Original Article

Endocardial Left Atrial Appendage Closure for Stroke Prevention in Patients Undergoing Cardiac Surgery: Meta-Analysis

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Abstract

Background: **Prior studies have confirmed that left atrial appendage closure (LAAC) reduces stroke risk. However, most analyses combined various closure techniques. The specific effect of the endocardial suture technique alone remains unclear. Furthermore, follow-up showed variable rates of complete closure after endocardial suturing. Whether it could consistently prevent stroke in real-world practice was debated.**

Objective: **This study aimed to evaluate the effectiveness and safety of concomitant endocardial LAAC during cardiac surgery, with or without other cardiac conditions, to prevent cerebrovascular events.**

Methods: **Adhering strictly to PRISMA guidelines, we systematically searched PubMed, EMBASE, and other databases (from inception to January 2025) for studies comparing stroke risk in patients undergoing cardiac surgery with versus without LAAC. Literature screening was performed independently by two investigators, with disagreements resolved by a third. To assess robustness, we performed a sensitivity analysis stratified by study design using a random-effects REML model with Knapp-Hartung adjustment. A two-sided alpha level of 0.05 was set for hypothesis testing in the meta-analysis. Four studies involving 1853 patients (LAAC group: n=1074; no LAAC group: n=779) were included.**

Results: **The incidence of strokes was significantly lower in the LAAC group than in the no-LAAC group, resulting in a 73% relative risk reduction. There was no significant difference in all-cause mortality between the two groups (p=0.75). Heterogeneity analysis indicated stable results. In the sensitivity analysis, the RCTs subgroup did not reach statistical significance (p=0.22), while the RCSs subgroup showed borderline significance (p=0.05); the overall significant result was driven by increased statistical power when pooling all studies.**

Conclusion: **Concomitant endocardial LAAC was associated with a significant reduction in the risk of cerebrovascular events (1.5% vs. 5.8%, OR=0.27, 95% CI: 0.16–0.46, p<0.01). Sensitivity analysis confirmed the direction of benefit across study designs, though evidence from RCTs remains limited.**

Keywords: **Left Atrial Appendage Closure; Cardiac Surgical Procedures; Transient Ischemic Attack.**

Introduction

Since 1940, surgical closure of the left atrial appendage (LAA) has been considered for stroke prevention.[1] However, debate persisted regarding the efficacy of LAA closure in preventing stroke until Whitlock's multicenter, double-blind, randomized trial definitively established that surgical LAA closure effectively prevents postoperative stroke. Surgical LAA closure techniques evolved into multiple approaches. These include surgical LAA excision, epicardial patch closure, stapler resection, endocardial suture closure, and LAA clip exclusion. Among these techniques, suture-based methods (including endocardial suturing) yield an average cost savings of $851 per patient.[2]

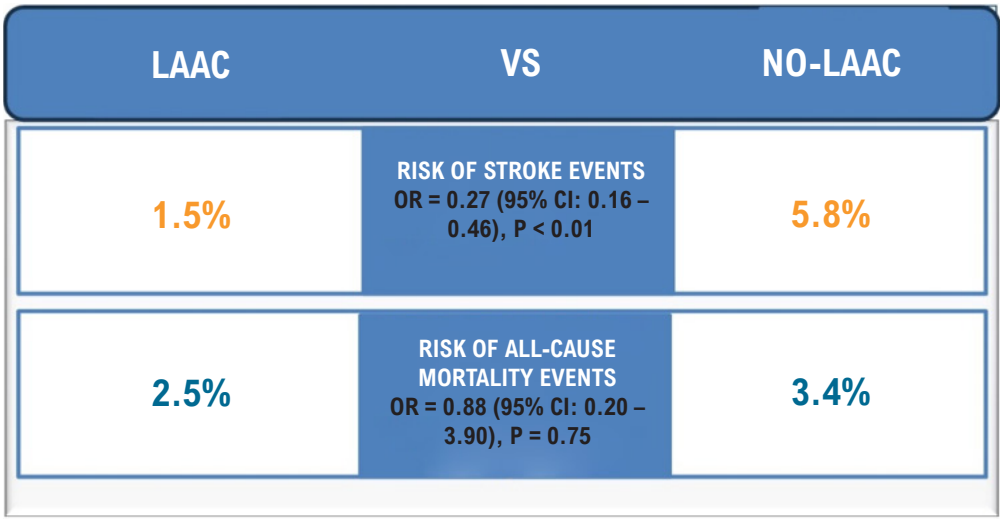
Endocardial suture closure was widely employed clinically, particularly in procedures involving intracardiac access to the left atrium, such as mitral valve surgery, or when performed via a right thoracotomy approach (which limits adequate external visualization of the LAA), as in minimally invasive thoracotomy or robotic-assisted mitral valve replacement.[3-9] This technique required cardioplegic arrest and atriotomy to perform a continuous suture closure from within the left atrial cavity.

