



The Gap of Activated Clotting Time Recommendation Level Between Left Atrial Appendage Occlusion and Atrial Fibrillation Ablation:

Is it necessary to close it?



Kexin Wang

The First Affiliated Hospital Of Nanjing Medical University, China

Korean Heart Rhythm Society

COI Disclosure

Kexin Wang

The authors have no financial conflicts of interest
to disclose concerning the presentation



Disclosure

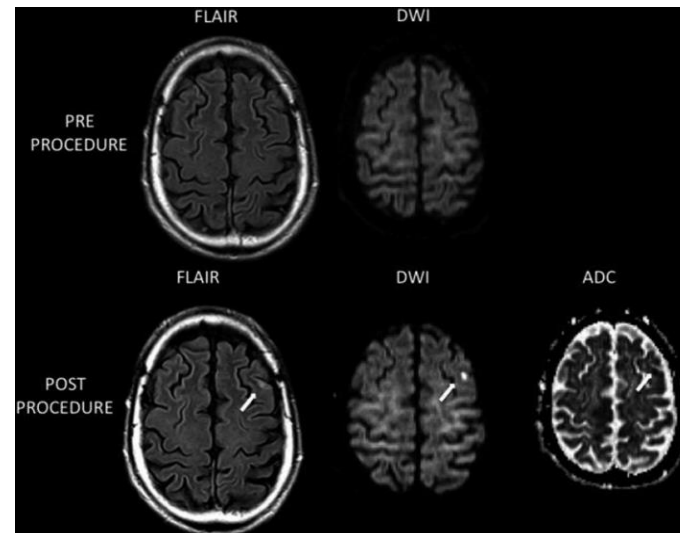
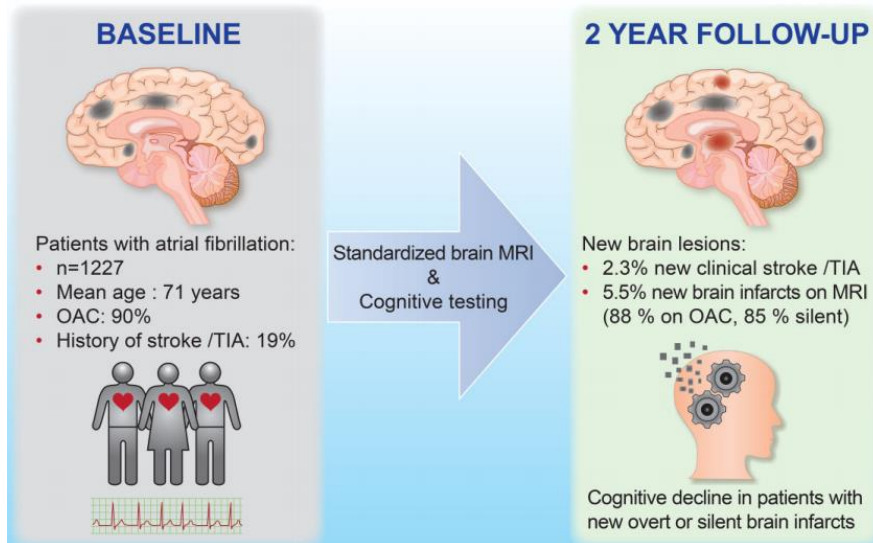
Relationships with commercial interests:

- Grants/Research Support: None.
- Consulting Fees: None.
- Other: None.



