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*Original Article*

# Post-procedural anticoagulation enhances cognitive function and reduces stroke risk in atrial fibrillation patients after left atrial appendage occlusion

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**Abstract:** Objective: To investigate the effect of post-left atrial appendage (LAA) occlusion anticoagulation strategy adjustments on cognitive function in atrial fibrillation (AF) patients, showing the influence of these adjustments on long-term brain health. Methods: In this retrospective cohort study, a total of 210 patients with AF subjected to left atrial appendage (LAA) closure between January 2022 and January 2025 were included. Among them, 103 patients received anticoagulation treatment following the procedure (observation group) and 107 did not (control group). The primary outcome - cognitive function - was evaluated using the Mini-Mental State Examination (MMSE) scale and other cognitive tests. The secondary outcomes, including major adverse events (stroke [ischemic, hemorrhagic], transient ischemic attack, major bleeding, and venous thrombotic event), blood biochemical values (fasting blood glucose [FBG], low-density lipoprotein [LDL], high-density lipoprotein (HDL), triglycerides (TG), prothrombin time [PT], activated partial thromboplastin time [aPTT], fibrinogen, and D-Dimer), and quality-of-life scores (Physical, Mental Health, and Social Functioning) were also recorded and compared between groups. Results: Post-procedure anticoagulation therapy significantly improved both cognitive function and clinical outcomes in AF patients undergoing LAA occlusion. The observation group demonstrated significantly better performances in the MMSE, attention, working memory, and visual-spatial abilities (all P<0.001). The FBG and LDL levels (both P<0.001) were significantly lower in the observation group compared to the control group, as was the incidence of ischemic stroke (1.9 vs. 5.6%) (P = 0.032). Quality of life scores, including physical, mental, and social functioning, were all significantly better in the observation group (P<0.001). Anticoagulation effects were evident, with significantly prolonged PT and aPTT in the observation group (P<0.001). Logistic regression analysis identified anticoagulation therapy as a significant predictor of reduced cognitive impairment (OR = 0.940, 95% CI: 0.910-0.972, P<0.001), indicating its potential benefit in preserving cognitive function after LAA occlusion. Conclusion: Post-procedural anticoagulation therapy significantly improves cognitive function, reduces ischemic stroke incidence, and enhances quality of life in AF patients following LAA occlusion, highlighting its clinical value in management.

**Keywords:** Left atrial appendage occlusion, anticoagulation strategy, cognitive function, atrial fibrillation, postoperative management

## Introduction

Atrial Fibrillation (AF) is the most common sustained cardiac arrhythmia, with its prevalence increasing globally due to an aging population and the rising burden of cardiovascular risk factors [1, 2]. AF significantly elevates the risk of thromboembolic events, particularly ischemic stroke, making stroke prevention a primary goal in the AF management [3]. Standard preventive therapies, including warfarin and direct oral anticoagulants (DOACs), effectively reduce thromboembolic risk [4, 5]. However, long-term anticoagulation increases the risk of bleeding complications, especially in patients at high bleeding risk.

To mitigate these risks, left atrial appendage (LAA) occlusion has emerged as a promising alternative for stroke prevention, particularly in

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patients with contraindications to chronic anticoagulation therapy [6, 7]. The procedure mechanically isolates the LAA, a common site of thrombus formation in AF patients, thereby reducing the likelihood of stroke without the need for long-term anticoagulation [8]. Although LAA occlusion has shown procedural success in preventing stroke, the post-procedure anticoagulation management remains controversial. Current strategies for anticoagulation following LAA occlusion vary, with some patients receiving tailored anticoagulation therapy and others without [9]. The effect of post-procedure anticoagulation strategies on patient outcomes, including cognitive function, remain unclear.

Cognitive dysfunction is an increasingly recognized complication in AF patients, both as a direct consequence of arrhythmia and as a side effect of long-term anticoagulation therapy. AF has been associated with a higher incidence of cognitive decline, including memory impairment, executive dysfunction, and an increased risk of dementia [10, 11]. While anticoagulation therapy is known to reduce thromboembolic events, its effect on cognitive outcomes is complex, with some studies suggesting potential cognitive benefits, while others report negative effects [12]. This underscores the need for further investigation into how different anticoagulation strategies, particularly those following LAA occlusion, affect cognitive function.

This study aimed to address this matter by examining the effect of post-LAA occlusion anticoagulation strategies on cognitive function in AF patients. Specifically, we compared two treatment approaches: individualized anticoagulation therapy versus no routine anticoagulation following the procedure. The novelty of this study lies in its focus on post-LAA occlusion anticoagulation and its effect on cognitive outcome, a topic that remains insufficiently explored. By evaluating cognitive function in patients with different anticoagulation regimens, this study will show how personalized anticoagulation therapy can optimize both stroke prevention and cognitive health. These findings are expected to inform clinical decision-making, thereby improving overall quality of life for AF patients undergoing LAA occlusion.