Given the cost-effectiveness and broad applicability of endocardial suture closure, whether it effectively prevented stroke in clinical practice was uncertain and needed further study. However, in current high-level evidence, the effect of this technique was often mixed with that of other simultaneous surgeries, making its precise stroke-prevention benefit hard to attribute. This meta-analysis aimed to assess the incidence of strokes in patients with atrial fibrillation (AF) undergoing cardiac surgery with or without concomitant endocardial suture closure.

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Central Illustration: Endocardial Left Atrial Appendage Closure for Stroke Prevention in Patients Undergoing Cardiac Surgery: Meta-Analysis



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Methods

Ethical considerations

As this study involved the analysis of previously published data and did not include individual patient participation, approval from an institutional review board and patient consent were not required. The datasets generated and analyzed during this study were available from the corresponding author upon reasonable request.

Literature search strategy

A systematic literature search was conducted using the following key terms and combinations:

#1 ("left atrial appendage"[MeSH Terms] OR "left atrial appendage"[Title/Abstract] OR ("left"[Title/Abstract] AND "atrial appendage"[Title/Abstract]))

#2 ("occlusion"[Title/Abstract] OR "exclusion"[Title/Abstract] OR "amputation"[Title/Abstract] OR "closure"[Title/Abstract] OR "ligation"[Title/Abstract] OR "obliteration"[Title/Abstract])

#3 ("endocardial"[Title/Abstract] OR "intracardiac"[Title/Abstract])

#4 ("stroke"[MeSH Terms] OR "stroke"[Title/Abstract] OR "stroke"[Title/Abstract] OR "stroke"[Title/Abstract] OR "brain vascular accident"[Title/Abstract] OR "apoplexy"[Title/Abstract] OR "randomized controlled trial"[Publication Type] OR "randomized controlled trial"[Title/Abstract] OR "RCT"[Title/Abstract] OR "randomised"[Title/Abstract])

#5 #1 AND #2 AND #3 AND #4

This systematic review was conducted in line with PRISMA guidelines. Figure 1 shows the study selection flow. We searched PubMed and EMBASE from their inception to January 2025 for studies comparing stroke risk in patients with AF undergoing cardiac surgery with or without concomitant left atrial appendage closure (LAAC) via the endocardial suture technique. We also manually screened reference lists of relevant studies and reviews. Two investigators independently selected studies, resolving disagreements through discussion with a third investigator.

Selection criteria

Two investigators jointly assessed the methodological quality of observational studies and randomized controlled trials (RCTs). The National Institutes of Health (NIH) Quality Assessment Tool was used for observational studies. Study quality was categorized as Good, Fair, or Poor. All other study types were excluded. Conference abstracts, meeting reports, review articles, editorials, letters to the editor, and commentaries were also excluded from this systematic review.