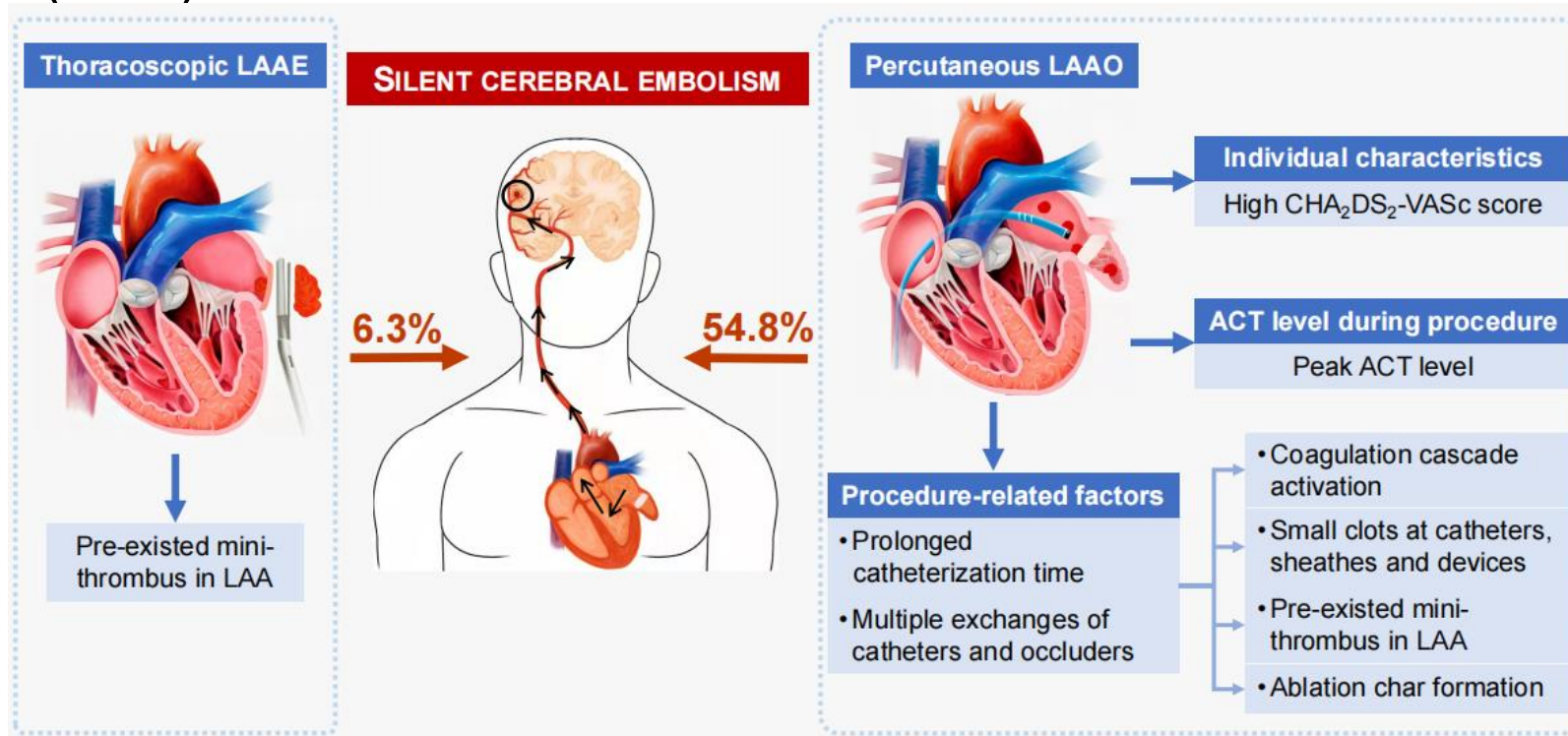
Background

- Atrial fibrillation (AF) is known to cause microembolisms throughout its long clinical course, which may increase the risk of Alzheimer's disease and decrease quality of life.
- **Interventional treatment** for AF, including either catheter ablation or left atrial appendage occlusion (LAAO) have been shown to be associated with a high incidence of acute **silent cerebral embolisms (SCE)**



Background

- Possible reasons for SCE development include thromboembolic clots, char formation or tissue clots and air embolism.
- Our previous study identified the following **risk factors** for SCE during LAAO procedure: high CHA₂DS₂-VASc score, left atrial procedure duration and peri-procedure activated clotting time (ACT) level.