## Patients and methods

### *Patient selection*

This retrospective cohort study included 210 patients with AF who LAA occlusion at Shanghai Pudong New Area People's Hospital between January 2022 and January 2025. Patients were divided into two groups based on their anticoagulation therapy following the procedure: 103 patients received post-procedure anticoagulation therapy (observation group), and 107 patients did not (control group). This study was approved by the Ethics Committee from Shanghai Pudong New Area People's Hospital. Patient inclusion procedures are illustrated in **Figure 1**.

Inclusion criteria: (1) age ≥18 years; (2) diagnosis of AF confirmed by clinical diagnosis and electrocardiogram (ECG) [13], (3) successful LLA occlusion (LAAO), (4) at least one follow-up visit assessing cognitive function within 6 months after the procedure, and (5) documented anticoagulation strategy before and after LAAO. Exclusion criteria: (1) history of significant cognitive impairment or dementia prior to the procedure; (2) incomplete medical records or missing follow-up data; (3) contraindications to anticoagulation therapy; (4) concomitant cardiac surgeries or procedures during the same hospitalization; and (5) history of stroke or transient ischemic attack (TIA) prior to LAAO.

### *Treatment protocol*

Patients in the control group did not receive routine anticoagulation therapy following LAAO. These patients were monitored for thromboembolic events or complications, and anticoagulation therapy was initiated only when clinically indicated (e.g., signs of ischemic stroke or transient ischemic attack [TIA]). Routine follow-up assessments included cognitive evaluations and clinical monitoring for any thromboembolic events. In some cases, low-dose aspirin or other antiplatelet therapies were prescribed for stroke prevention based on individual stroke risk, but this was not part of the standard management protocol.

Patients in the observation group received individualized anticoagulation regimen following LAAO according to their clinical profiles and risk factors. Following the procedure, anticoagula-

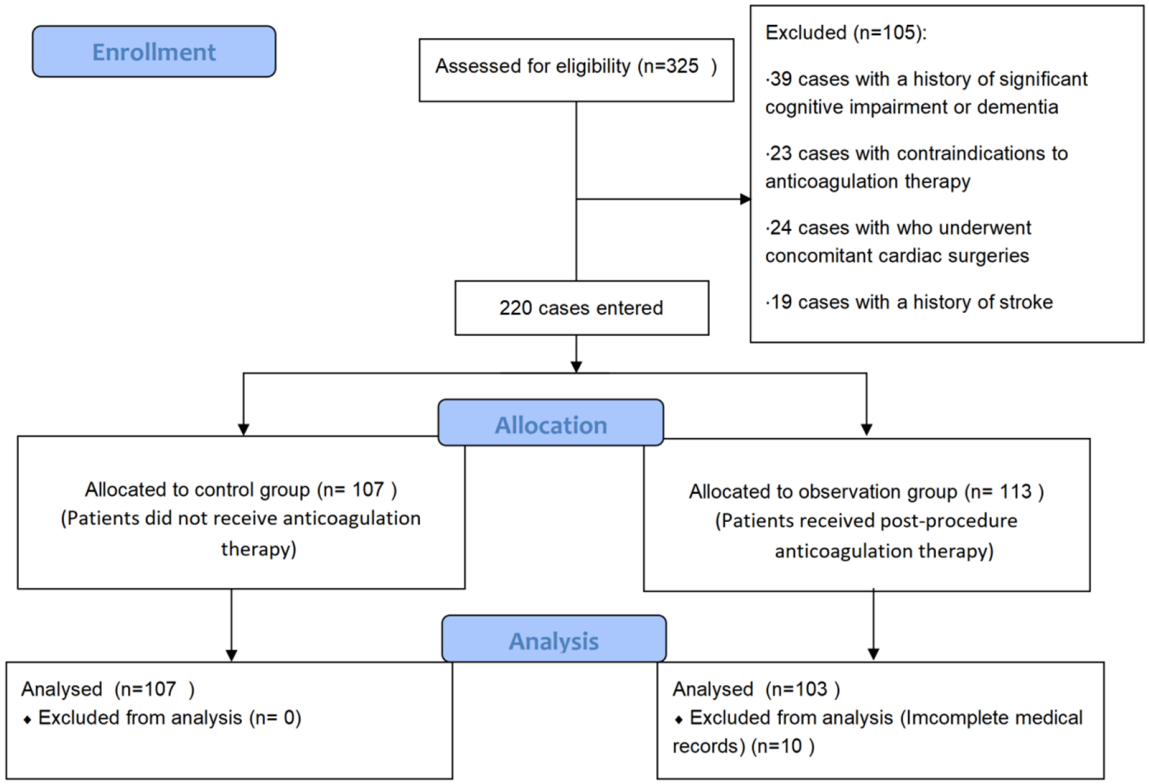


**Figure 1.** Flow diagram detailing patient selection.

tion was initiated with either a direct oral anticoagulant (DOACs, e.g., apixaban or rivaroxaban, or a vitamin K antagonist (warfarin), depending on the patient's renal function, bleeding risk, and history of thromboembolic events. The choice of anticoagulants was determined by the attending physician, considering contraindications or comorbidities. For patients on warfarin, the international normalized ratio (INR) was maintained within the therapeutic range of 2.0-3.0 through regular monitoring and dose adjustment. For those on DOACs, renal function was periodically assessed, and dosages were modified as recommended by current clinical guidelines. The duration of anticoagulation therapy was individualized, with a typical duration of 3-6 months post-procedure. At each follow-up, the anticoagulation regimen was assessed, and proper adjustments were made based on clinical evaluations, including any adverse effects, thromboembolic events, or bleeding complications.