To address duplicate data, the study periods of multiple publications originating from the same research center were examined. Following these selection criteria, for dichotomous outcomes, the pooled risk ratio (RR) with its 95% confidence interval (CI) was used to analyze the effect size. We compared concomitant LAAC versus standard cardiac surgery alone for the following outcomes: strokes and all-cause mortality.

The present study implemented rigorous quality control criteria during the literature screening process: we required all included studies to clearly report stroke or transient ischemic attack outcomes; we excluded studies with mixed surgical techniques that precluded isolation of the effect of endocardial LAAC alone; and we prioritized studies with low risk of bias to ensure the validity of the meta-analysis. This strict selection strategy, although resulting in only 4 eligible studies from an initial 2,706 records, underscores the high quality of the synthesized evidence and highlights the considerable difficulty in identifying suitable studies in this field.

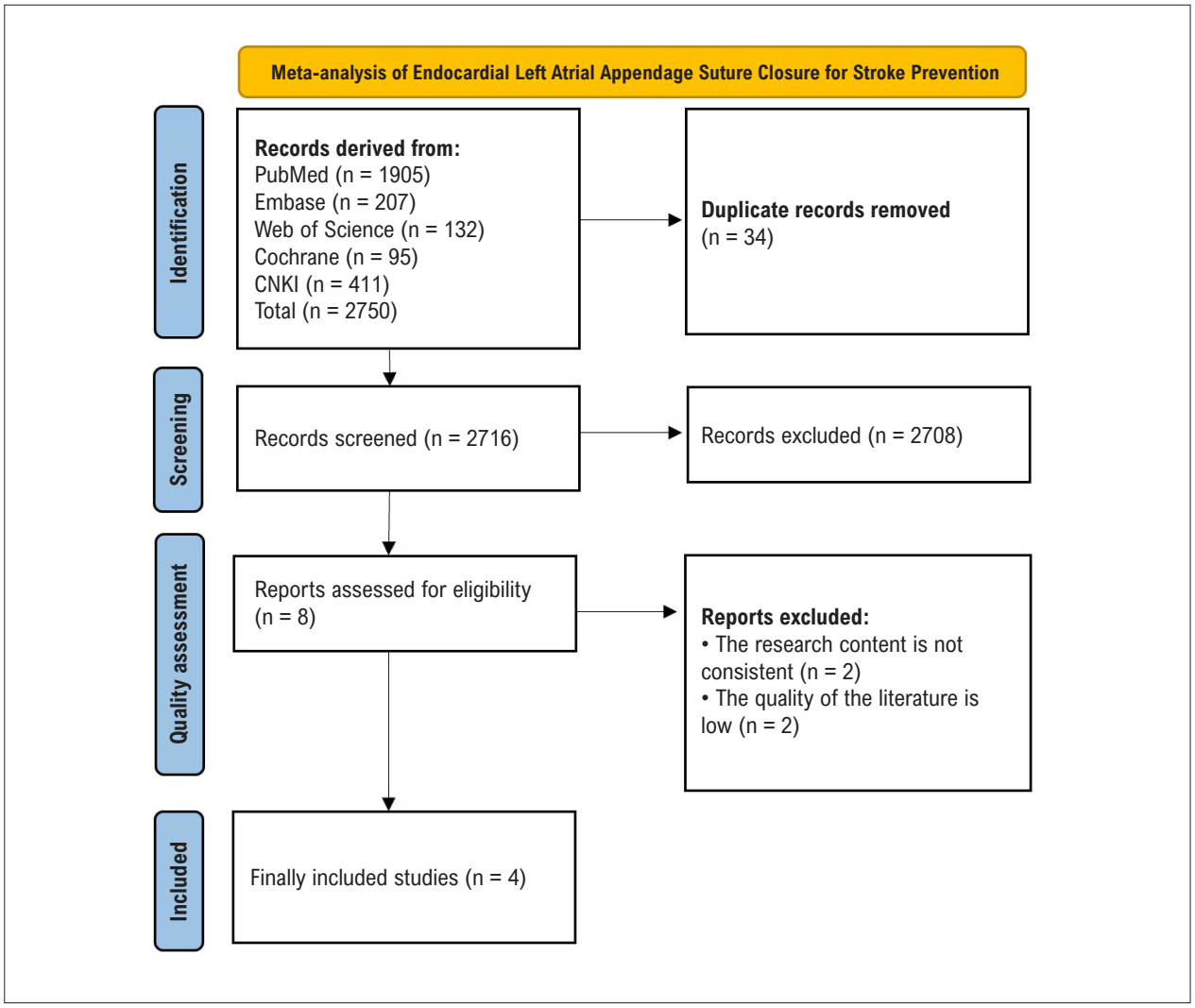


Figure 1 – *PRISMA guidelines.*

Data extraction and critical appraisal

After the study selection, data extraction was performed using Microsoft Excel. Categorical variables are presented as counts (percentages), and continuous variables are reported as mean ± standard deviation (SD). Data extracted included the study period, research center, country, study design, and sample size. The included studies showed some variability in the information reported. Specifically, each article provided a distinct set of variables, some of which were unique to that study and not reported by the others. For each included variable, whether categorical or continuous, the reporting method was recorded.

For stroke and all-cause mortality outcomes, we directly extracted the number of events and the total sample size for each treatment group from each study. For any study with zero events in one arm, a continuity correction of 0.5 was applied to both arms to enable calculation of odds ratios. All extracted data were independently double-checked against the original publications by two investigators, with discrepancies resolved by consensus or a third investigator. The aggregate data used for the meta-analysis are available from the corresponding author upon reasonable request.