Background

- Because of the **high incidence** of SCE and its **long-term impact on cognitive function**, preventive strategies should be taken to minimize the risk of SCE.
- Procedural manipulation-related factors can be surpassed with the refinement of technology. Learning curves can be even shorter with the innovative device and delivery system.
- However, **there remains no consensus regarding** the most appropriate ACT level for the LAAO procedure.
- **Guideline-recommended** ACT level for AF catheter ablation is **≥ 300 s.**
- **Expert consensus recommended** ACT level for LAAO is **≥ 250 s.**



Background

- **Guideline-recommended ACT level for AF catheter ablation is ≥ 300 s.**
- **Expert consensus recommended regarding the ACT level for LAAO is ≥ 250 s.**
- Deeply concerned about **the gap** in recommended ACT levels **between** AF ablation and LAAO implantation.
- We wondered if **increasing the targeted ACT level of LAAO to the same level as AF ablation** could decrease the incidence of peri-procedure minor thromboembolism without increasing the bleeding risk.
- Thus, we designed this prospective observational study to answer this question and to identify the most appropriate ACT patterns for LAAO procedures.



Methods

Study Population

- This prospective cohort study was performed at the First Affiliated Hospital of Nanjing Medical University between January 2021 and December 2022.
- AF patients receiving Watchman implantation were consecutively enrolled.
- The **inclusion criteria** were as follows:
 - 1) ≥ 18 years of age;
 - 2) previous ischemic stroke or a CHA₂DS₂-VASc score ≥ 3 ;
 - 3) unwilling or unable to take oral anticoagulant (OAC);
 - 4) no contraindications to MRI scan.



Methods

Study Population

- Prospective cohort study:
- Patients enrolled during 2021 were assigned to
- **Group 250 (maintaining the target ACT ≥ 250 s during LAAO implantation)**
- Patients enrolled during 2022 were assigned to
- **Group 300 (maintaining the target ACT ≥ 300 s during LAAO implantation)**



Methods

Electrophysiologic procedures

- All procedures were performed under **conscious sedation**.
- If AF ablation was combined, pulmonary vein isolation and substrate modification (if needed) were routinely performed. After AF ablation, LAAO was performed in all patients using the WATCHMAN device. The entire procedure was guided by intracardiac echocardiogram (ICE).
- **Total procedure time** was defined as the time between the first puncture of the femoral vein and the end of the procedure.
- **Left atrial (LA) procedure time** was calculated from the successful transseptal puncture to the withdrawal of all sheaths and catheters from the LA.
- **LAAO placement time** was defined as the time between inserting the delivery system and successful release of the LAAO device.



Methods

Periprocedure antithrombotic therapy and assessments of ACT

- All patients received uninterrupted anticoagulation therapy with rivaroxaban (15 mg) for at least 3 weeks before the procedure.
- Rivaroxaban was not interrupted during the whole procedure.
- Left atrial thrombi were routinely screened by transesophageal echocardiography before the procedure.
- After implantation, all patients were treated with rivaroxaban (15 mg) and aspirin (100 mg) for at least 45 days.



Methods

Periprocedure antithrombotic therapy and assessments of ACT

- **Group 250:** a weight-adjusted bolus of first dose heparin (**80 IU/kg**) was administered upon TSP. If AF ablation was combined, the additional heparin dosage was adjusted as needed to maintain the **ACT ≥ 300 s** during the ablation procedure. After ablation, heparin was only supplemented when the ACT level was < 250 s during LAAO implantation (**target ACT ≥ 250 s**).
- **Group 300:** a bolus of heparin (**100 IU/kg**) was administered upon TSP and supplemented as needed to maintain a **target ACT of ≥ 300 s** during the whole procedure.
- ACT was monitored every 10-15 min.



