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Elevated risk of perioperative ischemic stroke in noncardiac surgery patients with atrial fibrillation: a retrospective cohort study

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Abstract

Background Stroke is still a significant and growing challenge of global health, however, the impact of Atrial Fibrillation (AF) on the risk of perioperative stroke remains unclear.

Aim This study aims to evaluate the clinical prognostic value of AF in patients undergoing noncardiac surgery, with perioperative ischemic stroke as the primary prognostic indicator.

Methods A retrospective cohort study was conducted on patients who underwent noncardiac surgery between January 2008 and August 2019 at The First Medical Center of Chinese People's Liberation Army (PLA) General Hospital. The study included patients with a procedure duration exceeding one hour. Participants were categorized into two groups: an AF group and a non-AF group, based on the presence or absence of AF. The primary outcome was the occurrence of perioperative ischemic stroke. To determine whether AF is an independent prognostic indicator, primary and subgroup analyses were performed. Logistic regression models were used to identify risk factors. Besides, sensitivity analysis, propensity score matching (PSM) analysis were applied to mitigate potential residual confounding effects and assess the robustness of the findings.

Results The primary analysis demonstrated that patients in the AF group had a significantly higher risk of perioperative ischemic stroke (OR: 6.843; 95% CI: 3.73–11.413; $P<0.001$). Further modeling analyses confirmed a significant correlation between AF and perioperative ischemic stroke across various models: model 2 (OR: 1.789; 95% CI: 0.958–3.053; $P<0.05$), model 3 (OR: 5.121; 95% CI: 2.749–8.716; $P<0.001$), and model 4 (OR: 2.122; 95% CI: 1.123–3.677; $P<0.05$). Sensitivity analysis excluding neurosurgeries were conducted. The adjusted OR of perioperative ischemic stroke in neurosurgery patients with the AF was 1.623(95% CI: 0.359–5.165; $P=0.463$). While, the association between AF and perioperative ischemic stroke remained stable in those non-neurosurgical patients (OR: 2.154;95% CI: 1.044–3.964; $P=0.023$). After PSM adjustments, the association between AF and perioperative ischemic stroke remained significant (OR: 2.106; 95% CI: 1.003–4.159; $P<0.05$). Subgroup analyses revealed that AF significantly

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increased the risk of perioperative ischemic stroke, particularly in males, patients aged ≥ 60.5 years, those with an ASA score ≥ 3, those with hypertension, and those not on antiplatelet medication.

Conclusion Atrial fibrillation is an independent prognostic risk factor for perioperative ischemic stroke in patients undergoing noncardiac surgery, especially pronounced in specific subgroups, including males, elderly patients, those with high ASA scores, with hypertension, and not receiving antiplatelet therapy. These findings emphasize the need for heightened awareness and prompt clinical intervention in these high-risk patients.

Keywords Atrial fibrillation (AF), Perioperative ischemic stroke, Noncardiac surgery, Prognostic indicator, Risk factor, Propensity score matching (PSM)

Introduction

Stroke represents a significant and growing global health challenge, responsible for approximately 6.2 million deaths annually, positioning cerebrovascular disease as the leading cause of premature death and disability worldwide [1–3]. Perioperative stroke, a severe complication occurring either during surgery or within 30 days post-operation, has a prevalence ranging from 0.08% to 10% [4, 5]. Recent studies indicate that the mortality associated with perioperative stroke is alarmingly high, with rates between 20 and 60%, depending on patient demographics, the type of stroke, and the nature of the surgery [1]. Compared to strokes that occur within the general community, the prognosis of perioperative stroke is significantly worse, with a twofold increase in 30-day mortality, higher rates of disability, and a diminished quality of life among survivors [1, 6]. Consequently, preventing and treating perioperative stroke is crucial to improving surgical outcomes.

Cardioembolism is a leading cause of acute ischemic stroke (AIS), with atrial fibrillation (AF) being the predominant source of cardioembolic stroke [7, 8]. AF, characterized by irregular heart rhythms, remains a critical public health concern due to its association with an elevated risk of stroke and systemic embolism [9]. In the United States, the number of AF patients is estimated to be between three and six million, with projections suggesting an increase to 6 to 16 million by 2050 [10]. Without appropriate treatment, approximately one in three AF patients may eventually suffer an ischemic stroke [11]. AF substantially increases the risk of ischemic stroke by a factor of 3 to 5, and it is estimated to account for 15% of all strokes globally [12].

A meta-analysis has demonstrated that the prophylactic reduction of AF can decrease the incidence of perioperative stroke [13]. Villareal and colleagues found that postoperative AF is associated with an increased risk of early stroke [14]. Additionally, perioperative AF has been linked to a heightened long-term risk of ischemic stroke, particularly following noncardiac surgery [15]. However, there is a lack of research examining the relationship between AF and the occurrence of perioperative stroke across various types of surgeries within large, population-based samples in China.

In this study, we present the first systematic investigation exploring the correlation between AF, as a categorical variable, and the risk of perioperative ischemic stroke. This retrospective study includes 223,415 Chinese patients who underwent noncardiac surgery, aiming to elucidate the complex relationship between AF and perioperative ischemic stroke. Given the distinct ethnic differences in AF prevalence and the lack of studies addressing this issue in the Chinese surgical population, our research provides essential insights that may enhance the global understanding of perioperative ischemic stroke risks.

Materials and methods

The study protocol was reviewed and approved by the Institutional Ethics Committee of the Chinese People's Liberation Army General Hospital (Ethics No. S2021-493–01). The requirement for informed consent was waived. This article adheres to the principles outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.

Inclusion and exclusion criteria

Patients who underwent noncardiac surgery at the General Hospital of the People's Liberation Army between January 2008 and August 2019 were initially screened using a perioperative retrospective database. The inclusion criteria were as follows: (1) noncardiac surgery; (2) general anesthesia; (3) operative time > 60 min; and (4) age ≥ 18 years. Patients were excluded if they met the following criteria: (1) American Society of Anesthesiologists (ASA) class V; (2) surgery under regional anesthesia; (3) missing clinical data; (4) age < 18 years; or (5) duration of surgery ≤ 60 min. For patients who underwent multiple surgeries during the study period, only