The quality of included non-randomized studies of interventions was assessed using the Risk Of Bias In non-randomized Studies of Interventions (ROBINS-I) tool (Table 1).[10] For RCTs, the risk of bias was assessed using the Cochrane Collaboration's Risk of Bias tool version 2 (RoB 2) (Table 2).[11] The certainty of evidence for conclusions derived from the comparative meta-analysis was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework (Table 3).[12]

Statistical analysis

The primary endpoint was the occurrence of stroke, analysed as a binary outcome based on the extracted event counts from each study's aggregate data. For each included study, the original authors' definition of cerebrovascular events was used.

For categorical variables, the odds ratio (OR) with 95% confidence interval (95% CI) was calculated from the number of events in each

Table 1 – ROBINS-I

Study	Bias due to Confounding	Selection Bias	Bias in Classification of Interventions	Bias due to Deviations from Intended Interventions	Bias due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of the Reported Result	Overall Risk of Bias
Chikwe et al. (2024)[13]	High risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	High risk
Jiang et al. (2020)[14]	High risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	High risk

Table 2 – RoB 2

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other biases	Overall risk of bias
Nagpal et al. (2009)[15]	Low risk	Low risk	Unclear	Unclear	Low risk	Low risk	Low risk	Unclear
Park-Hansen et al. (2018)[16]	Low risk	Unclear	High risk	High risk	Low risk	Low risk	Low risk	High risk

Table 3 – GRADE

GRADE Factor	Effect on Evidence Quality
Study design	Low
Risk of bias	Downgrade by 1 level
Inconsistency	No downgrade
Indirectness	No downgrade
Imprecision	No downgrade
Publication bias	No downgrade
Large effect size	Upgrade by 1 level
Dose-response gradient	No upgrade
All plausible residual confounding would reduce a demonstrated effect	Upgrade by 1 level
Qualidade geral das evidências	Moderado

group. The weight assigned to each study was determined by the inverse of the variance of its effect size estimate. Given the small number of included studies, a random-effects model was fitted using the restricted maximum likelihood (REML) method to estimate the between-study variance, with the Knapp-Hartung adjustment applied to the standard errors of the pooled effect. This approach is recommended for meta-analyses with few studies, as it provides more robust variance estimation and better control of Type I error rates compared to the conventional DerSimonian-Laird method.

