida 2005;

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Marto et al. 2022).

Among the different routes for interventional procedures, femoral artery puncture is commonly the preferred due to its high success rate, thick and straight structure, and relative stability, compared to the radial artery puncture which is less invasive but more prone to spasm and rupture (Chen et al. 2021). The percutaneous puncture of the common femoral artery is widely used across various medical fields, including vascular surgery, cardiology, interventional radiology, and neuroradiology (Uhl et al. 2022). To minimize access site complications during femoral artery puncture, the recommended puncture site is typically located between the common femoral artery bifurcation and 1-2 cm below the inguinal ligament (Kim et al. 2018). Minimally invasive interventional treatments for CVD often involve catheter insertion through the groin into the femoral artery, providing access to the brain without the need for open surgery (Uno et al. 2023), which is particularly advantageous in the treatment of acute ischemic stroke where time is critical for the removal of blood clots obstructing cerebral blood flow (Kobayashi et al. 2022).

Nevertheless, femoral artery puncture carries the risk of bleeding at the puncture site (Chisci et al. 2011). Puncture site bleeding, as one of the femoral access site complications, can have severe consequences such as prolonged hospitalization, increased medical costs, and higher mortality rates (Ozono et al. 2020; Akioka et al. 2022). Therefore, the prevention of puncture site bleeding is crucial to enhance the safety and effectiveness of interventional CVD treatment. The purpose of this study is to identify risk factors associated with puncture site bleeding after femoral artery puncture during interventional treatment of CVD and evaluate the effectiveness of a preventive strategy based on these risk factors. The findings of this study have the potential to improve early diagnosis and treatment, prevent further brain damage, and enhance outcomes for CVD patients.

Methods

Ethical statement

Research involving human participants, human material, or human data, were performed in accordance with the Declaration of Helsinki. This study was conducted with approval from the ethics committees of Hunan Provincial People's Hospital (The First-Affiliated Hospital of Hunan Normal University). Informed consent was waived due to the study's retrospective nature.

Participants

This retrospective study included a total of 710 CVD patients who underwent interventional treatment via femoral artery puncture consecutively at our hospital between January 2018 and December 2022. The inclusion criteria were as follows: 1) patients with CVD (such as stroke, intracerebral hemorrhage, subarachnoid hemorrhage, carotid artery stenosis/occlusion, cerebral arteriovenous malformation, etc.) who underwent interventional surgery via femoral artery puncture; 2) adult patients aged 18 years or older; and 3) patients with complete clinical data. The exclusion criteria were: 1) patients who did not meet the age requirements of the study; and 2) patients with severe renal insufficiency, cancer, severe infectious diseases, or other conditions that could not tolerate surgery. All operators who performed the femoral artery punctures were surgeons from the same group within the Department of Interventional Vascular Surgery. It is important to note that these operators were equally experienced in interventions involving femoral access. Out of the 710 patients, 26 (3.66%) experienced puncture site bleeding and were classified into the bleeding group, while 684 patients (96.34%) did not experience bleeding and were classified into the non-bleeding group. Puncture site bleeding was defined as the occurrence of bleeding at the site of femoral artery puncture, with a bleeding volume greater than 10 mL or the presence of a subcutaneous hematoma. After the puncture sheath removal, the doctor should manually press the puncture point for 10-20 minutes according to the size of the vascular sheath, and then change the elastic bandage to press the puncture point.

Data collection

Data collection involved gathering general information, including sex and age (in year), use of closure device, time of limb immobilization (in hours), repeated puncture (number of times), and sheath size (in French), and bleeding risk score were collected for each patient. Body mass index (BMI, calculated as weight in kilograms divided by height in meters squared, kg/m^2) was also recorded. Vascular conditions were assessed using digital subtraction angiography (DSA). Repeated puncture referred to the act of performing multiple punctures into the femoral artery during interventional treatment of cerebrovascular disease. It indicated that the operators had to make more than one attempt to access the femoral artery.

Risk score and factors for femoral artery puncture site bleeding

A risk assessment tool designated by our hospital was utilized for femoral artery puncture bleeding to evaluate the possibility of bleeding after the procedure (Table 1). This assessment involves evaluating two main factors: physiological and coagulation factors. Physiological factors take into account various aspects such as consciousness level, age, systolic blood pressure (SBP) and diastolic blood pressure (DBP) on the day of the procedure (mmHg), body mass index (BMI), and local vascular condition. Coagulation factors encompass parameters including thromboelastography, prothrombin time (PT) in seconds, activated partial thromboplastin time (APTT) in seconds, international normalized ratio (INR), platelet count, and the duration of anticoagulant or antiplatelet therapy in days. Each factor is also assigned a score ranging from 0 to 3. The total score obtained from adding up the individual

Table 1. Risk score and factors for femoral artery puncture site bleeding.