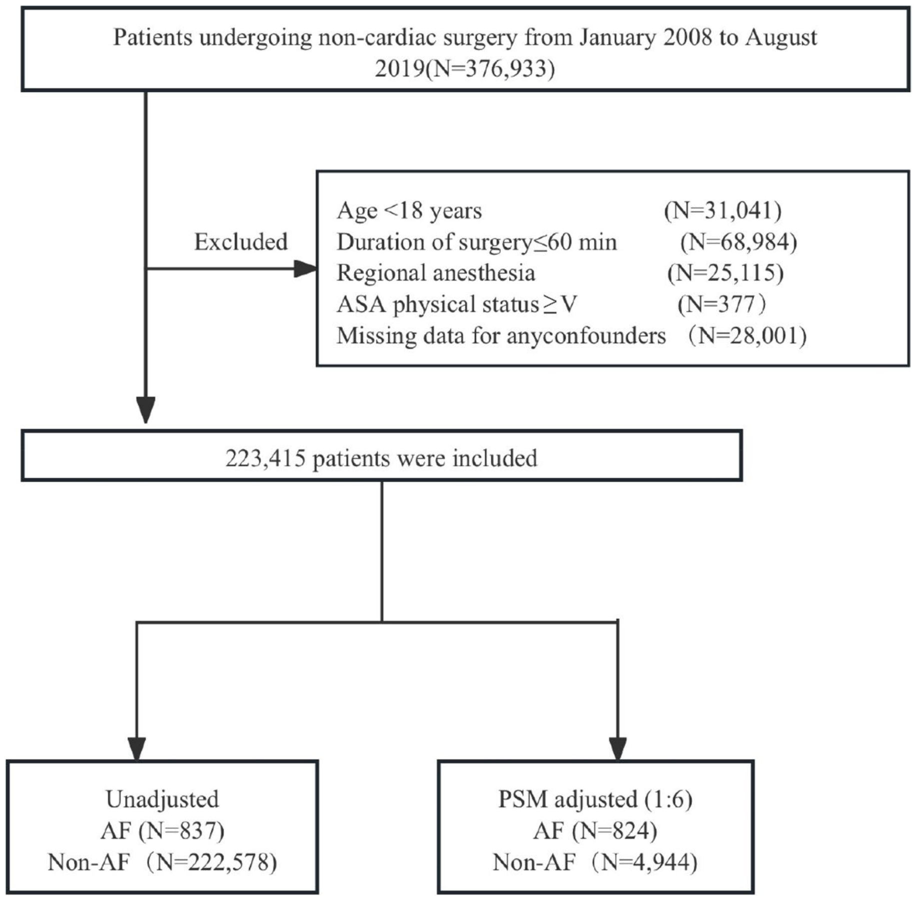

Fig. 1 Flowchart

the first eligible surgery was considered. A flow chart of the patient selection process is provided in Fig. 1.

Clinical outcome

The primary outcome was perioperative ischemic stroke, defined as an episode of neurological dysfunction (e.g., motor, sensory, or cognitive impairment) occurring within 30 days following surgery, resulting from a focal cerebral, spinal cord, or retinal infarction [16].

Definition of variables and data collection

Patients were classified based on the occurrence of atrial fibrillation (AF), with AF coded as 1 and non-AF as 0. For further analysis, AF was treated as a categorical variable. Preoperative covariates of interest included age, gender, body mass index (BMI), ASA classification, hypertension, diabetes mellitus, previous perioperative ischemic stroke, coronary artery disease, valvular heart disease, peripheral vascular disease, renal dysfunction, malignant tumor, and preoperative use of β-blockers, aspirin, ACE inhibitors (ACEI), angiotensin receptor blockers (ARB), or steroid hormones. Additionally, preoperative laboratory data such as hemoglobin, serum albumin, total bilirubin, prothrombin time (PT), glucose, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and fibrinogen-to-albumin ratio (FAR) were collected. Intraoperative data included mean arterial pressure (MAP), surgical technique, duration of surgery, estimated blood loss, intraoperative hypotension (MAP ≤ 65 mmHg), administration of crystalloids or colloids, blood product transfusion, use of glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs), cumulative opioid intake, and use of volatile anesthetics.

Propensity score-matched analysis and adjustment

To mitigate the confounding effects of demographic and clinical differences that could bias the results, propensity score matching (PSM) was employed. A multivariate logistic regression model was used to generate the propensity score, which is a composite score reflecting the probability of patients having different levels of AF based on their baseline characteristics [17]. After generating the propensity scores, patients with clinical outcomes indicative of AF were matched to those without AF in a

6:1 ratio using greedy nearest-neighbor matching, with a maximum caliper width of 0.1. Propensity score kernel density plots were utilized to verify the equivalency of matched pairs. Baseline differences between the two groups were assessed using the Standardized Mean Difference (SMD), with values below 0.1 indicating negligible differences.

Clinical data collection

A clinical data warehouse was developed through a collaborative program between Army Medical University (Beijing, China) and Hangzhou Le9 Healthcare Technology Co., Ltd. Data were extracted every 24 h using Lex Clinical Data Application 3.2 (Hangzhou Lejiu Healthcare Technology Co., Ltd) from the Hospital Health Information System (HIS) into a dedicated clinical data warehouse. This warehouse included data such as admission, transfer, discharge information, laboratory orders and results, medication orders, administration events, flow sheet entries, procedures, medical reports, admission notes, progress notes, and discharge summaries. All original unstructured data (e.g., pathology reports, radiology reports, progress notes, admit/discharge summaries) were converted into a standardized structured format. Core elements of the data warehouse were fully de-identified to ensure that all queries and analyses could be conducted without exposing confidential health information, although users with sufficient privileges could re-identify data to support operational and quality improvement initiatives.

Lex Clinical Data Application 3.2 is a self-service data access tool designed to query the clinical data warehouse and return tabular data for analysis and visualization. It allows investigators and data analysts with minimal computer training to identify study cohorts of interest based on their research hypotheses and study protocols. More complex queries can be conducted by experienced users or database managers using Structured Query Language (SQL). Lex outputs data in formats such as comma-separated values (CSV), tab-separated values (TSV), and attribute-related files, suitable for transfer to statistical analysis software and visualization tools.

Statistical analysis

Statistical analyses were conducted using R statistical software (R version 4.0.5, R Foundation for Statistical Computing) and IBM SPSS Statistics for Windows version 26.0 (IBM Corp.). Continuous variables were summarized using mean [standard deviation (SD)] or median [interquartile range (IQR)], while categorical data were represented as numbers and percentages. The clinical outcomes of AF in perioperative ischemic stroke patients were evaluated using an extended multivariate logistic regression model. To assess the robustness of our findings, we performed a sensitivity analysis, limiting the sample to non-neurosurgical patients based on the type of surgery. The primary association between AF and perioperative ischemic stroke was further examined by analyzing subgroups based on operative time, age, gender, ASA classification, intraoperative hypotension, and use of antiplatelet medications. In this study, patients without AF at the time of the clinical outcome were considered the control group unless otherwise specified. A two-sided *P*-value of less than 0.05 was considered statistically significant for all tests.