Methods

Cerebral MRI acquisition and analysis

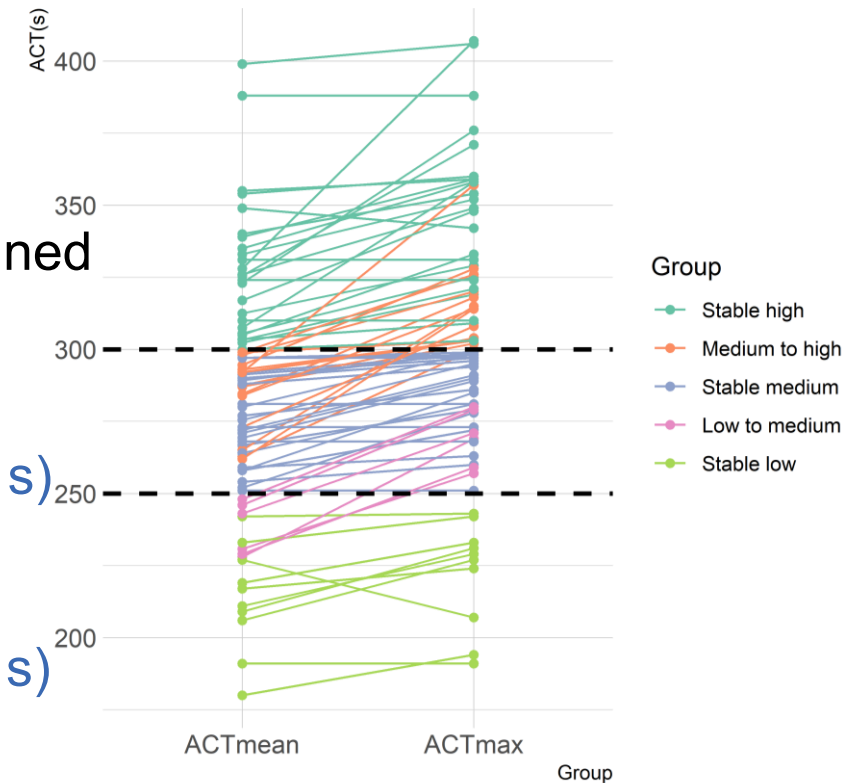
- All patients underwent cerebral MRI with a 1.5T scanner, slice thickness 2 mm before procedure, and within 7 days after procedure.
- MRI images were analysed by an independent neuroradiologist blinded to the clinical information. All lesions were carefully assessed and recorded for size, depth, and location.



Methods

Statistical Analysis

- To minimize potential selection bias and enhance the comparability of study subjects between two groups, we applied an IPTW matching procedure.
- We categorized ACT into **three levels**:
 $ACT < 250$ s; $250 \text{ s} \leq ACT < 300$ s; $ACT \geq 300$ s.
- Using ACT_{mean} and ACT_{peak} levels during procedure, we defined **Five ACT change patterns**:
 - Stable low (both < 250 s)
 - Low to medium ($ACT_{mean} < 250$ s and $250 \text{ s} \leq ACT_{peak} < 300$ s)
 - Stable medium ($250 \text{ s} \leq$ both ACT < 300 s)
 - Medium to high ($250 \text{ s} \leq ACT_{mean} < 300$ s and $ACT_{peak} \geq 300$ s)
 - Stable high (both ≥ 300 s)
- Multivariate logistic regression analysis was used to examine the relationship between different ACT level patterns during the procedure and the incidence of new SCE.



Results Patient Characteristics

Between Jan 2021 and Dec 2022, 81 patients were enrolled and underwent pre- and postprocedure MRI