Risk factors	Evaluation Criteria	3 points	2 points	1 point	0 points
Physical factors	Altered mental status	Altered consciousness/agitation, inability to cooperate	Alert	Alert	Alert
	Age (year)	≥ 70	65-69	60-64	< 60
	Preoperative BP (mmHg)	SBP ≥ 180 or DBP ≥ 110	SBP: 160-179 or DBP: 100-109	SBP: 140-159 or DBP: 90-99	SBP: < 140 or DBP: < 90
	BMI (kg/m^2)	≥ 28	24-27.9	≤ 18.5	18.6-23.9
	Local Vascular Conditions	History of lower limb arterial disease; or intraoperative imaging showing femoral artery sclerosis/anomaly	Diminished dorsalis pedis pulse or skin color/temperature changes	-	-
Coagulation factors	Thromboelastography (Comprehensive parameter: −3.0 to 3.0)	< 3.0	-	-	-
	PT (s)	≥ 30	23-29	18-22	≤ 17
	APTT (s)	≥ 70	56-69	47-55	≤ 46
	INR	≥ 2.5	2.0-2.49	1.60-1.99	≤ 1.59
	Platelets	≤ 50	51-75	76-99	≥ 100
	Anticoagulant/Antiplatelet therapy	> 7 days	3-7 days	< 3 days	None

SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio.

scores determines the risk level of post-puncture bleeding. A total score of ≤ 4 indicates a low risk, a score of 5-9 indicates a moderate risk, and a score ≥ 10 indicates a high risk of bleeding.

Statistical analysis

Statistical analysis was conducted using SPSS version 20.0. Descriptive statistics were employed to analyze the clinical characteristics of patients. Categorical variables were compared using the χ^2 test and Fisher's exact test (two-sided). The distribution of continuous variables was assessed using the 1-sample Kolmogorov-Smirnov and Shapiro-Wilk tests. The Mann-Whitney U test was utilized to compare two independent samples (presented as median ± interquartile range, IQR) when the data did not follow a normal distribution, while the t-test was used for normally distributed data (presented as mean ± standard deviation, SD). Receiver operating characteristic (ROC) analysis was performed to determine the diagnostic accuracy of the bleeding risk score in identifying cases of bleeding at the femoral artery puncture site. A binary logistic regression model was constructed to account for potential confounding factors related to postoperative puncture site bleeding. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and statistical significance was defined as $P < 0.05$.

Results

A comparison between the non-bleeding group and the bleeding group in terms of various factors related to femoral artery puncture site bleeding

As shown in Table 2, there was no significant difference in sex distribution (Fisher's exact test, $P = 0.359$) or average age (Independent *t*-test, $P = 0.662$). However, the bleeding group had higher blood pressure, lower platelet counts, and longer PT and APTT, all of which were statistically significant (Independent *t*-test, all $P < 0.05$), indicating that these factors were associated with a higher likelihood of bleeding at the femoral artery puncture site. The bleeding group also had a higher prevalence of larger sheath sizes and a different timing of anticoagulant and antiplatelet therapy administration, both of which were statistically significant (χ^2 test, both $P < 0.05$). There were no significant differences in the use of closure devices, duration of sheath insertion, or post-procedural bed rest time between the two groups (all $P > 0.05$).

Comparison of bleeding risk score between the bleeding and non-bleeding groups

We conducted a comparison of bleeding risk scores between the bleeding and non-bleeding groups. Our findings revealed that the bleeding group exhibited higher scores in various factors including preoperative blood pressure, vascular conditions, PT, platelet count, as well as the administration of anticoagulant and antiplatelet therapy (all $P < 0.05$, Mann-Whitney U test, Fig. 1A). Notably, the total score of the bleeding group (median: 10, IQR: 8-11) was significantly higher than that of the non-bleeding group (median: 4, IQR: 2-6, $P < 0.001$, Mann-Whitney U test). Moreover, ROC analysis revealed that the total score exhibited a diagnostic sensitivity of 84.62% and a specificity of 86.55% in accurately identifying cases of bleeding at the femoral artery puncture site. To categorize patients into bleeding or non-bleeding groups, a specified cut-off value of 7.5 was employed as a threshold (Fig. 1B).

Table 2. A comparison between the non-bleeding group and the bleeding group in terms of various factors related to femoral artery puncture site bleeding.