Results

Study population

This study included a total of 376,933 individuals who underwent noncardiac surgery between January 2008 and August 2019. Based on the inclusion and exclusion criteria, 223,415 patients were deemed eligible for analysis. The patient selection process is illustrated in Fig. 1. Among the eligible patients, 109,912(49.2%) were female, and 113,503 (50.8%) were male (Supplementary Table 1).

In the entire cohort, 525 patients (0.23%) experienced a perioperative ischemic stroke within 30 days post-surgery. Of these, 13 patients (2.5%) had atrial fibrillation (AF), while 512 patients (97.5%) did not. The stroke rate observed in this study aligns with previously reported rates of 0.1–0.7% for noncardiac surgeries [17, 18].

The study population was further stratified into two groups: those with AF ($n=837$, 3.7%) and those without AF ($n=222{,}578$, 99.6%). Supplementary Table 2 highlights the differences between these two groups. The median age of the AF group was 67 years [Interquartile Range (IQR): 61.00, 74.00]. In the AF group, 13 patients (1.6%) experienced a perioperative ischemic stroke, while 824 (98.4%) did not.

Baseline characteristics varied between the AF and non-AF groups. While some traits were comparable, others showed significant differences, such as gender, age, type of procedure, ASA classification, and comorbidities like hypertension, coronary artery disease, and prior perioperative ischemic stroke. The AF group had higher rates of cardiovascular comorbidities, including diabetes mellitus, hypertension, peripheral vascular disease, and coronary artery disease, as well as higher rates of long-term β-blocker and aspirin use compared to the non-AF group.

Primary analysis: correlation between perioperative ischemic stroke and AF

The primary analysis examined the association between AF and perioperative ischemic stroke. Univariate analysis revealed that AF was strongly associated with an increased risk of perioperative ischemic stroke [Odds Ratio (OR): 6.843; 95% Confidence Interval (CI): 3.73–11.413; $P<0.001$] (Supplementary Table 3). Other independent risk factors for perioperative ischemic stroke included gender, age, type of surgery, ASA classification, BMI, hypertension, coronary artery disease, arrhythmia, prior transient ischemic attack (TIA) or stroke, myocardial infarction, coronary stenting, peripheral vascular disease, malignancy, and the use of β-blockers, aspirin, and NSAIDs. In contrast, variables such as trauma surgery, dentistry, urology, thoracic surgery, chronic obstructive pulmonary disease (COPD), certain preoperative lab data, and the use of inhalational anesthetics and glucocorticoids did not significantly predict perioperative ischemic stroke (Supplementary Table 3). Further analysis using an extended multivariate logistic regression model assessed the OR of perioperative ischemic stroke in patients with AF across four different models (Table 1):

Propensity score-matched analysis and adjustment

To further evaluate the predictive value of AF, we conducted a propensity score-matched (PSM) analysis. Before matching, the median propensity score for patients with AF was 0.014 (IQR: 0.005–0.038), while for older patients without AF, the median propensity score was approximately 0.001 (IQR: 0.00029–0.003). After matching, we identified 824 patients with AF and 4,944 patients without AF. Figure 2 illustrates the distribution of propensity scores in the AF and non-AF groups before and after matching. Post-matching, the mean (SD) propensity scores were nearly identical between the non-AF [0.032 (0.049)] and AF [0.032 (0.049)] groups, indicating a successful matching process.

Except for TIA, stroke, COPD, and preoperative plasma plasminogen time measurements, all covariates had standardized mean differences (SMDs) below 0.10, suggesting that baseline demographic and clinical characteristics were well-balanced between the two groups (Table 2). Moreover, after adjusting for multifactorial logistic regression post-PSM ($n=10{,}826$), the correlation between AF and perioperative ischemic stroke remained significant (OR: 2.106; 95% CI: 1.003–4.159; $P<0.05$), as shown in Supplementary 5.

Sensitivity analysis

Given the significant correlation between perioperative ischemic stroke and the complexity of surgical procedures, prior research has demonstrated that neurosurgery (3.153%) are associated with the highest incidence of perioperative ischemic stroke,followed by spine surgery(0.837%)and joint arthroplasty (0.631%) [19]. To further test the robustness of our results, we

Table 1 An analysis of propensity scores and logistic regression models to assess the relationship between atrial fibrillation and perioperative ischemic stroke

Analysis methods	OR	95%CI	*P*-value
Univariate regression analysis			
Model 1 (Univariate analysis of AF and PIS)[a]	6.843	3.730–11.413	< 0.001
Logistic regression analysis ($n=223{,}415$)			
Model 2 (Baseline conditions and preoperative laboratory biochemical covariates adjusted)[b]	1.789	0.958–3.053	< 0.001
Model 3 (Surgical and intraoperative covariates adjusted)[c]	5.121	2.749–8.716	< 0.001
Model 4 (Comprehensively adjusted)[d]	2.122	1.123–3.677	< 0.05
Propensity score analysis (multivariate)			
Model PSM ($n=5{,}768$)[e]	2.106	1.003–4.159	< 0.05

AF Atrial Fibrillation index, *PIS* perioperative ischemic stroke, *OR* odds ratio, *CI* confidence interval, *PSM* propensity score matching

[a] Model 1 illustrates the univariate regression results between AF n(%) and PIS n(%)

[b] Model 2 included peripheral vascular disease n(%), ASA classification III n(%), AF n(%), diabetes n(%), ASA classification II n(%),perioperative nonsteroidal anti-inflammatory drugs n(%), Myocardial infarction n(%, preoperative antiplatelet drugs n(%), coronary stenting n(%), NLR[Median (IQR)], age[Median (IQR)], systolic blood pressure[Median (IQR)], preoperative plasma prothrombin time measurement[Median (IQR)], preoperative Hemoglobin[Median (IQR)], PLR[Median (IQR)], preoperative total bilirubin[Median (IQR)], coronary heart disease n(%), BMI[Median (IQR)], preoperative mean erythrocyte hemoglobin volume[Median (IQR)], preoperative serum albumin[Median (IQR)], preoperative ARBs n(%), preoperative potassium[Median (IQR)], Intraoperative fluid albumin[Median (IQR)]