*Data collection*

Data were systematically retrieved from the electronic medical record, including demographics (age, sex), clinical history (hypertension, diabetes, previous stroke or TIA), baseline comorbidities (cardiovascular risk factors), and in-hospital information. Procedural details of LAAO (e.g., date of operation, type of device, and post-procedure management), were recorded. Information regarding anticoagulation therapy included the type of anticoagulant, duration of treatment, and regimen adjustments during the follow-up. Cognitive outcomes were assessed at baseline and 12 months post-procedure using standardized cognitive tests, including the Mini-Mental State Examination (MMSE) [14], Visual-Spatial Ability, Attention and Working Memory, Verbal Fluency, and Digit Symbol Substitution tests. Routine laboratory data collected at the follow-up included fasting blood glucose (FBG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG) and total cholesterol (TC). Coagulation values were collected including prothrombin time (PT), activated partial thromboplastin (aPTT), international normalized ratio (INR), fibrinogen, and D-Dimer, were also extracted. Besides, adverse events, including ischemic stroke, hemorrhagic stroke,

and transient TIA, major bleeding events, venous thromboembolism (VTE) and other significant clinical events. Event incidences were followed up for 12 months after LAA occlusion.

All data were extracted by trained personnel using a standardized data collection form to ensure consistency and accuracy. Each record was independently reviewed for completeness, and discrepancies were resolved by consulting with the attending physicians. This meticulous extraction process ensured data reliability and integrity.

The primary outcome was cognitive function. The secondary outcome measures included the incidence of major adverse events (MAEs) (ischemic stroke, hemorrhagic stroke, TIA, major bleeding events, intracranial bleeding, gastrointestinal bleeding, and VTE), blood routine (e.g., FBG, LDL, HDL, TC, TC), and coagulation values (PT, aPTT, INR, fibrinogen, and D-Dimer), and quality of life (Physical Health Score, Mental Health Score, Question of Social Functioning, and Overall Quality of Life Score). These measures enabled evaluation of the effect of post-procedural anticoagulant therapy on both cognitive and clinical health outcomes.

*Statistical analysis*

All statistical analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as means ± standard deviations (SD), while categorical variables were expressed as frequencies and percentages. Data normality was assessed using the Shapiro-Wilk test.

For normally distributed continuous variables, between-group comparisons were made using independent t-tests; otherwise, the Mann-Whitney U tests was applied. Categorical data were evaluated using either the chi-square test or Fisher's exact test, as appropriate. For repeated cognitive assessments, a repeated-measures ANOVA was used to compare cognitive scores over time between groups.

To identify predictors of cognitive impairment, logistic regression analysis with a stepwise backward elimination method was employed to identify the independent risk factors. Results were reported as odds ratio (OR) with 95% confidence intervals (CI). A *p*-value of <0.05 was considered significant.

## Results

*Baseline characteristics*

There were no significant differences between the two groups in terms of age (68.85 ± 7.24 vs. 70.92 ± 9.12 years, P = 0.072) or gender distribution (male: 60.2% vs. 60.7%, P = 0.935). The prevalence of hypertension (82.5% vs. 81.3%, P = 0.819), diabetes mellitus (43.7% vs. 44.9%, P = 0.864), and history of stroke (21.4% vs. 23.4%, P = 0.727) was comparable between the two groups.

Similarly, no significant differences were observed between the two groups in terms of $CHA_2DS_2$-VASc scores (4.84 ± 0.40 vs. 4.86 ± 0.54, P = 0.705), left ventricular ejection fraction (58.64 ± 6.52 vs. 58.65 ± 8.56, P = 0.990), or atrial fibrillation duration (31.15 ± 9.93 vs. 32.21 ± 10.54 months, P = 0.454). The proportions of paroxysmal AF (53.4% vs. 48.6%, P = 0.487) and persistent AF (46.6% vs. 51.4%, P = 0.487) were also comparable between the two groups.

In addition, there were no significant differences in antithrombotic therapy prior to the procedure (warfarin: 80.6% vs. 75.7%; DOACs: 19.4% vs. 24.3%; P = 0.393) (**Table 1**). These results indicate that the two groups were well-matched at baseline, allowing for a reliable comparison of the effects of post-procedure anticoagulation strategies on cognitive function.