	Non-Bleeding Group (n = 684)	Bleeding Group (n = 26)	*P*
Sex			
Male	332 (48.5%)	15 (57.7%)	
Female	352 (51.5%)	11 (42.3%)	0.359
Age (years)	56.30 ± 13.94	54.58 ± 19.74	0.662
SBP (mmHg)	141.83 ± 20.65	176.85 ± 18.26	9.84E-17
DBP (mmHg)	81.19 ± 11.39	90.04 ± 11.16	1.08E-04
BMI (kg/m^2)	22.59 ± 4.75	24.52 ± 7.14	0.047
PT (s)	13.28 ± 4.21	15.9 ± 3.38	0.002
APTT (s)	30.07 ± 7.43	33.12 ± 8.78	0.042
INR	1.12 ± 0.55	1.16 ± 0.20	0.69
Platelets	258.65 ± 120.07	145.31 ± 81.02	1.49E-07
Sheath size			
5F	506 (74.0%)	17 (65.4%)	
6F	165 (24.1%)	5 (19.2%)	
7F	5 (0.7%)	3 (11.5%)	
8F	8 (1.2%)	1 (3.8%)	4.00E-06
Anticoagulant and antiplatelet therapy			
0 day	380 (55.6%)	8 (30.8%)	
1-2 days	160 (23.4%)	3 (11.5%)	
3-7 days	59 (8.6%)	7 (26.9%)	
> 7 days	85 (12.4%)	8 (30.8%)	1.86E-04
Sheath time (h)	1.56 ± 0.66	1.75 ± 0.85	0.167
Bed rest time (h)	12.07 ± 3.06	12.00 ± 2.94	0.909
Closure device used			
Yes	140 (20.5%)	4 (15.4%)	
No	544 (79.5%)	22 (84.6%)	0.628

Data are shown as n (%) or mean ± SD. SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio.

Binary logistic regression analysis

The results of a univariate binary regression analysis demonstrated that several factors were identified as risk factors for bleeding at the puncture site after cerebral vascular intervention via femoral artery puncture. These factors include the bleeding risk total score (OR = 1.773; 95% CI: 1.51-2.08, *P* = 2.59E-12), SBP (OR = 1.094; 95% CI: 1.07-1.12, *P* = 3.46E-11), DBP (OR = 1.077; 95% CI: 1.04-1.12, *P* = 2.04E-04), PT (OR = 1.057; 95% CI: 1.01-1.11, *P* = 0.015), and anticoagulant/antiplatelet therapy (3-7 days vs. 0 day: OR = 5.636; 95% CI: 1.97-16.12, *P* = 0.001; > 7 days vs. 0 day: OR = 4.471; 95% CI: 1.63-12.25, *P* = 0.004). Additionally, factors such as repeated puncture, larger sheath sizes, and serious vascular conditions were also identified as risk factors. These findings emphasize the importance of considering these variables in a multivariable binary regression analysis, which revealed that the bleeding risk total score, SBP, repeated puncture, and vascular conditions remained as significant risk factors for bleeding at the puncture site after cerebral vascular intervention via femoral artery puncture (Table 3).

Effect of salt bag compression on postoperative puncture site bleeding in patients with intermediate to high bleeding risk scores

We conducted an analysis to evaluate the impact of salt bag compression on postoperative puncture site bleeding in patients (n = 79) with intermediate to high bleeding risk scores. Immediately after catheterization, a total of 75 patients with intermediate to high bleeding risk scores underwent a 2-hour salt bag compression application. The patient demographics included sex (male/female: 44/31), sheath size (5F/6F/7F/8F: 70/4/0/1), duration of anticoagulant and antiplatelet therapy (0 day/1-2 days/3-7 days/> 7 days: 14/30/17/14), closure device used (yes/no: 21/54), age (60.60 ± 13.39 years), SBP (149.21 ± 20.25 mmHg), DBP (83.80 ± 10.97 mmHg), BMI (22.71 ± 7.18 kg/m^2), PT (17.20 ± 7.37 seconds), APTT (30.89 ± 7.05 seconds), INR (1.13 ± 0.21), platelets (204.75 ± 151.06) and sheath time (1.17 ± 0.42 hours). The incidence of bleeding was 4.00% in the salt bag compression group and 50.00% in the no salt bag compression group, showing a significant difference (*P* = 0.019, Fig. 2). Importantly, no adverse effects or compli-