	All Patients			IPTW		
	Group250(n=38)	Group300(n=43)	P value	Group250(n=25.66)	Group300(n=24.92)	P value
Age(year)	69.13±7.48	67.67±7.73	0.393	67.71±6.69	67.43±8.20	0.877
Male	19(50.0%)	28(65.1%)	0.25	13.5 (52.6%)	13.1 (52.5%)	0.993
Hypertension	26(68.4%)	27(62.8%)	0.766	16.6 (64.7%)	16.6 (66.6%)	0.871
CAD	12(31.6%)	13(30.2%)	1	8.1 (31.7%)	8.2 (32.8%)	0.925
Diabetes	11(28.9%)	6(14.0%)	0.167	5.4 (20.9%)	5.1 (20.4%)	0.963
NPAF	25(65.8%)	28(65.1%)	1	16.0 (62.3%)	14.4 (57.6%)	0.704
Prior Ischemic stroke	28(73.7%)	41(95.3%)	0.015	23.6 (92.1%)	22.9 (92.0%)	0.98
CHA2DS2-VASc Score	4.26±1.72	4.47±1.24	0.543	4.42±1.61	4.63±1.29	0.552
HASBLED Score	2.45±0.86	2.33±0.78	0.506	2.53±0.81	2.32±0.78	0.275
LAD (mm)	43.16±4.53	44.65±4.63	0.147	43.57±4.30	43.39±4.43	0.858
LVEF (%)	62.89±3.03	62.88±4.38	0.992	62.67±3.38	62.65±4.78	0.985
LAAO placement time (min)	45.18±25.70	40.93±19.02	0.396	43.99±25.28	42.23±19.07	0.749
LA procedure time (min)	110.87±60.19	110.44±49.55	0.972	114.38±60.16	112.10±48.11	0.865
Entire procedure time (min)	137.68±66.36	147.79±55.99	0.459	142.98±64.75	150.30±54.89	0.62
new SCE	21 (55.3%)	14 (32.6%)	0.067	16.2 (63.2%)	9.2 (37.0%)	0.038
Baseline ACT (s)	140.87±32.46	136.56±32.37	0.552	138.51±32.20	137.96±33.58	0.946
Average ACT (s)	272.13±51.22	292.54±29.29	0.028	265.82±46.43	294.31±28.22	0.002
Peak ACT (s)	288.37±51.76	311.70±35.21	0.019	283.68±49.13	312.23±34.52	0.006

55.3%



32.6%

P=0.038



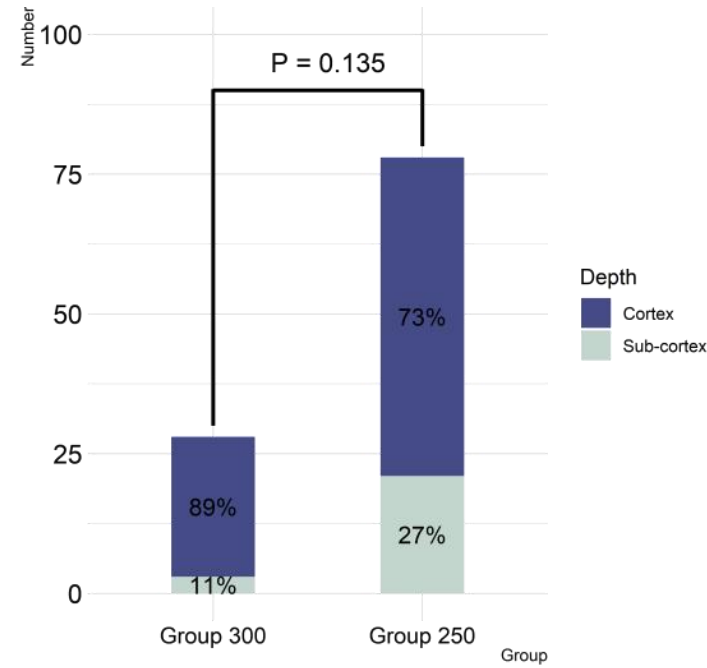
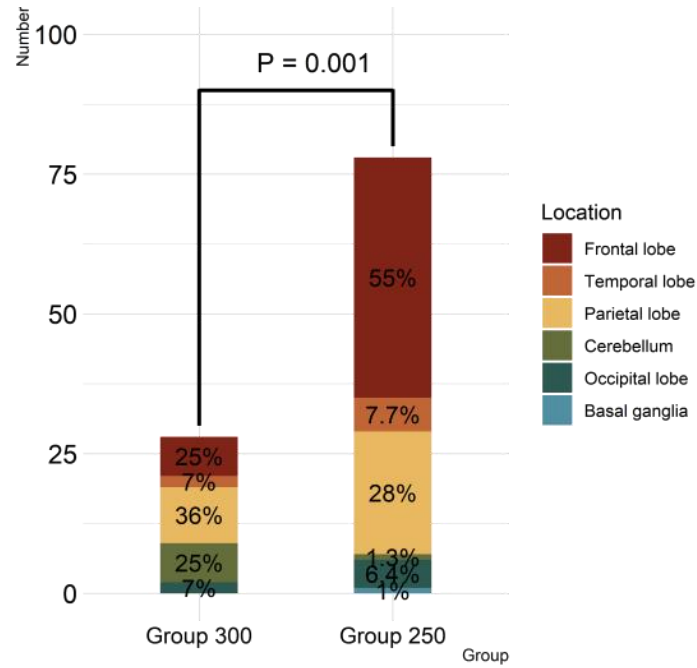
Results