*Blood biochemical indicators*

FBG levels were significantly lower in the observation group compared to the control group after the intervention (P<0.001), whereas no significant difference was observed at baseline (**Figure 2A**). HDL levels remained unchanged in both groups throughout the study (**Figure 2B**). In contrast, LDL was significantly lower in the observation group compared to the control group after intervention (P<0.001, **Figure 2C**). TG and TC levels remained comparable between the two groups throughout the observation period (**Figure 2D**, **2E**).

**Table 1.** Comparison of baseline characteristics between the two groups

| | Observation Group (n = 103) | Control Group (n = 107) | $t/\chi^2$ | *P*-value |
|---|---|---|---|---|
| Age (years) | 68.85 ± 7.24 | 70.92 ± 9.12 | 1.810 | 0.072 |
| Sex | | | 0.007 | 0.935 |
| Male | 62 (60.2%) | 65 (60.7%) | | |
| Female | 41 (39.8%) | 42 (39.3%) | | |
| Hypertension (%) | 85 (82.5%) | 87 (81.3%) | 0.052 | 0.819 |
| Diabetes Mellitus (%) | 45 (43.7%) | 48 (44.9%) | 0.029 | 0.864 |
| History of Stroke (%) | 22 (21.4%) | 25 (23.4%) | 0.121 | 0.727 |
| CHA2DS2-VASc Score | 4.84 ± 0.40 | 4.86 ± 0.54 | 0.379 | 0.705 |
| Left Ventricular Ejection Fraction (%) | 58.64 ± 6.52 | 58.65 ± 8.56 | 0.013 | 0.990 |
| Atrial Fibrillation Duration (months) | 31.15 ± 9.93 | 32.21 ± 10.54 | 0.750 | 0.454 |
| Antithrombotic Therapy prior to Procedure | 83 (80.6%) on warfarin, 20 (19.4%) on DOACs | 81 (75.7%) on warfarin, 26 (24.3%) on DOACs | 0.731 | 0.393 |
| Paroxysmal AF (%) | 55 (53.4%) | 52 (48.6%) | 0.484 | 0.487 |
| Persistent AF (%) | 48 (46.6%) | 55 (51.4%) | 0.484 | 0.487 |