Heterogeneity was assessed using the Cochran Q test and the I^2 statistic. Publication bias was evaluated both visually (by examining funnel plots) and through testing for small-study effects. In all analyses, the no-LAAC group served as the reference. A two-sided alpha level of 0.05 was set for hypothesis testing.

Sensitivity analysis

To assess the robustness of the primary findings and to explore potential heterogeneity arising from different study designs, we conducted a pre-specified sensitivity analysis stratified by study type. All included studies were categorized into two groups: RCTs and two retrospective cohort studies (RCSs). For each subgroup, we recalculated the pooled effect estimate and 95% CI for stroke using the same REML random-effects model with Knapp-Hartung adjustment as in the primary analysis.

Results

The initial literature search yielded 2750 records. After removing duplicates, 2250 records underwent screening based on titles and abstracts. Subsequently, the full texts of 8 articles were assessed for eligibility. Ultimately, four studies[13–16] comprising 1853 patients (1074 in the LAAC group and 779 in the no-LAAC group) were included in the final analysis.

All studies were published between 2009 and 2024. Detailed characteristics and baseline patient data are presented in Tables 4 and 5. The selection comprised two RCTs and two RCSs.

For stroke and mortality outcomes, event counts were extracted directly from the reported aggregate data in each study; the corresponding funnel plots and Egger tests for small-study effects are shown in Figures 2–5 (stroke: Figures 2 and 3; all-cause mortality: Figures 4 and 5)

Meta-analysis results of adverse clinical events

Concomitant endocardial LAAC was associated with a significantly lower incidence of stroke compared to the no-LAAC group (Figure 6). The all-cause mortality rate was numerically lower in the LAAC group, but this difference was not statistically significant (Figure 7).

Sensitivity analysis results

Subgroup analysis by study design (RCT vs. RCS) consistently favored LAAC for stroke prevention across all strata, although neither subgroup individually reached conventional statistical significance. In the RCT subgroup, one study demonstrated a significant protective effect while the other showed a non-significant trend in the same direction (Figure 8). In the RCS subgroup, the pooled effect was borderline, with both studies individually demonstrating significant protection (Figure 9). Overall, the significant protective effect observed in the primary analysis was driven by the increased statistical power achieved when pooling all four studies.

Discussion

This meta-analysis synthesized data from four studies involving 1853 patients. In patients who underwent cardiac surgery, the addition of transendocardial LAAC was associated with a significantly lower stroke rate during follow-up compared to those who did not receive LAAC. However, a significant survival advantage was not observed despite this reduction in stroke incidence.

Table 4 - Outline of the Included Studies

Study	Year	Study type	Country	Surgery
Nagpal et al.[15]	2009	RCTs	Canada	Mitral valve surgery
Park-Hansen et al.[16]	2018	RCTs	Denmark	Any cardiac surgery
Chikwe et al .[13]	2024	RCSs	America	Mitral valve surgery
Jiang et al[14]	2020	RCSs	China	Mitral valve surgery

RCTs: randomized controlled trials; RCSs: retrospective cohort studies.

Table 5 – Patients' Baseline Characteristics of the Included Studies

Characteristic	Park-Hansen, 2018[16]		Jiang, 2020[14]		Nagpal, 2009[15]		Chikwe, 2024[13]	
	no LAAC (n=86)	LAAC (n=100)	no LAAC (n=339)	LAAC (n=521)	no LAAC (n=21)	LAAC (n=22)	no LAAC (n=333)	LAAC (n=431)
Age, y; mean (SD)	69(9)	67(9)	52(12)	53(11)	59(12)	58(13)	57(10)	62(10)
Sex (Female), n (%)	11(12.8)	18(18.0)	153(45.)	293(56.)	9(42.9)	11(50.0)	108(32.4.)	137(31.8)
Previous AF, n (%)	9(11.1)	16(16.3)	182(53.7)	355(68.1)	4(19.0)	4(18.2)	0(0)	0(0)
CHA2 DS2-VASc, median (IQR)	3 (2,4)	3(2,4)	NR	NR	NR	NR	1(1-2)	2(1-2)
Anticoagulation at discharge, n (%)	21(24.4)	27(27.3)	NR	NR	NR	NR	12(3.6)	32(7.4)
Postoperative AF,n (%)	42(48.8)	38(38.0)	NR	NR	NR	NR	84(25.5)	137(31.8)
Hypertensio, n (%)	NR	NR	66(19.5)	63(12.1)	0(0)	1(4.5)	NR	NR