[c] Model 3 included preoperative AF n(%), perioperative nonsteroidal drugs n(%), vascular surgery n(%), neurosurgery n(%), dentistry n(%), spine n(%), joint surgery n(%), urology n(%), obstetrics and gynecology n(%), thoracic surgery n(%), trauma surgery n(%), laparoscopic surgery n(%), general surgery n(%), other surgery types n(%), intraoperative antihypertensive drug n(%), blood products n(%), Total intraoperative fluids individualization[Median (IQR)], preoperative MAP[Median (IQR)], Total time with $MAP=60$[Median (IQR)], Total time for $MAP=65$[Median (IQR)], Total time with $MAP=75$[Median (IQR)], Total time with $MAP=80$[Median (IQR)], Intraoperative methylprednisolone dose[Median (IQR)], crystals[Median (IQR)], colloid[Median (IQR)], bleeding[Median (IQR)], duration of procedures[Median (IQR)], inhalation anesthesia usage[Median (IQR)], crystals Individualized[Median (IQR)], glucocorticoid[Median (IQR)], remifentanil individualization[Median (IQR)]

[d] Model 4 included all the variables. Multivariate results are shown in Supplementary Table 4

[e] 5,786 pairs were matched using the propensity score method. Multivariate results are shown in Supplementary Table 5

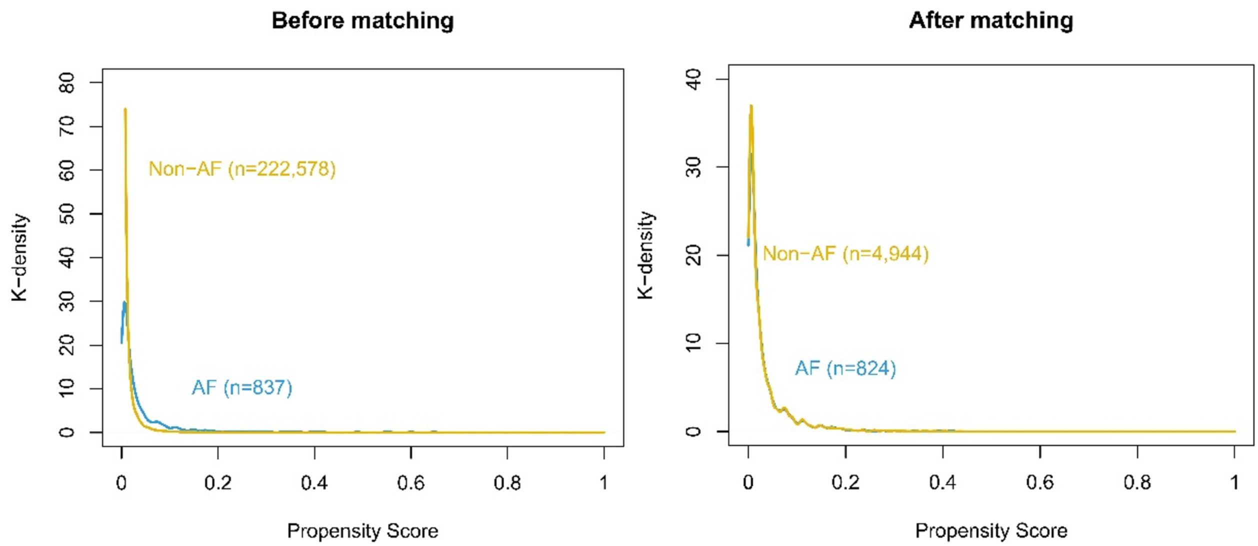

Fig. 2 Distribution of propensity scores before and after matching

performed a sensitivity analysis excluding neurosurgeries. The adjusted OR of perioperative ischemic stroke in neurosurgery patients with the AF was 1.623(95% CI: 0.359–5.165; $P=0.463$). The association between AF and perioperative ischemic stroke remained stable in those non-neurosurgical patients (OR: 2.154;95% CI: 1.044–3.964; $P=0.023$) (Table 3).

Subgroup analyses

Among the 837 perioperative patients in the AF group, 638 (76.2%) were aged ≥ 60.5 years, 291 (34.8%) were female, 380 (45.4%) had an ASA classification > 3, 480 (57.3%) had hypertension, and 164 (19.6%) received intraoperative antiplatelet medication. Subgroup analyses were conducted to evaluate the risk of perioperative ischemic stroke associated with AF based on age, sex, ASA classification, hypertension, and antiplatelet medication use (Fig. 3).

The risk of perioperative ischemic stroke was significantly higher in the AF group (OR: 2.122; 95% CI: 1.123–3.677; $P=0.012$), particularly in patients aged ≥ 60.5 years (OR: 2.272; 95% CI: 1.133–4.115; $P=0.012$). Additionally, male patients exhibited an increased risk (OR: 3.000; 95% CI: 1.462–5.593; $P=0.001$). AF was also significantly associated with perioperative ischemic stroke in patients with an ASA classification ≥ 3 (OR: 2.917; 95% CI: 1.407–5.506; $P=0.002$) and in those with hypertension (OR: 2.423; 95% CI: 1.181–4.507; $P=0.009$). Furthermore, the absence of antiplatelet medication use was significantly linked to an increased risk of perioperative ischemic stroke (OR: 2.413; 95% CI: 1.197–4.389; $P=0.007$) in the AF group.

Discussion

Perioperative ischemic stroke remains a serious complication for patients undergoing noncardiac surgery, particularly those with preexisting conditions such as AF, valvular disease, renal impairment, or a history of stroke [20]. Understanding the mechanisms and risk factors associated with perioperative ischemic stroke is crucial for the development of effective preventive strategies, which can ultimately lead to better clinical outcomes and reduced healthcare costs. Previous studies, such as those by Gialdini et al. [21] and Shu et al. [22], have established a clear connection between AF and an increased long-term risk of ischemic stroke, especially in the context of noncardiac surgery. However, the specific relationship between AF and perioperative ischemic stroke, along with the associated risk factors, has not been extensively explored, leaving significant gaps in our understanding.

In our study, the association between AF and the risk of perioperative ischemic stroke in patients undergoing noncardiac surgery remained significantly. Our findings are consistent with those of previous studies that have demonstrated a heightened risk of perioperative ischemic stroke in patients with AF [22, 23].