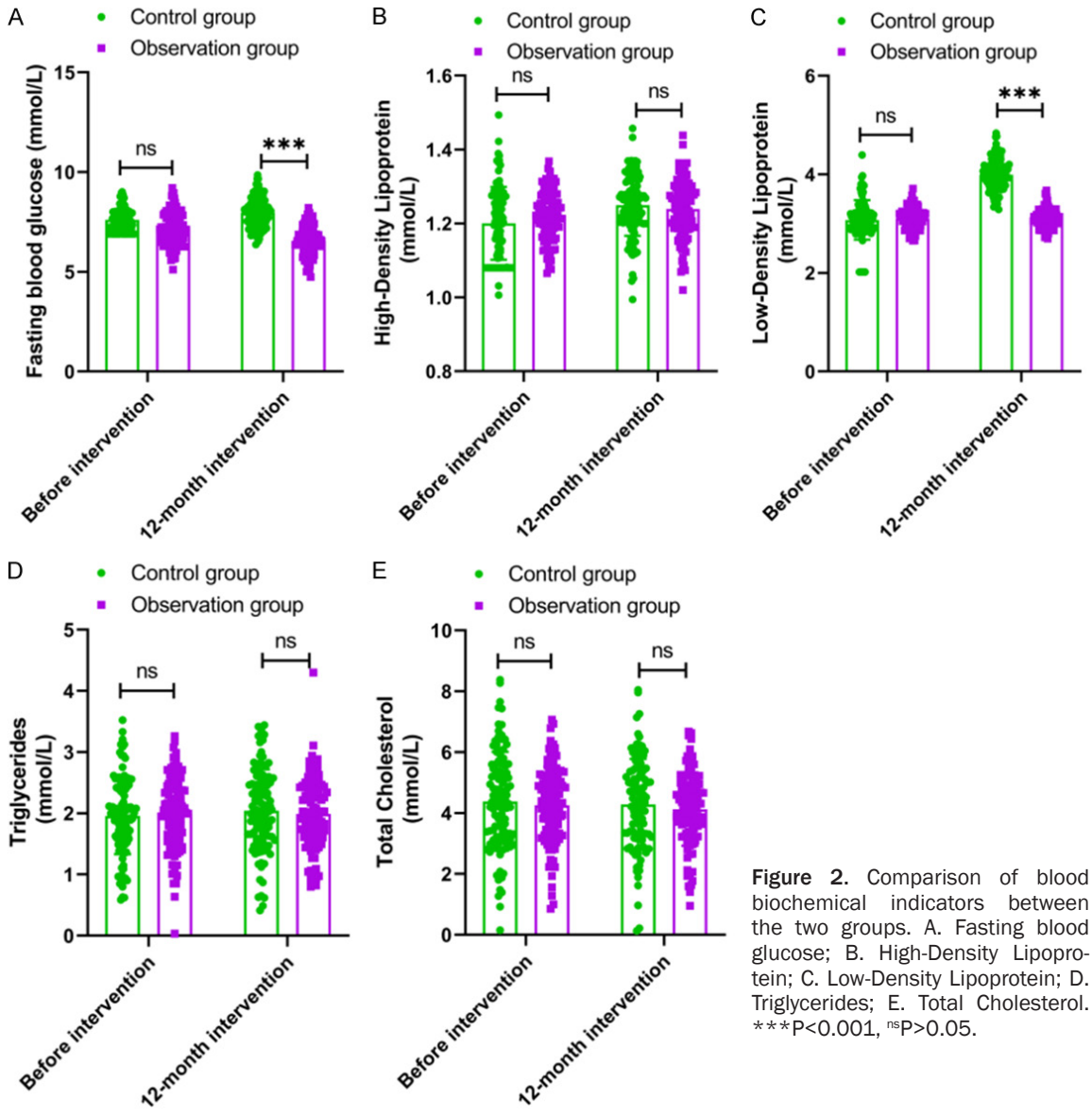


**Figure 2.** Comparison of blood biochemical indicators between the two groups. A. Fasting blood glucose; B. High-Density Lipoprotein; C. Low-Density Lipoprotein; D. Triglycerides; E. Total Cholesterol. ***P<0.001, $^{ns}$P>0.05.

*Cognitive functions*

Before the intervention, the two groups were comparable in cognitive function (all P>0.05). After the intervention, the observation group demonstrated significantly higher MMSE scores (**Figure 3A**), Visual-Spatial Ability scores (**Figure 3B**), Attention and Working Memory scores (**Figure 3C**), Verbal Fluency scores (**Figure 3D**), and Digit Symbol Substitution scores (**Figure 3E**) compared to the control group (all P<0.001). These findings suggest that post-procedure anticoagulation therapy significantly improved cognitive function across multiple cognitive domains.

*Incidence of MAEs*

The overall incidence of MAEs was lower in the observation group compared with the control group, though the difference was not significant (11.7% vs. 16.8%) (P = 0.284). Specifically, the incidence of ischemic stroke (1.9% vs. 5.6%, P = 0.165), hemorrhagic stroke (1.0% vs. 1.9%, P = 0.583), and TIA (1.0% vs. 2.8%, P = 0.331), intracranial bleeding (1.0% vs. 2.8%, P = 0.331), gastrointestinal bleeding (1.9% vs. 3.7%, P = 0.435), acute myocardial infarction (0% vs. 0.9%, P = 0.325), VTE (1.0% vs. 0%, P = 0.307), and new arrhythmic events (including new atrial fibrillation or flutter) (1.9% vs. 3.7%,