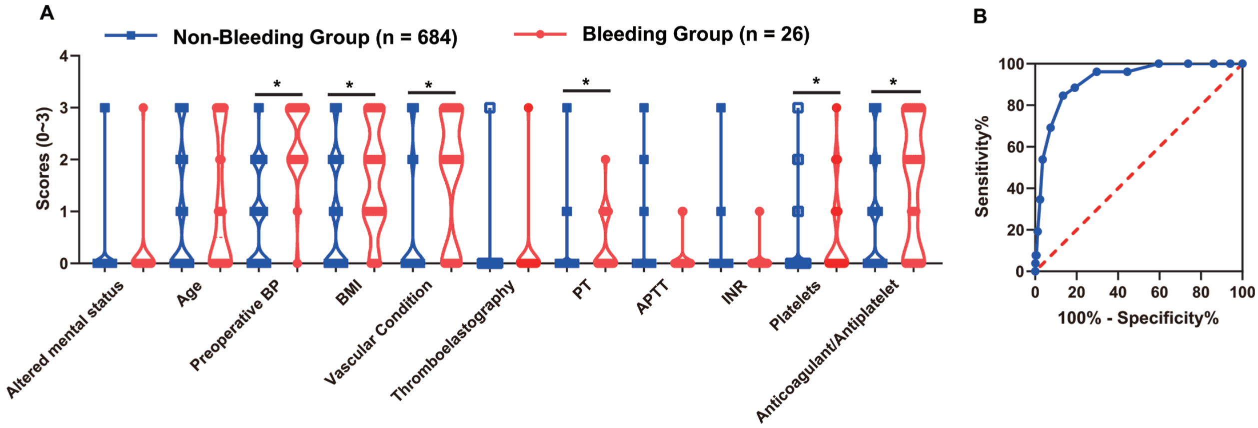

Fig. 1. Risk score and factors for femoral artery puncture site bleeding.
A. The bleeding group demonstrated higher scores for preoperative blood pressure, vascular conditions, prothrombin time (PT), platelet count, as well as the administration of anticoagulant and antiplatelet therapy compared to the non-bleeding group. *$P < 0.05$. The data were presented as median ± interquartile range (IQR) and calculated by Mann-Whitney U test. B. Receiver operating characteristic (ROC) analysis demonstrated that the total score exhibited a diagnostic sensitivity of 84.62% and a specificity of 86.55% in accurately identifying cases of bleeding at the femoral artery puncture site.

cations were observed in the patients who received salt bag compression for postoperative puncture site bleeding.

Discussion

In this study, we aimed to investigate the risk factors for puncture site bleeding after interventional treatment of CVD via femoral artery puncture and explore potential preventive measures to reduce the incidence of bleeding complications. As reported, the incidence of puncture site bleeding varies widely among different studies, for example, puncture site hemorrhage occurred in 15 patients (5.9%) after neuroendovascular treatment (Tamari et al. 2021). Being consistently, our retrospective analysis of 710 patients who underwent interventional treatment for CVD via CFA revealed that 26 patients (3.66%) experienced femoral artery puncture site bleeding.

Advancements in stent technology have introduced smaller sheath sizes, offering alternative approaches for access and closure of the common femoral arteries (Lonn et al. 2010). It is worth mentioning that the bleeding group in our study had a higher prevalence of larger sheath sizes. Larger sheath sizes have consistently been identified as a risk factor for access site complications, including bleeding. Prior studies have reported associations between sheath size and access site complications, including bleeding. For instance, Cantor et al. (2007) conducted a study in patients with acute coronary syndrome undergoing early invasive management and found that larger sheath sizes were significantly associated with higher rates of access site bleeding, non-coronary artery bypass graft-related thrombolysis in myocardial infarction (TIMI) major bleeding, and transfusion. Another randomized trial by Metz et al. (1997) demonstrated fewer femoral access site complications with 6 F sheaths compared to 7/8 F sheaths in percutaneous coronary intervention (PCI) procedures. Additionally, Madden et al. (2019) reported that percutaneous brachial artery access was associated with a 10% complication rate, with an increased risk of complications associated with increasing sheath size. Collectively, these studies suggest that larger sheath sizes pose a higher risk of access site complications, including bleeding. The mechanisms underlying this association may involve increased vascular trauma, impaired hemostasis, and the potential for more extensive tissue damage during sheath removal.

Combined anticoagulant and antiplatelet therapy use has been associated with increased bleeding risk (Tinkham et al. 2020). In our study, the bleeding group had a different timing of anticoagulant and antiplatelet therapy administration as compared to the non-bleeding group. In our study, the bleeding group exhibited a different timing of anticoagulant and antiplatelet therapy administration compared to the non-bleeding group. Interestingly, our binary logistic regression analysis did not identify anticoagulant and antiplatelet therapy administration as a significant risk factor, which contrasts some prior studies. For instance, a study of 31,836 patients who underwent neuroendovascular therapy found that the use of antiplatelet drugs was associated with a higher incidence of puncture site vascular complications, including hemorrhagic complications (Sato et al. 2014b). Conversely, Hwang et al. (2014, 2015) reported that triple antiplatelet therapy in patients with high on-treatment platelet reactivity could lead to oozing at the femoral puncture site or a local groin hematoma without any serious bleeding complications. Another retrospective review conducted by Tamari et al. (2021) involving 255 patients who underwent endovascular treatment identified patients with an activated clotting time of ≥ 300 seconds before postoperative sheath removal, those receiving triple antiplatelet therapy, or those administered postoperative heparin as being at an increased risk of puncture site hemorrhage. Furthermore, Sato et al. (2014a) reported that postprocedural puncture site hemorrhage was common with carotid artery stenting and percu-

Table 3. Univariate and multivariable binary regression analysis.