The increased risk of perioperative ischemic stroke in AF patients can be attributed to several mechanisms. First, surgical trauma and systemic inflammation during the perioperative period can activate the coagulation system, resulting in hypercoagulability and exacerbating inflammatory responses [24, 25]. Hemodynamic changes during surgery, including fluctuations in blood pressure and alterations in blood flow rates, can further contribute to abnormal coagulation, particularly in patients with AF. Additionally, inflammatory mediators such as

Table 2 An analysis of propensity scores and logistic regression models to assess the relationship between atrial fibrillation and perioperative ischemic stroke

Characteristic	Unadjusted sample ($n=223{,}415$)				PSM adjusted (1:6)($n=5{,}768$)			
	Non-AF	AF	*P*-value	SMD	Non-AF	AF	*P*-value	SMD
Demographics								
Sex (%)								
Male	112957 (50.7)	546 (65.2)	< 0.001	0.297	3251 (65.8)	538 (65.3)	0.825	0.010
Female	109621 (49.3)	291 (34.8)			1693 (34.2)	286 (34.7)		
Age (median [IQR])	52.00 [41.00, 62.00]	67.00 [61.00, 74.00]	< 0.001	1.317	68.00 [61.00, 74.00]	67.00 [61.00, 73.25]	0.063	0.056
BMI (median [IQR])	24.22 [21.88, 26.64]	25.14 [22.72, 27.58]	< 0.001	0.242	24.91 [22.66, 27.28]	25.10 [22.67, 27.55]	0.13	0.054
ASA classification (%)								
Class I	32478 (14.6)	9 (1.1)	< 0.001	1.004	27 (0.5)	9 (1.1)	0.165	0.063
Class II	170313 (76.5)	448 (53.5)			2745 (55.5)	448 (54.4)		
Class III	19787 (8.9)	380 (45.4)			2172 (43.9)	367 (44.5)		
Past medical history								
Hypertension (%)								
0	178845 (80.4)	357 (42.7)	< 0.001	0.84	2106 (42.6)	357 (43.3)	0.724	0.015
1	43733 (19.6)	480 (57.3)			2838 (57.4)	467 (56.7)		
Coronary heart disease (%)								
0	214590 (96.4)	641 (76.6)	< 0.001	0.606	3866 (78.2)	638 (77.4)	0.654	0.018
1	7988 (3.6)	196 (23.4)			1078 (21.8)	186 (22.6)		
TIA (%)								
0	216891 (97.4)	737 (88.1)	< 0.001	0.368	4526 (91.5)	725 (88.0)	0.001	0.118
1	5687 (2.6)	100 (11.9)			418 (8.5)	99 (12.0)		
Stroke (%)								
0	217473 (97.7)	727 (86.9)	< 0.001	0.415	4501 (91.0)	717 (87.0)	< 0.001	0.129
1	5105 (2.3)	110 (13.1)			443 (9.0)	107 (13.0)		
Myocardial infarction (%)								
0	221685 (99.6)	818 (97.7)	< 0.001	0.163	4839 (97.9)	805 (97.7)	0.838	0.012
1	893 (0.4)	19 (2.3)			105 (2.1)	19 (2.3)		
Coronary stenting (%)								
0	220652 (99.1)	802 (95.8)	< 0.001	0.213	4739 (95.9)	789 (95.8)	0.968	0.005
1	1926 (0.9)	35 (4.2)			205 (4.1)	35 (4.2)		
Peripheral vascular disease (%)								
0	214203 (96.2)	724 (86.5)	< 0.001	0.352	4318 (87.3)	715 (86.8)	0.693	0.017
1	8375 (3.8)	113 (13.5)			626 (12.7)	109 (13.2)		
COPD (%)								
0	220845 (99.2)	806 (96.3)	< 0.001	0.199	4853 (98.2)	793 (96.2)	0.001	0.117
1	1733 (0.8)	31 (3.7)			91 (1.8)	31 (3.8)		
Cancers (%)								
0	121878 (54.8)	366 (43.7)	< 0.001	0.222	2076 (42.0)	357 (43.3)	0.496	0.027
1	100700 (45.2)	471 (56.3)			2868 (58.0)	467 (56.7)		
Preoperative laboratory tests								
Preoperative mean erythrocyte hemoglobin volume (median [IQR])	30.40 [29.30, 31.40]	30.80 [29.50, 32.00]	< 0.001	0.192	30.70 [29.60, 31.80]	30.80 [29.50, 32.00]	0.515	0.027
Renal insufficiency or preoperative creatinine > 177 (%)								
0	220453 (99.0)	814 (97.3)	< 0.001	0.133	4827 (97.6)	801 (97.2)	0.541	0.027
1	2125 (1.0)	23 (2.7)			117 (2.4)	23 (2.8)		

Table 2 (continued)