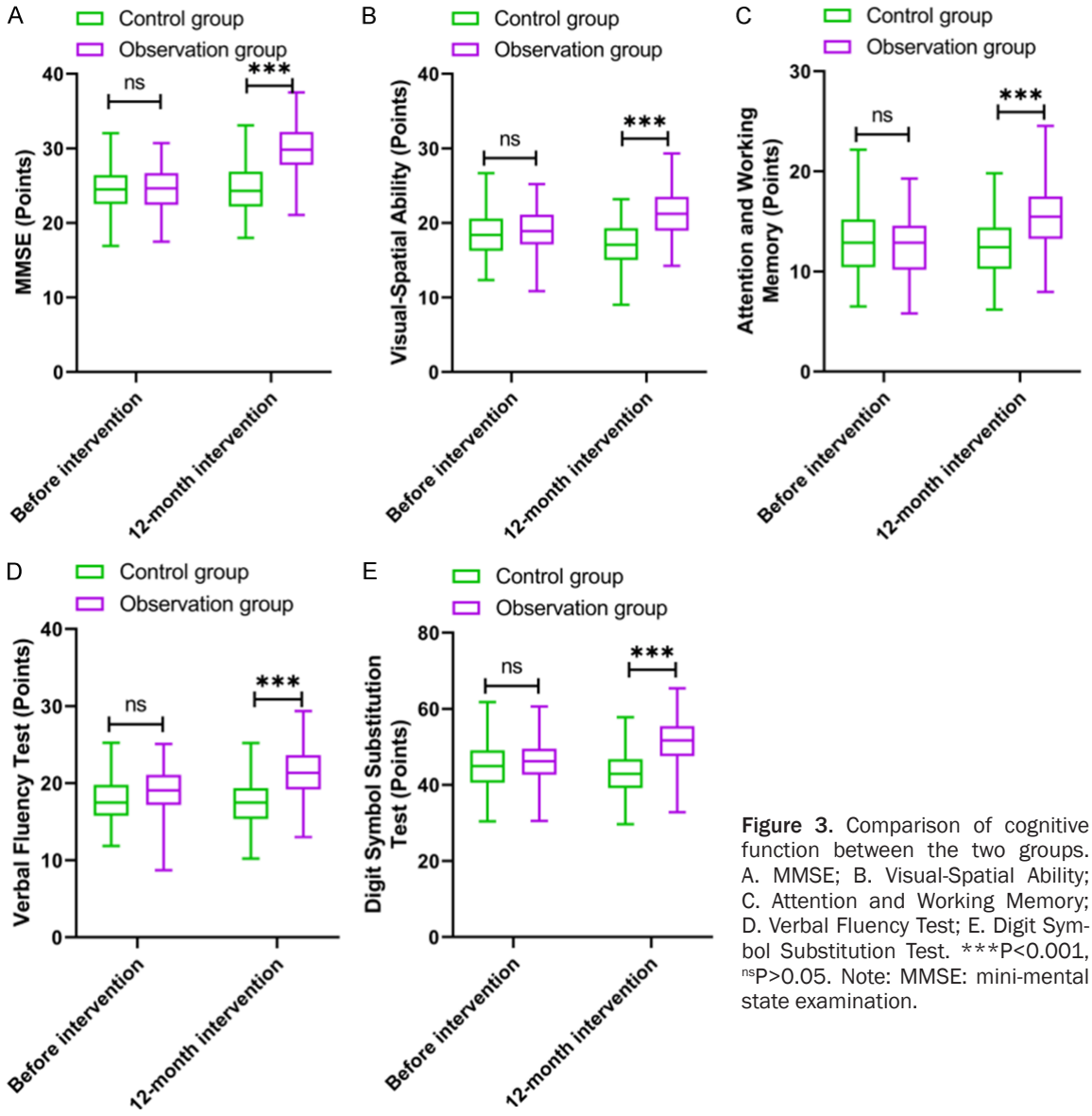


**Figure 3.** Comparison of cognitive function between the two groups. A. MMSE; B. Visual-Spatial Ability; C. Attention and Working Memory; D. Verbal Fluency Test; E. Digit Symbol Substitution Test. ***P<0.001, $^{ns}$P>0.05. Note: MMSE: mini-mental state examination.

P = 0.435) was comparable between the two groups (**Table 2**). In addition, there was also no significant difference in all-cause mortality (2.9% vs. 4.7%, P = 0.505) or cardiac arrest (1.0% vs. 1.9%, P = 0.583) between the two groups. These findings suggest that while post-procedure anticoagulation therapy did not significantly alter the overall rate of major adverse events, it was associated with a lower incidence of ischemic stroke, suggesting clinical benefit in preventing stroke in AF patients.

*Quality-of-life scores*

The Physical Health Score and Mental Health Score showed marked improvements in the observation group (P<0.001 for both). Similarly, the Social Functioning Score and Overall Quality of Life Score were significantly better in the observation group after 12 months (P<0.001 for both), while the control group showed no significant improvement (**Figure 4**). These findings suggest that post-procedure anticoagulation improves cognition and overall quality of life in AF patients.

*Blood coagulation values*

Patients in the observation group exhibited significantly prolonged PT and aPTT (P<0.001) compared to the control group, indicating an enhanced anticoagulation effect. Furthermore,

**Table 2.** Comparison of the incidence of major adverse events between the two groups

| | Observation Group (N = 103) | Control Group (N = 107) | $\chi^2$ | *P*-Value |
|---|---|---|---|---|
| Major Adverse Events (Total) | 12 (11.7%) | 18 (16.8%) | 1.146 | 0.284 |
| Ischemic Stroke | 2 (1.9%) | 6 (5.6%) | 1.925 | 0.165 |
| Hemorrhagic Stroke | 1 (1.0%) | 2 (1.9%) | 0.301 | 0.583 |
| Transient Ischemic Attack (TIA) | 1 (1.0%) | 3 (2.8%) | 0.944 | 0.331 |
| Major Bleeding Events | 4 (3.9%) | 7 (6.5%) | 0.747 | 0.387 |
| Intracranial Bleeding | 1 (1.0%) | 3 (2.8%) | 0.944 | 0.331 |
| Gastrointestinal Bleeding | 2 (1.9%) | 4 (3.7%) | 0.610 | 0.435 |
| Death (All-Cause) | 3 (2.9%) | 5 (4.7%) | 0.444 | 0.505 |
| Cardiac Arrest | 1 (1.0%) | 2 (1.9%) | 0.301 | 0.583 |
| Acute Myocardial Infarction | 0 (0%) | 1 (0.9%) | 0.967 | 0.325 |
| Venous Thromboembolism (VTE) | 1 (1.0%) | 0 (0%) | 1.044 | 0.307 |
| Arrhythmic Events (New AF/Flutter) | 2 (1.9%) | 4 (3.7%) | 0.610 | 0.435 |