- Thirty-two patients (18 in group 250 and 14 in group 300) who received LAAO alone were in AF rhythm during postprocedure MRI scanning periods.
- **No serious complications** (including closure-device disengagement, stroke, major bleeding and severe pericardial tamponade) occurred during the peri-procedural period.
- Three patients in group 250 and 5 patients in group 300 suffered from **bruising or mild hematoma formation** at the venepuncture site ($p = 0.850$), which resolved gradually with conservative treatment.



Results

Results of MRI images

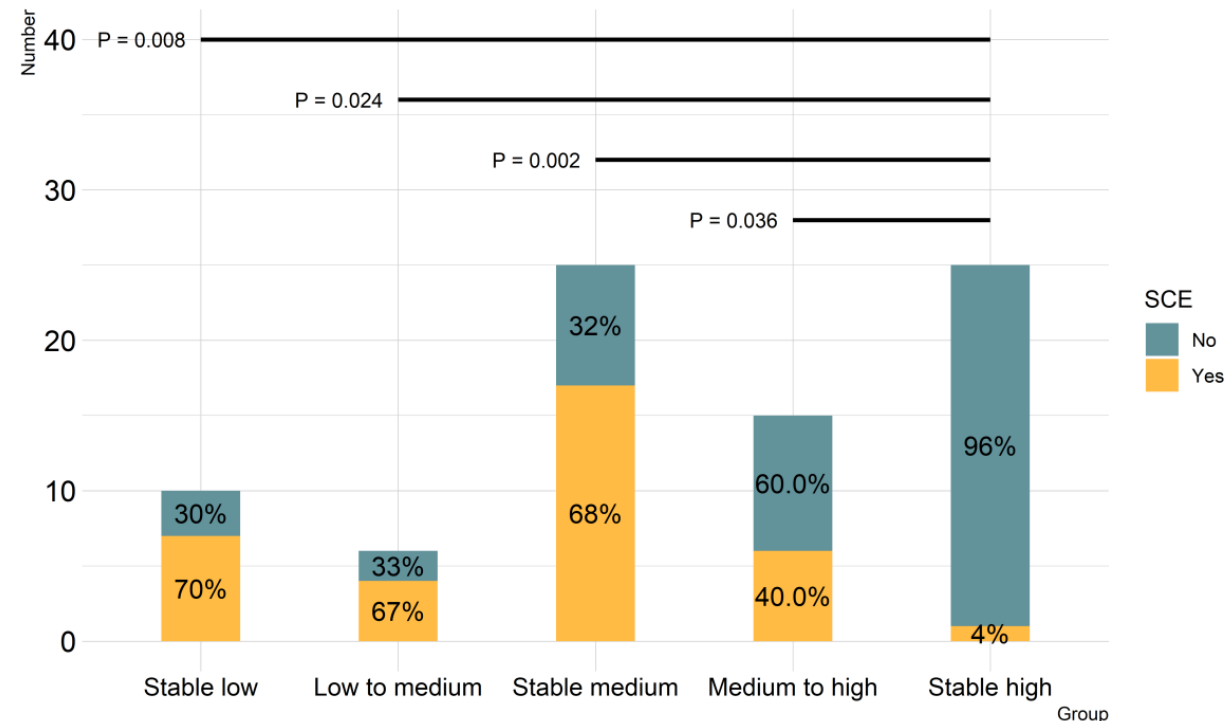


- MRI found a total of 106 lesions, including 28 lesions among 14 patients in group 300 and 78 lesions among 21 patients in group 250.
- 11 patients in group 250 and 5 patients in group 300 suffered from multiple lesions.
- A total of 77.4% (82/106) of the lesions were located in the cortex. 47.2% (50/106) located in the frontal lobe, and 30.1% (32/106) located in the parietal lobe.
- No significant differences were observed between these two groups in lesion size (4.02 mm vs. 4.35 mm, $p = 0.49$), location or depth.



Results

Relations of peri-procedure ACT level patterns with the incidence of SCE



- Using the stable low group as the reference. As expected, stable high ACT levels had decreased risks of SCE incidence ($p = 0.008$), and the other 3 groups had no significant difference from the stable low group.
- Stable high group was significantly different from the other groups ($p = 0.036, 0.002, 0.024,$ and 0.008 , respectively) (Figure 3).
- No significant interaction was found between ACT level patterns and LAAO placement time (p interaction = 0.472) or CHA2DS2-VASc score (p interaction = 0.592).



Discussion

- This prospective observational study is the first to investigate the relationship between the incidence of LAAO procedure-related SCE and different ACT levels and patterns in Asian individuals.
- Five ACT patterns in terms of ACT_{mean} and ACT_{peak} levels during the LAAO procedure were innovatively defined to explore the most appropriate ACT level.
- **Important findings:**
 1. Increasing the peri-procedure ACT level by increasing the first dose bolus of heparin upon TSP can significantly decrease the incidence of SCE without additional risk of bleeding compared with traditional practice.
 2. Only participants in the stable high group (ACT_{peak} ≥300 s and ACT_{mean} ≥300 s) had the lowest risk of SCE incidence.