Characteristic	Unadjusted sample ($n = 223,415$)				PSM adjusted (1:6)($n = 5,768$)			
	Non-AF	AF	*P*-value	SMD	Non-AF	AF	*P*-value	SMD
Preoperative hemoglobin measurement (median [IQR])	134.00 [122.00, 146.00]	135.00 [121.00, 147.00]	0.736	0.001	135.00 [123.00, 146.00]	134.50 [121.00, 147.00]	0.679	0.021
Preoperative serum albumin (median [IQR])	41.50 [39.10, 43.80]	40.00 [37.20, 42.60]	< 0.001	0.391	40.10 [37.30, 42.60]	40.00 [37.27, 42.52]	0.47	0.013
Preoperative total bilirubin (median [IQR])	10.70 [8.00, 14.40]	12.50 [9.40, 17.70]	< 0.001	0.117	11.40 [8.60, 15.53]	12.40 [9.30, 17.70]	< 0.001	0.01
Preoperative potassium (median [IQR])	3.98 [3.78, 4.20]	4.01 [3.78, 4.27]	0.004	0.134	4.01 [3.78, 4.27]	4.01 [3.78, 4.27]	0.884	0.011
Preoperative plasma prothrombin time measurement (median [IQR])	13.10 [12.60, 13.60]	13.50 [13.00, 14.30]	< 0.001	0.472	13.25 [12.70, 13.90]	13.50 [13.00, 14.30]	< 0.001	0.184
Preoperative ARB medications (%)								
0	213894 (96.1)	683 (81.6)	< 0.001	0.473	4059 (82.1)	677 (82.2)	1	0.002
1	8684 (3.9)	154 (18.4)			885 (17.9)	147 (17.8)		
Preoperative antiplatelet agents (%)								
0	216788 (97.4)	673 (80.4)	< 0.001	0.562	4030 (81.5)	667 (80.9)	0.735	0.015
1	5790 (2.6)	164 (19.6)			914 (18.5)	157 (19.1)		
Perioperative NSAIDs (%)								
0	83423 (37.5)	191 (22.8)	< 0.001	0.324	1256 (25.4)	188 (22.8)	0.122	0.061
1	139155 (62.5)	646 (77.2)			3688 (74.6)	636 (77.2)		
Preoperative systolic blood pressure (median [IQR])	122.00 [111.00, 134.00]	130.00 [119.00, 140.00]	< 0.001	0.382	130.00 [120.00, 140.00]	130.00 [119.00, 140.25]	0.768	0.022
Preoperative MAP (median [IQR])	91.33 [83.33, 99.33]	96.33 [88.33, 104.00]	< 0.001	0.361	96.00 [88.67, 103.33]	96.00 [88.33, 104.00]	0.86	0.02
Surgical procedures (%)								
ENT	21807 (9.8)	31 (3.7)	< 0.001	0.603	155 (3.1)	31 (3.8)	0.997	0.062
Trauma Surgery	6633 (3.0)	20 (2.4)			107 (2.2)	20 (2.4)		
Obstetrics and Gynecology	15395 (6.9)	23 (2.7)			133 (2.7)	23 (2.8)		
Abdominal Surgery	57295 (25.7)	346 (41.3)			2091 (42.3)	341 (41.4)		
Joint Surgery	15854 (7.1)	59 (7.0)			356 (7.2)	58 (7.0)		
Spine Surgery	18255 (8.2)	48 (5.7)			288 (5.8)	48 (5.8)		
Stomatology	9458 (4.2)	19 (2.3)			121 (2.4)	19 (2.3)		
Urology	18543 (8.3)	77 (9.2)			451 (9.1)	77 (9.3)		
General Surgery	16979 (7.6)	29 (3.5)			150 (3.0)	29 (3.5)		
Neurosurgery	20307 (9.1)	41 (4.9)			212 (4.3)	38 (4.6)		
Thoracic Surgery	15218 (6.8)	67 (8.0)			437 (8.8)	67 (8.1)		
Vascular Surgery	2151 (1.0)	57 (6.8)			307 (6.2)	53 (6.4)		
Others	4683 (2.1)	20 (2.4)			136 (2.8)	20 (2.4)		
Duration of surgery (median [IQR])	148.00 [100.00, 215.00]	150.00 [105.00, 215.00]	0.294	0.008	155.00 [109.00, 219.00]	153.00 [105.00, 216.25]	0.306	0.04
Intraoperative and anesthetic factors								
Aspirin medicine (%)								
0	213687 (96.0)	633 (75.6)	< 0.001	0.611	3880 (78.5)	625 (75.8)	0.1	0.063
1	8891 (4.0)	204 (24.4)			1064 (21.5)	199 (24.2)		

Table 2 (continued)

Characteristic	Unadjusted sample ($n = 223,415$)				PSM adjusted (1:6)($n = 5,768$)			
	Non-AF	AF	P-value	SMD	Non-AF	AF	P-value	SMD
Days off preoperative aspirin (median [IQR])	9999.00 [9999.00, 9999.00]	9999.00 [999.00, 9999.00]	< 0.001	0.672	9999.00 [9999.00, 9999.00]	9999.00 [999.00, 9999.00]	0.065	0.069
Inhalation anaesthetics (Yes or No) (%)								
0	13,561 (6.1)	74 (8.8)	0.001	0.105	459 (9.3)	73 (8.9)	0.745	0.015
1	209017 (93.9)	763 (91.2)			4485 (90.7)	751 (91.1)		
Bleeding volume (median [IQR])	100.00 [50.00, 200.00]	100.00 [50.00, 200.00]	0.365	0.072	100.00 [50.00, 200.00]	100.00 [50.00, 200.00]	0.885	0.043
Colloid (median [IQR])	500.00 [0.00, 1000.00]	500.00 [0.00, 500.00]	0.061	0.084	500.00 [0.00, 1000.00]	500.00 [0.00, 500.00]	0.094	0.065
Crystals (median [IQR])	1500.00 [1000.00, 2100.00]	1600.00 [1100.00, 2100.00]	< 0.001	0.14	1600.00 [1100.00, 2100.00]	1600.00 [1100.00, 2100.00]	0.869	0.001
Intraoperative methylprednisolone dose (median [IQR])	0.00 [0.00, 40.00]	0.00 [0.00, 40.00]	< 0.001	0.116	0.00 [0.00, 40.00]	0.00 [0.00, 40.00]	< 0.001	0.005
Total time with MAP = 80 (median [IQR])	75.00 [40.00, 130.00]	65.00 [35.00, 110.00]	< 0.001	0.189	67.50 [35.00, 115.00]	65.00 [35.00, 111.25]	0.982	0.007
Total time with MAP = 75 (median [IQR])	45.00 [20.00, 95.00]	35.00 [15.00, 75.00]	< 0.001	0.219	35.00 [15.00, 75.00]	35.00 [15.00, 75.00]	0.603	0.003
Total time with MAP = 65 (median [IQR])	10.00 [0.00, 25.00]	10.00 [0.00, 20.00]	0.351	0.137	10.00 [0.00, 20.00]	10.00 [0.00, 20.00]	0.178	0.011
Total time with MAP = 60 (median [IQR])	5.00 [0.00, 15.00]	5.00 [0.00, 15.00]	0.68	0.065	5.00 [0.00, 15.00]	5.00 [0.00, 15.00]	0.373	0.01
Diabetes (%)								
0	195159 (87.7)	613 (73.2)	< 0.001	0.37	3586 (72.5)	603 (73.2)	0.731	0.015
1	27,419 (12.3)	224 (26.8)			1358 (27.5)	221 (26.8)		
NLR (median [IQR])	1.81 [1.37, 2.52]	2.07 [1.53, 3.15]	< 0.001	0.189	2.07 [1.54, 2.96]	2.07 [1.53, 3.13]	0.399	0.044
PLR (median [IQR])	116.81 [91.62, 152.32]	118.28 [91.62, 157.21]	0.4	0.059	118.94 [91.39, 156.36]	118.31 [91.52, 157.43]	0.881	0.001
Blood products (Yes or No) (%)								
0	196643 (88.3)	724 (86.5)	0.108	0.056	4386 (88.7)	713 (86.5)	0.079	0.066
1	25935 (11.7)	113 (13.5)			558 (11.3)	111 (13.5)		
Crystal_individualisation (median [IQR])	8.41 [6.17, 11.40]	8.32 [5.96, 11.00]	0.029	0.122	8.26 [6.03, 11.11]	8.38 [6.08, 11.02]	0.962	0.017
Total intraoperative fluid volume_individualised (median [IQR])	11.50 [8.59, 15.10]	10.75 [8.15, 14.15]	< 0.001	0.189	11.11 [8.27, 14.40]	10.82 [8.25, 14.23]	0.351	0.02
Intraoperative pressure-raising drugs (%)								
0	178791 (80.3)	549 (65.6)	< 0.001	0.336	3260 (65.9)	544 (66.0)	0.995	0.002
1	43787 (19.7)	288 (34.4)			1684 (34.1)	280 (34.0)		
Oral morphine (median [IQR])	120.00 [90.00, 150.00]	135.00 [90.00, 162.00]	0.197	0.016	135.00 [90.00, 165.00]	135.00 [90.00, 165.00]	0.226	0.037
Individualised remifentanil (median [IQR])	0.17 [0.13, 0.20]	0.15 [0.11, 0.18]	< 0.001	0.373	0.15 [0.12, 0.18]	0.15 [0.11, 0.18]	0.536	0.005
Ischaemic stroke (%)								
0	222066 (99.8)	824 (98.4)	< 0.001	0.141	4908 (99.3)	812 (98.5)	0.054	0.07
1	512 (0.2)	13 (1.6)			36 (0.7)	12 (1.5)		
Intraoperative fluid albumin(median [IQR])	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.625	0.023	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]	0.369	0.01