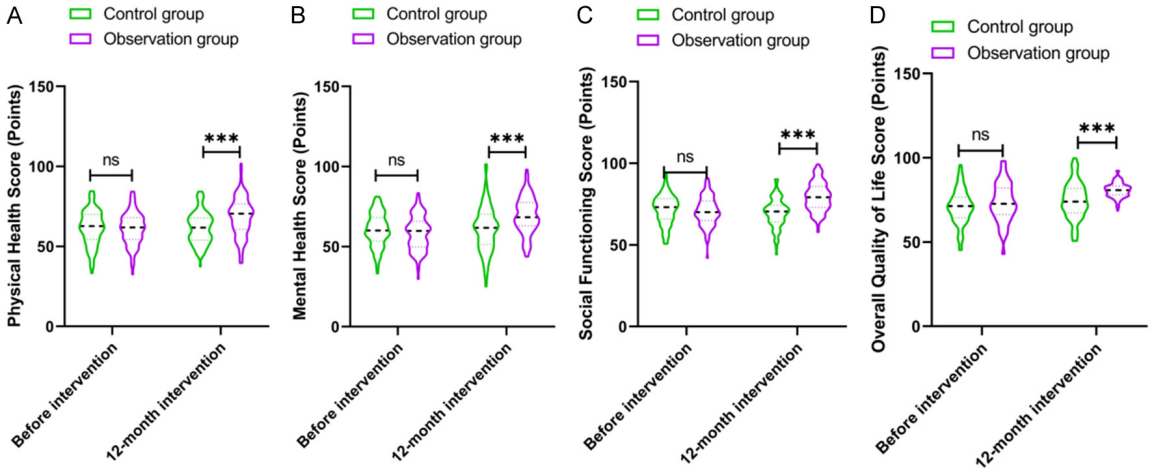


**Figure 4.** Comparison of Quality-of-Life scores between the two groups. A. Physical Health; B. Mental Health; C. Social Functioning; D. Overall Quality of Life. ***P<0.001, $^{ns}$P>0.05.

the INR was significantly higher in the observation group (P<0.001), further confirming effective anticoagulation. In contrast, the fibrinogen levels in the observation group were significantly lower, while D-dimer levels were significantly higher (both P<0.001) (**Figure 5**), suggesting that anticoagulation therapy not only affects coagulation factors but may also alter fibrinolytic activity.

*Logistic regression analysis of factors associated with cognitive impairment*

Logistic regression analysis was performed to identify independent factors affecting cognitive impairment in AF patients. The results revealed that anticoagulation therapy was a significant protective factor, with an OR of 0.940 (95% CI: 0.910-0.972, P<0.001) (**Table 3**).

## Discussion

This study explored theeffect of post-LAA occlusion anticoagulation strategies on cognitive function in AF patients. Our results demonstrated that anticoagulation therapy after LAA occlusion is effective in enhancing cognitive function, as evidenced by higher scores on MMSE, Attention and Working Memory, Visual-Spatial ability tests. These findings indicate that post-procedural anticoagulation therapy not only aids in stroke prevention but also exerts notable cognitive advantages. The novelty of this study lies in its focus on a compara-