	Univariate binary regression analysis			Multivariable binary regression analysis		
	P	OR	95% CI	*P*	OR	95% CI
Sex	0.362	1.446	0.65-3.19			
Age	0.542	0.992	0.97-1.02			
Bleeding risk total score	2.59E-12	1.773	1.51-2.08	3.46E-11	1.094	1.07-1.12
Altered mental status	0.927	1.100	0.14-8.46			
SBP	3.46E-11	1.094	1.07-1.12	4.76E-04	1.082	1.04-1.13
DBP	2.04E-04	1.077	1.04-1.12	0.109	1.060	0.99-1.14
BMI	0.587	1.100	0.78-1.55	0.128	1.103	0.97-1.25
PT	0.015	1.057	1.01-1.11	0.126	1.087	0.98-1.21
APTT	0.362	1.022	0.98-1.07			
INR	0.697	1.104	0.67-1.82			
Anticoagulant/Antiplatelet therapy						
< 3 days vs. 0 day	0.865	0.891	0.23-3.4	0.217	.258	0.03-2.22
3-7 days vs. 0 day	0.001	5.636	1.97-16.12	0.954	1.067	0.12-9.55
> 7 days vs. 0 day	0.004	4.471	1.63-12.25	0.600	1.821	0.19-17.12
Repeated puncture (times)						
1 vs.0	4.57E-05	8.431	3.02-23.5	0.005	14.437	2.28-91.32
3 vs.0	2.03E-06	24.525	6.55-91.82	0.002	32.105	3.4-302.92
4 vs.0	1.69E-07	44.963	10.8-187.16	0.030	32.917	1.41-767.5
5 vs.0	1.52E-04	33.722	5.46-208.23	0.017	225.481	2.6-19,531.5
Sheath sizes						
6F vs. 5F	0.842	0.902	0.33-2.48	0.229	.317	0.05-2.06
7F vs. 5F	1.84E-04	17.859	3.94-80.9	0.259	9.267	0.19-442.71
8F vs. 5F	0.228	3.721	0.44-31.44	0.367	3.444	0.23-50.59
Duration of sheath insertion	0.169	1.437				
Vascular Conditions						
Diminished dorsalis pedis pulse or skin color/temperature changes vs. Normal	1.09E-05	9.156	3.41-24.56	1.32E-04	83.039	8.61-800.86
History of lower limb arterial disease or intraoperative imaging showing femoral artery sclerosis/anomaly vs. Normal	1.54E-04	6.612	2.49-17.59	0.007	19.691	2.22-174.49
Time of limb immobilization	0.908	0.992	0.86-1.14			
Use of closure devices	0.529	0.706	0.24-2.08			

OR, odds ratio; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; PT, prothrombin time; APTT, activated partial thromboplastin time; INR, international normalized ratio.

taneous transluminal angioplasty, which was attributed to intraoperative heparinization, preoperative administration of multiple antiplatelet agents, and large sheath size. These findings highlight both discrepancies and agreements with prior studies, indicating the need for further investigation into the relationship between anticoagulant and antiplatelet therapy administration, and bleeding risk.

Our findings also suggested that the bleeding risk total score, SBP, repeated puncture, and vascular conditions remained significant risk factors for bleeding at the puncture site. These findings highlight the importance of considering these variables when assessing the risk of bleeding in patients undergoing cerebral vascular intervention via femoral artery puncture. Similarly, Hackl et al. (2015) revealed that age, procedure duration > 45 minutes, procedures performed below the knee intervention, uncontrolled hypertension, and impaired coagulation were risk factors for puncture site complications (including bleeding) after endovascular procedures in patients with peripheral arterial disease. Increased vascular fragility and vascular lesions caused by chronic hypertension exerted by elevated blood pressure (Coutard and Osborne-Pellegrin 1991), and it might be an explanation that arterial hypertension was independently associated with the risk of access-site bleeding (bleeds or hematomas arising from the site of vascular access and those spreading from the access site to the adjacent tissues, i.e., from femoral artery puncture site to retroperitoneal space) occurring over 30 days following PCI procedure (Ndrepepa et al. 2016).

Salt bag compression refers to the application of external pressure using a salt bag or similar device at the site where a medical procedure, such as a femoral artery punc-

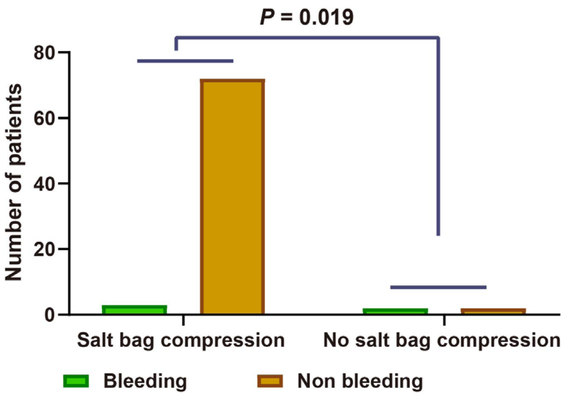

Fig. 2. Effect of salt bag compression on postoperative puncture site bleeding in patients with intermediate to high bleeding risk scores.
The data was compared using the Fisher's exact test (two-sided).