Table 2 (continued)

Characteristic	Unadjusted sample ($n = 223{,}415$)				PSM adjusted (1:6)($n = 5{,}768$)			
	Non-AF	AF	*P*-value	SMD	Non-AF	AF	*P*-value	SMD
Glucocorticoids (%)								
0	54131 (24.3)	254 (30.3)	< 0.001	0.136	1551 (31.4)	251 (30.5)	0.63	0.02
1	168447 (75.7)	583 (69.7)			3393 (68.6)	573 (69.5)		

The data are presented as median (inter0quartile range), mean (standard deviation) or n(%)

Table 3 Sensitivity analysis of the association between AF and perioperative ischemic stroke (adjustment through multivariate logistic regression)

	Non-AF and PIS cases, n	AF and PIS cases, n	OR	95%CI	*P*-value
Entire cohort ($n = 223{,}415$; PIS = 525)	222578 (512)	837 (13)	2.122	1.123–3.677	0.012
Type of Surgery					
Neurosurgery ($n = 20{,}348$; PIS = 200)	20307 (197)	41 (3)	1.623	0.359–5.165	0.463
Non-Neurosurgery ($n = 203{,}067$; PIS = 325)	202271 (315)	796 (10)	2.154	1.044–3.964	0.023

Abbreviations: AF Atrial Fibrillation, *PIS* perioperative ischemic stroke, *OR* odds ratio, *CI* confidence interval

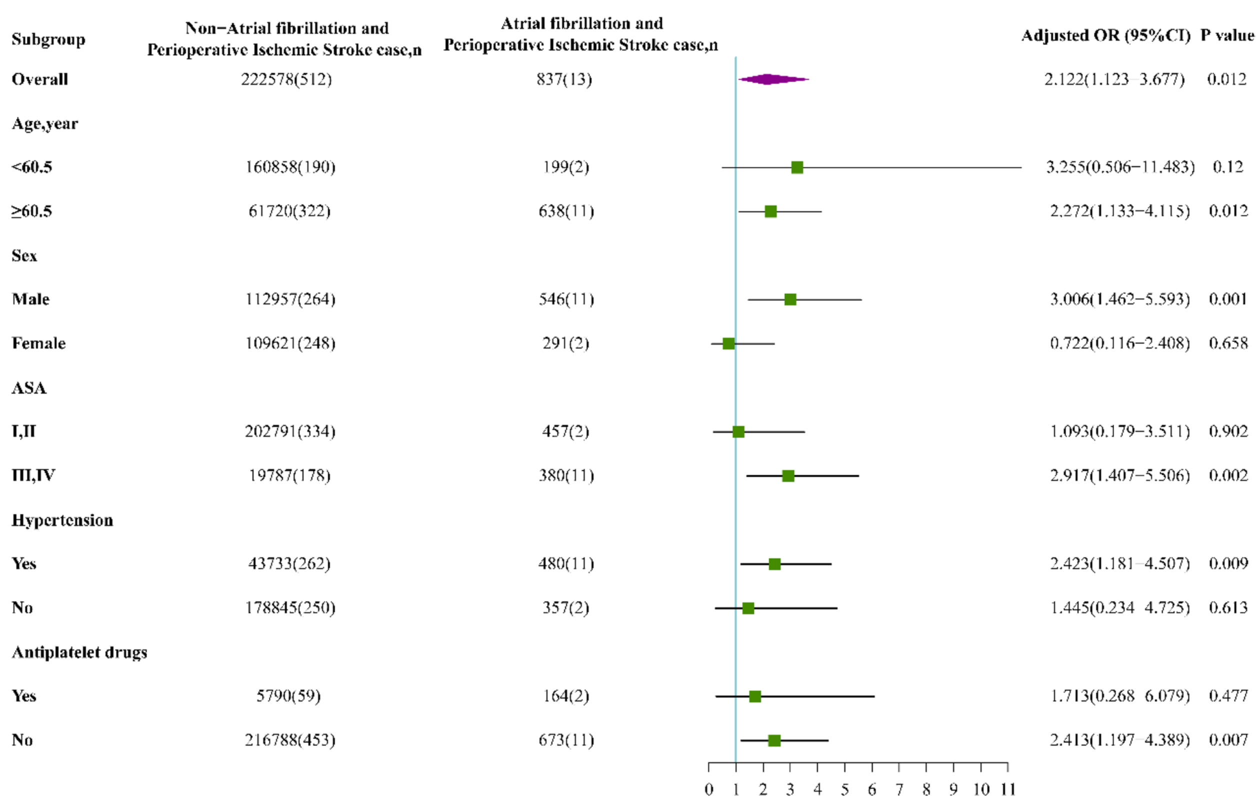

Fig. 3 Subgroup analyses of the correlation between atrial fibrillation and perioperative ischemic stroke. OR, odds ratio