- These findings underscore the importance of maintaining a stable high level of ACT during the LAAO procedure, especially in patients with a high risk of stroke and in patients with a prolonged procedure duration.



Discussion

- Previous studies have demonstrated that LAAO has a surprisingly high incidence of peri-procedural SCE detected by thin-layer MRI scans, even **higher than catheter ablation**.
- Transcatheter LAAO was introduced with the aim of preventing thromboembolism and improving cognitive status and quality of life. Therefore, **avoidance of periprocedural SCE is of great importance**.
- **Raising the targeted ACT level of LAAO to the same level as AF ablation significantly decreases the incidence of SCE without sacrificing the bleeding risk.**
- Therefore, it might be reasonable and necessary to apply a more intensive anticoagulation therapy to increase the target ACT to ≥ 300 seconds.



Discussion

- Additionally, for patients with multiple exchanges of devices and prolonged catheter manipulation, which was reported to be associated with a higher SCE risk, enhanced heparinization to a target ACT to ≥ 300 seconds can still decrease the risk of procedure-related SCE.
- Patients with more cardiovascular comorbidities reflecting more impaired LA endothelial function might also need a higher target ACT level.
- In the ACT stable high group, the SCE incidence was as low as 4%. These results suggest that LAAO with the WATCHMAN device can be a safe procedure under enhanced heparinization.



Limitations

- Overall sample size was relatively small. The small sample size might increase the stochasticity of the incidence of adverse events. However, the primary findings were still statistically significant even with the small sample size.
- Non-randomly designed. We enrolled consecutive eligible patients and propensity score matching was used to avoid the bias.
- The long-term improvement on cognitive function of this measure should be further evaluated during follow-up based on the present results.



Conclusion

Raising the targeted ACT level of LAAO to 300 s reduces the risk of SCE without increasing the major bleeding events compared to the conventional 250 s strategy. Only a stable high ACT level can result in a significantly lower SCE incidence. Future studies assessing the long-term effect of this proposal on cognitive function are necessary.





THANKS