ture, was performed (King et al. 2008; Kordestani et al. 2012; Bakhshi et al. 2014). In this study, the application of salt bag compression for a duration of 2 hours significantly reduced the occurrence of postoperative puncture site bleeding in patients with intermediate to high bleeding risk scores. This finding is consistent with the study by Christensen et al. (1998) where the use of a salt bag weighing between 2.3 to 4.5 kg on the femoral access site helped decrease bleeding at the arteriotomy site. Additionally, patients who were verbally instructed to keep their leg straight and still had a significantly higher incidence of bleeding compared to those who had a salt bag applied to the femoral site (Hogan-Miller et al. 1995). These findings collectively highlight that salt bag compression provides external pressure, promoting hemostasis and minimizing bleeding complications at the puncture site.

This study has several strengths that enhance its validity and contribute to the understanding of risk factors for puncture site bleeding after cerebral vascular intervention via femoral artery puncture. Firstly, the relatively large sample size of 710 patients provides robust statistical power and increases the generalizability of the findings to a broader population. Additionally, the study employed a comprehensive analysis approach, combining descriptive statistics and binary logistic regression analysis, which allows for a thorough exploration of the risk factors associated with bleeding. Moreover, the investigation of the effect of salt bag compression on postoperative bleeding provides valuable insights into practical management strategies for patients with intermediate to high bleeding risk scores. However, it is important to consider the limitations of the study. The retrospective design introduces inherent biases and potential limitations in data collection and analysis, and the findings may be influenced by confounding factors and the accuracy of recorded information. Furthermore, the evaluation of the effect of salt bag compression was limited to a specific subgroup of patients, which restricts the generalizability of the findings to the entire population undergoing cerebral vascular intervention.

In conclusion, our study found that blood pressure, platelet counts, PT, APTT, sheath sizes, and different timing of anticoagulant and antiplatelet therapy administration were associated with bleeding at the femoral artery puncture site. The bleeding risk score was effective in predicting bleeding risk, with higher scores observed in the bleeding group. Salt bag compression for 2 hours significantly reduced postoperative puncture site bleeding in patients with intermediate to high bleeding risk scores. These findings suggest the importance of considering these factors and implementing preventive measures to reduce bleeding complications.

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Conflict of Interest

The authors declare no conflict of interest.

References

Akioka, H., Yufu, K., Harada, T., Akamine, K., Uemura, T., Takahashi, M., Nishimizu, K., Hirota, K., Ishii, Y., Kira, S., Yonezu, K., Abe, I., Tawara, K., Kondo, H., Saito, S., et al. (2022) Reduction of bleeding complications on puncture site after percutaneous coronary intervention using a 6.5-French sheathless guiding catheter. *Heart Vessels*, **37**, 954-960.

Bakhshi, F., Namjou, Z., Andishmand, A., Panabadi, A., Bagherinasab, M. & Sarebanhassanabadi, M. (2014) Effect of positioning on patient outcomes after coronary angiography: a single-blind randomized controlled trial. *J. Nurs. Res.*, **22**, 45-50.

Cantor, W.J., Mahaffey, K.W., Huang, Z., Das, P., Gulba, D.C., Glezer, S., Gallo, R., Ducas, J., Cohen, M., Antman, E.M., Langer, A., Kleiman, N.S., White, H.D., Chisholm, R.J., Harrington, R.A., et al. (2007) Bleeding complications in patients with acute coronary syndrome undergoing early invasive management can be reduced with radial access, smaller sheath sizes, and timely sheath removal. *Catheter. Cardiovasc. Interv.*, **69**, 73-83.

Chen, H.Z., Liang, W.S., Yao, W.F. & Liu, T.X. (2021) Compression methods after femoral artery puncture: a protocol for systematic review and network meta-analysis. *Medicine* (*Baltimore*), **100**, e24506.

Chisci, E., Setacci, F., Giubbolini, M., de Donato, G. & Setacci, C. (2011) Stroke and pulmonary embolism following manual and bandage compression after bleeding from a common femoral artery access site. *J. Cardiovasc. Surg.* (*Torino*), **52**, 849-851.

Christensen, B.V., Manion, R.V., Iacarella, C.L., Meyer, S.M., Cartland, J.L., Bruhn-Ding, B.J. & Wilson, R.F. (1998) Vascular complications after angiography with and without the use of sandbags. *Nurs. Res.*, **47**, 51-53.