cytokines and chemokines can damage atrial endothelial cells, promote collagen deposition, and trigger atrial myocardial remodeling, leading to unstable atrial electrical activity and sustaining AF [25]. The aforementioned recommendations emphasize that surgical teams should prioritize minimally invasive techniques during procedures to mitigate or prevent direct nerve injury, vascular traction, and tissue damage. During thrombus aspiration, heightened vigilance is imperative to avoid air or debris embolization, which may precipitate a stroke. The deployment of hemodynamic support devices should be judiciously evaluated in accordance with their specific indications. Furthermore, rigorous perioperative blood pressure monitoring is essential to avert hypotension, thereby diminishing the likelihood of ischemic stroke. Besides, Interruption of anticoagulation therapy significantly increases the likelihood of thrombus formation in AF patients [26]. Thus, the resumption of anticoagulation therapy postoperatively must be carefully managed to avoid further complications. Upon detection of AF, anticoagulation therapy should be considered within an appropriate timeframe to mitigate the risk of thromboembolic events. Furthermore, during the perioperative period, patients often experience physiological stress responses and sympathetic activation, which can lead to cerebral hypoperfusion, hypovolemia, anemia, and stress-induced arrhythmias. These conditions contribute to electrophysiological instability in the atria, increasing both the frequency and duration of AF episodes [27]. Stress responses and autonomic dysregulation are also implicated in stroke-mediated functional and structural alterations, including microvascular dysfunction, myocardial necrosis, coronary artery hypoxia, and arrhythmias [28]. These factors collectively elevate the risk of thrombus formation and perioperative ischemic stroke. It is imperative that we maintain vigilant surveillance over these factors to ensure optimal patient outcomes.

Our study has significant clinical implications, particularly for the early identification and management of AF patients at risk of perioperative ischemic stroke. The sensitivity analysis revealed that the association between AF and perioperative ischemic stroke remained stable. In non-Neurosurgery patients, the relationship continued to demonstrate significant statistical relevance. However, within neurosurgery cases, the statistical significance was not evident, potentially due to the limited sample size (only 3 cases in the AF group), insufficient statistical power, and the inherently high risk of neurosurgery, which may obscure the independent impact of AF. Subgroup analyses revealed that certain populations are at higher risk, including males, patients aged $\geq$ 60.5 years, those with an ASA score $\geq$ 3, individuals with hypertension, and those not receiving antiplatelet medications. For these high-risk groups, targeted interventions should be considered.Males with AF were found to be more susceptible to perioperative ischemic stroke compared to females. This disparity may be attributed to the higher prevalence of cardiovascular disease in men and hormonal differences between sexes [29]. Therefore, for male patients, heightened attention should be directed towards their cardiovascular history to ensure comprehensive risk assessment and management. Elderly patients with AF are at an increased risk of perioperative ischemic stroke due to several factors. Aging is associated with a higher prevalence of comorbidities such as hypertension, diabetes, and cardiovascular disease, which complicate the management of anticoagulation therapy. The management of elderly patients with AF necessitates an individualized approach, with a particular focus on the safety of anticoagulation therapy, the management of comorbidities, the prevention of falls and bleeding, and the regular monitoring of cardiac and renal function. The ASA scoring system is a valuable tool for assessing a patient's overall health and anesthetic risk. Patients with an ASA score $\geq$ 3 are typically burdened with multiple comorbidities, including cardiovascular disease, pulmonary disorders, and diabetes, all of which inherently increase the risk of perioperative ischemic stroke [30]. For patients with a high ASA classification, it is crucial to rigorously manage comorbid conditions to optimize perioperative outcomes and minimize the risk of complications. In hypertensive patients, the risk of perioperative ischemic stroke is further elevated due to the structural and functional changes that hypertension induces in the blood vessel walls. Hypertension contributes to cardiac alterations such as left ventricular hypertrophy and dilation, which increase the likelihood of AF [31]. Chronic low-grade inflammation, commonly present in hypertensive patients, plays a significant role in the initiation and maintenance of hypertension [32]. Consequently, for hypertensive patients, it is crucial to intensify blood pressure management and minimize blood pressure variability to ensure optimal therapeutic outcomes. The non-use of antiplatelet medications significantly heightens the risk of thrombosis in AF patients. While oral anticoagulation therapy is effective in reducing the risk of ischemic stroke and systemic embolism, it is not infallible. Ischemic strokes can still occur in patients on anticoagulation therapy due to factors such as non-compliance, reduced pharmacological efficacy, or alternative stroke mechanisms, such as small vessel occlusion [33]. Therefore, it is essential to carefully determine the timing of anticoagulation therapy interruption and resumption prior to surgery, taking into account the bleeding risk associated with the procedure.

Our study has several strengths that contribute to its significance. First, to our knowledge, this is the first study conducted in China to assess the prognostic value of AF in perioperative ischemic stroke among patients undergoing noncardiac surgery. Given the low incidence of perioperative ischemic stroke, we included a large sample of 223,415 eligible patients, enhancing the study's power.

Second, we utilized PSM analysis to adjust for various potential confounders, including patient demographics, preoperative history, and laboratory data, ensuring a robust analysis. Third, our study employed multiple statistical methods, including subgroup analyses, to validate the role of AF as an independent prognostic factor for perioperative ischemic stroke.

However, this is not without limitations. Firstly, the observational nature of our study precludes the establishment of causality. While we identified a significant association between AF and perioperative ischemic stroke, prospective and well-designed studies are needed to confirm this relationship and explore causative mechanisms. Secondly, the study was conducted at a single center, which may limit the direct translation of our findings to a broader population. Consequently, our results should be interpreted as hypothesis-generating, and further research is required to develop precise risk stratification models or predictive tools. Thirdly, we did not account for certain factors known to influence ischemic stroke risk, such as smoking, lipid levels, family history of stroke, and congestive heart failure. The omission of these variables could introduce bias.

Conclusion

In summary, AF has emerged as a significant and independent prognostic risk factor for perioperative ischemic stroke in patients undergoing noncardiac surgery. Our study underscores the critical need for heightened vigilance and targeted management strategies for patients with AF, particularly those within high-risk subgroups. These include males, individuals aged 60.5 years or older, patients with an ASA score of 3 or higher, those with hypertension, and those not on antiplatelet therapy. By recognizing and addressing these specific risk factors, healthcare providers can implement more effective preventive measures, ultimately reducing the incidence of perioperative ischemic stroke and improving patient outcomes in this vulnerable population.

Supplementary Information

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Supplementary Material 1

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Authors' contributions

YL: Conceptualization, Resources. RX: Data curation, Writing–original draft. JW: Software, Validation, Visualization. HY: Writing–review and editing. MQ: Data curation, Writing–original draft. SL: Investigation. MS: Methodology. LS: Writing–review and editing. QF: Project administration, Resources, Funding acquisition. YM: Supervision, Writing–review and editing. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The database utilized in this study were reviewed and approved by the Medical Ethics Committee of the Chinese People's Liberation Army General Hospital (Ethics No. S2021-493–01). The Medical Ethics Committee of the Chinese People's Liberation Army General Hospital waived the requirement of written informed consent for participation. This study was conducted in accordance with the 1964 Declaration of Helsinki and its amendments. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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