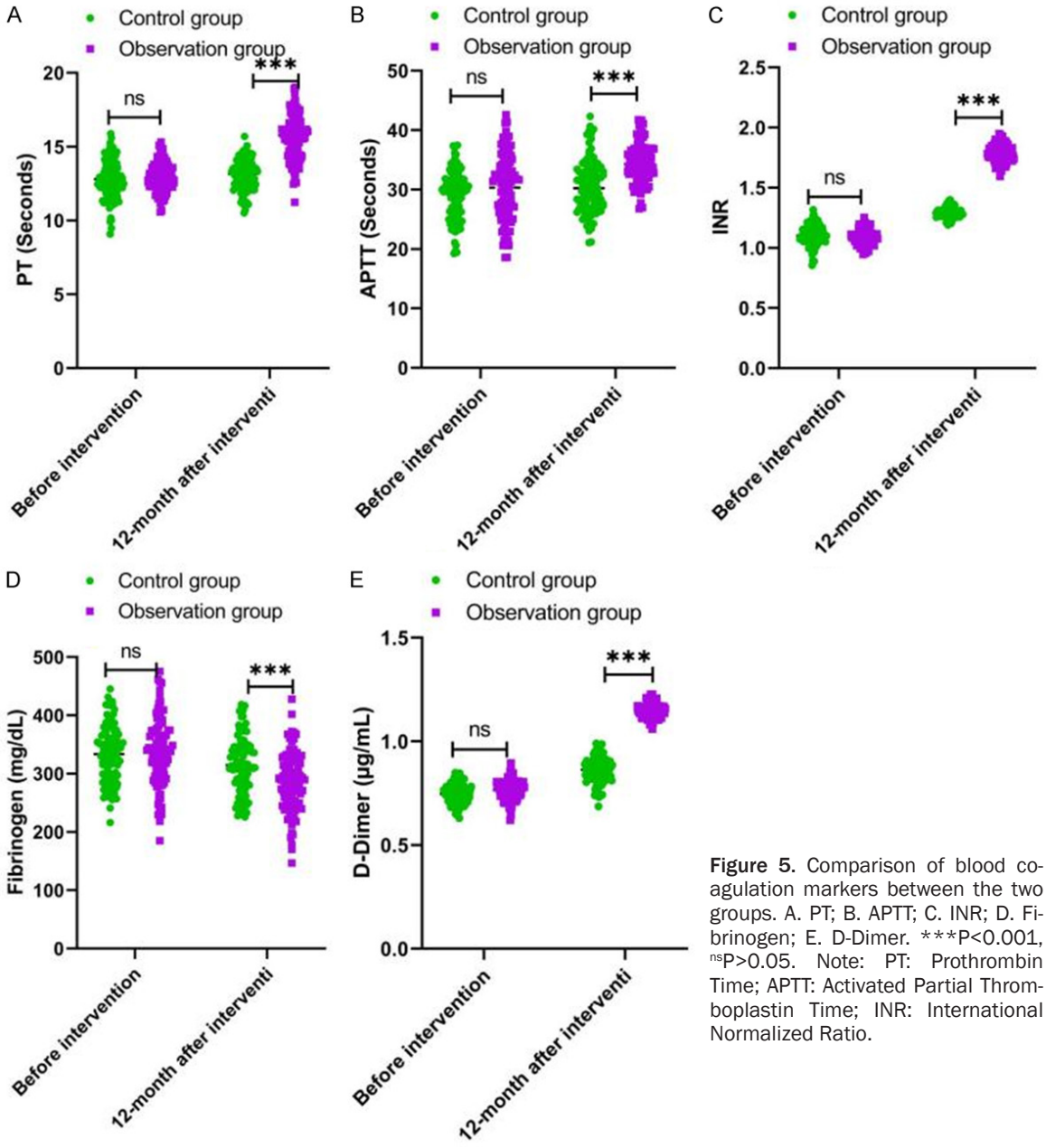


**Figure 5.** Comparison of blood coagulation markers between the two groups. A. PT; B. APTT; C. INR; D. Fibrinogen; E. D-Dimer. ***P<0.001, $^{ns}$P>0.05. Note: PT: Prothrombin Time; APTT: Activated Partial Thromboplastin Time; INR: International Normalized Ratio.

**Table 3.** Logistic regression analysis of the factors associated with cognitive impairment

| Variable | B | SE | Wald | P | OR | 95% CI |
|---|---|---|---|---|---|---|
| Anticoagulation therapy | 0.062 | 0.017 | 13.253 | <0.001 | 0.940 | 0.910-0.972 |
| Ischemic stroke | 0.048 | 0.042 | 1.264 | 0.261 | 1.049 | 0.965-1.140 |
| Constant | 2.807 | 1.824 | 2.369 | 0.124 | 16.448 | - |

tively underexplored domain of post-LAA occlusion management, providing new insight into the broader application of anticoagulation therapy.

A key finding of this study is the protective effect of post-LAAO anticoagulation on the cognitive performance in AF patients. This aligns with previous studies reporting that anticoagu-

lation therapy may mitigate cognitive decline, especially among high-risk populations with AF [15-18]. However, existing literature remains inconclusive. While some studies have demonstrated positive effects, others have found no explicit correlation between anticoagulation use and cognitive function [19-21]. Furthermore, our findings support the cognitive benefits of anticoagulation following LAA occlusion, where it exerts benefits in both stroke prevention and improved hemodynamics.

Our findings provide additional evidence that post-LAAO anticoagulation treatment produced favorable changes in coagulation and metabolic values, as evidenced by prolonged PT and aPTT, and decreased LDL level. These biomarkers demonstrate that anticoagulation treatment not only modulates coagulation factors but also influence lipid metabolism, potentially enhancing blood vessels health and reducing thrombotic risk [22, 23]. This observation is consistent with previous studies reporting wider implications of anticoagulation therapy in cardiovascular health management [24]. The mechanisms may involve the ability of anticoagulation to alleviate microvascular damage and enhance cerebral perfusion, a condition that appears to be clinically advantageous in patients with cardiovascular diseases [25].

Another striking finding of this study is the reduction in stroke incidence observed in the anticoagulation group. This is consistent with prior research demonstrating that anticoagulation following an LAAO protects against ischemic stroke [26, 27]. Although the overall incidence of MAEs did not differ greatly between the two groups, the lower rate in ischemic stroke is clinically meaningful and reinforces the protective effect of anticoagulation treatment.

Despite these encouraging findings, several limitations in this study should be acknowledged. First, its retrospective design limits the ability to establish a causal relationship between anticoagulation therapy following LAAO and cognitive outcomes. Second, although the sample size was adequate for statistical analysis, it may not accurately represent the long-term outcomes or the diversity of anticoagulation strategies in a broader population. Third, the type of anticoagulation agent was not uniform, which may affect the generalizability of the findings. There is a need to conduct prospective, multicenter design in future studies to validate these findings.

## Conclusion

Anticoagulation therapy following LAA occlusion in AF patients improved cognitive function and reduced the incidence of ischemic stroke, underscoring its benefits in cognitive and cardiovascular protection.

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## Disclosure of conflict of interest

None.

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