Coutard, M. & Osborne-Pellegrin, M. (1991) Rupture of the internal elastic lamina and vascular fragility in stroke-prone spontaneously hypertensive rats. *Stroke*, **22**, 510-515.

Eun, J. & Park, I.S. (2023) Outcomes and complications of cerebral aneurysms operated on by eyebrow incision according to aneurysm type and location. *BMC Surg.*, **23**, 50.

Faizy, T.D., Broocks, G., Heit, J.J., Kniep, H., Flottmann, F., Meyer, L., Sporns, P., Hanning, U., Kaesmacher, J., Deb-Chatterji, M., Vollmuth, P., Lansberg, M.G., Albers, G.W., Fischer, U., Wintermark, M., et al. (2023) Association between intravenous thrombolysis and clinical outcomes among patients with ischemic stroke and unsuccessful mechanical reperfusion. *JAMA Netw. Open*, **6**, e2310213.

Hackl, G., Gary, T., Belaj, K., Hafner, F., Eller, P. & Brodmann, M. (2015) Risk factors for puncture site complications after endovascular procedures in patients with peripheral arterial disease. *Vasc. Endovascular Surg.*, **49**, 160-165.

Higashida, R.T. (2005) Recent advances in the interventional treatment of acute ischemic stroke. *Cerebrovasc. Dis.*, **20** Suppl 2, 140-147.

Hogan-Miller, E., Rustad, D., Sendelbach, S. & Goldenberg, I. (1995) Effects of three methods of femoral site immobilization on bleeding and comfort after coronary angiogram. *Am. J. Crit. Care*, **4**, 143-148.

Hwang, G., Huh, W., Lee, J.S., Villavicencio, J.B., Villamor, R.B. Jr., Ahn, S.Y., Kim, J., Chang, J.Y., Park, S.J., Park, N.M., Jeong, E.A. & Kwon, O.K. (2015) Standard vs modified antiplatelet preparation for preventing thromboembolic events in patients with high on-treatment platelet reactivity undergoing coil embolization for an unruptured intracranial aneurysm: a randomized clinical trial. *JAMA Neurol.*, **72**, 764-772.

Hwang, G., Kim, J.G., Song, K.S., Lee, Y.J., Villavicencio, J.B., Suroto, N.S., Park, N.M., Park, S.J., Jeong, E.A. & Kwon, O.K. (2014) Delayed ischemic stroke after stent-assisted coil placement in cerebral aneurysm: characteristics and optimal duration of preventative dual antiplatelet therapy. *Radiology*, **273**, 194-201.

Johnston, S.C., Amarenco, P., Aunes, M., Denison, H., Evans, S.R., Himmelmann, A., Jahreskog, M., James, S., Knutsson, M., Ladenvall, P., Molina, C.A., Nylander, S., Rother, J. & Wang, Y.; THALES Investigators (2021) Ischemic benefit and hemorrhage risk of ticagrelor-aspirin versus aspirin in patients with acute ischemic stroke or transient ischemic attack. *Stroke*, **52**, 3482-3489.

Kellogg, J.X., Nesbit, G.M., Clark, W.M. & Barnwell, S.L. (1998) The role of angioplasty in the treatment of cerebrovascular disease. *Neurosurgery*, **43**, 549-555; discussion 555-546.

Kim, M., Kim, M.A., Kim, H.L., Lee, W.J., Lim, W.H., Seo, J.B., Kim, S.H. & Zo, J.H. (2018) Body mass index and the risk of low femoral artery puncture in coronary angiography under fluoroscopy guidance. *Medicine* (*Baltimore*), **97**, e0070.

King, N.A., Philpott, S.J. & Leary, A. (2008) A randomized controlled trial assessing the use of compression versus vasoconstriction in the treatment of femoral hematoma occurring after percutaneous coronary intervention. *Heart Lung*, **37**, 205-210.

Kobayashi, S., Osanai, T., Fujima, N., Hamaguchi, A., Sugiyama, T., Nakamura, T., Hida, K. & Fujimura, M. (2022) Efficacy of the MRA-based road mapping of the para-aortic access route before mechanical thrombectomy in patients with acute ischemic stroke. *Cerebrovasc. Dis. Extra*, **12**, 47-52.

Kordestani, S.S., Noohi, F., Azarnik, H., Basiri, H., Hashemi, M.J., Abdi, S., Mohebi, A., Madani, M. & Nayebhabib, F. (2012) A randomized controlled trial on the hemostasis of femoral artery using topical hemostatic agent. *Clin. Appl. Thromb. Hemost.*, **18**, 501-505.

Koueik, J., Wesley, U.V. & Dempsey, R.J. (2023) Pathophysiology, cellular and molecular mechanisms of large and small vessel diseases. *Neurochem. Int.*, **164**, 105499.

Lonn, L., Larzon, T. & Van Den Berg, J.C. (2010) From puncture to closure of the common femoral artery in endovascular aortic repair. *J. Cardiovasc. Surg.* (*Torino*), **51**, 791-798.

Madden, N.J., Calligaro, K.D., Zheng, H., Troutman, D.A. & Dougherty, M.J. (2019) Outcomes of brachial artery access for endovascular interventions. *Ann. Vasc. Surg.*, **56**, 81-86.

Marto, J.P., Salerno, A., Maslias, E., Lambrou, D., Eskandari, A., Strambo, D. & Michel, P. (2022) Stroke in the stroke unit: recognition, treatment and outcomes in a single-centre cohort. *Eur. J. Neurol.*, **29**, 2674-2682.

Metz, D., Meyer, P., Touati, C., Coste, P., Petiteau, P.Y., Durand, P., Faivre, R., Lefevre, T. & Elaerts, J. (1997) Comparison of 6F with 7F and 8F guiding catheters for elective coronary angioplasty: results of a prospective, multicenter, randomized trial. *Am. Heart J.*, **134**, 131-137.

Ndrepepa, G., Groha, P., Lahmann, A.L., Lohaus, R., Cassese, S., Schulz-Schupke, S., Kufner, S., Mayer, K., Bernlochner, I., Byrne, R.A., Fusaro, M., Laugwitz, K.L., Schunkert, H. & Kastrati, A. (2016) Increased bleeding risk during percutaneous coronary interventions by arterial hypertension. *Catheter. Cardiovasc. Interv.*, **88**, 184-190.

Oliveira, F.A.A. & Sampaio Rocha-Filho, P.A. (2019) Headaches attributed to ischemic stroke and transient ischemic attack. *Headache*, **59**, 469-476.

Ozono, I., Sakamoto, S., Okazaki, T., Oshita, J., Ishii, D. & Kurisu, K. (2020) Management of post-puncture bleeding after neurointerventional procedures performed with a large-bore sheath introducer. *J. Clin. Neurosci.*, **74**, 61-64.

Raymond, J., Gentric, J.C., Magro, E., Nico, L., Bacchus, E., Klink, R., Cognard, C., Januel, A.C., Sabatier, J.F., Iancu, D., Weill, A., Roy, D., Bojanowski, M.W., Chaalala, C., Barreau, X., et al. (2023) Endovascular treatment of brain arteriovenous malformations: clinical outcomes of patients included in the registry of a pragmatic randomized trial. *J. Neurosurg.*, **138**, 1393-1402.

Sato, M., Matsumaru, Y., Sakai, N. & Yoshimura, S.; JR-NET Study Group Affiliations (2014a) Detailed analysis of puncture site vascular complications in Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2. *Neurol. Med. Chir.* (*Tokyo*), **54** Suppl 2, 17-22.

Sato, M., Matsumaru, Y., Sakai, N. & Yoshimura, S.; JR-NET Study Group Affiliations (2014b) Detailed analysis of puncture site vascular complications in Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2. *Neurol. Med. Chir.* (*Tokyo*), **54**, 17-22.

Tamari, Y., Izumi, T., Nishihori, M., Imai, T., Ito, M., Tsukada, T., Ishida, M. & Wakabayashi, T. (2021) Case-control study of postprocedural arterial puncture site hemorrhage after neuroendovascular treatment. *Nagoya J. Med. Sci.*, **83**, 125-133.

Tinkham, T.T., Vazquez, S.R., Jones, A.E. & Witt, D.M. (2020) Direct oral anticoagulant plus antiplatelet therapy: prescribing practices and bleeding outcomes. *J. Thromb. Thrombolysis*, **49**, 492-496.

Uhl, C., Hatzl, J., Meisenbacher, K., Zimmer, L., Hartmann, N. & Bockler, D. (2022) Mixed-reality-assisted puncture of the common femoral artery in a phantom model. *J. Imaging*, **8**, 47.

Uno, T., Misaki, K., Nakajima, R., Nambu, I., Yoshikawa, A., Kamide, T. & Nakada, M. (2023) Factors related to high bifurcation level of common femoral artery. *J. Stroke Cerebrovasc. Dis.*, **32**, 106976.

Wang, S., Cai, Y., Meng, Z., Zhang, X., Yang, X. & Dong, Z. (2020) Finite element simulation of stent implantation and its applications in the interventional planning for hemorrhagic cardio-cerebrovascular diseases. *Sheng Wu Yi Xue Gong Cheng Xue Za Zhi*, **37**, 974-982 (in Chinese).

Winkler, E.A., Kim, C.N., Ross, J.M., Garcia, J.H., Gil, E., Oh, I., Chen, L.Q., Wu, D., Catapano, J.S., Raygor, K., Narsinh, K., Kim, H., Weinsheimer, S., Cooke, D.L., Walcott, B.P., et al. (2022) A single-cell atlas of the normal and malformed human brain vasculature. *Science*, **375**, eabi7377.