All included studies reported statistical significance at a two-sided alpha level of 0.05.NR: not reported; IQR: interquartile range; LAAC: left atrial appendage closure; AF: atrial fibrillation.

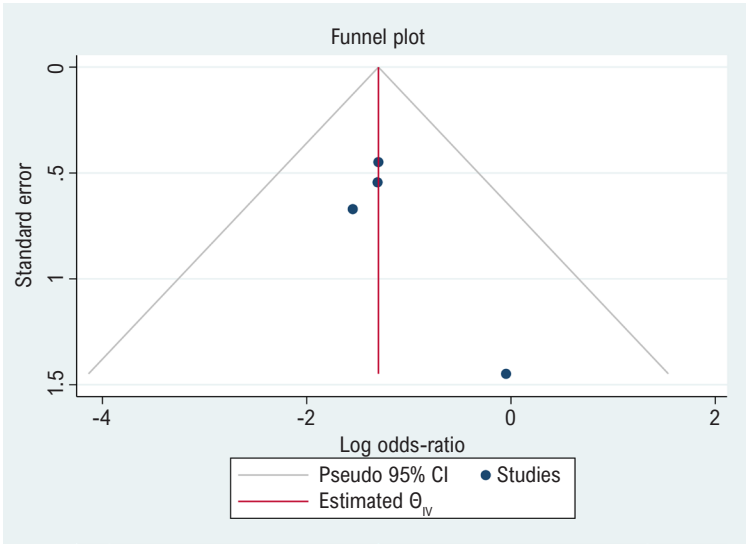


Figure 2 – *In the funnel plot for stroke, among the four studies represented by blue dots, those with greater precision (reflected by smaller standard errors) clustered near the pooled effect estimate (red vertical line). However, one study with lower precision was located to the right.*

Random-effects meta-regression — Number of obs = 4
Method: REML — Residual heterogeneity:
SE adjustment: Knapp-Hartung — tau2 = 3.9e-08
I2 (%) = 0.00
H2 = 1.00
R-squared (%) = 0.00
Model F(1,2) = 2.27
Prob > F = 0.2708

_meta_es	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
meta_se	1.005073	.6668985	1.51	0.271	-1.86436	3.874506
_cons	-1.866084	.4011281	-4.65	0.043	-3.591999	-.1401694

Test of residual homogeneity: Q_res = chi2(2) = 0.41 — Prob > Q_res = 0.8129

Regression-based Egger test for small-study effects
Random-effects model
Method: REML
SE adjustment: Knapp-Hartung

H0: beta1 = 0; no small-study effects
beta1 = 1.01
SE of beta1 = 0.667
t = 1.51
Prob > |t| = 0.2708

Figure 3 – *Small-Study Effects Test for Stroke: The tests for heterogeneity yielded the following results: tau² = 3.9e-08 (virtually zero), I²(%) = 0.00, and H² = 1.00. These values indicate no statistical heterogeneity among the studies. This conclusion is further supported by the residual heterogeneity test (Q_ res = 0.41, p = 0.8129). Regarding small-study effects, the regression coefficient was 1.005. However, this was not statistically significant (P > |t| = 0.271), and the 95% confidence interval [-1.86, 3.87] included zero. This indicates no significant association between study precision (sample size) and the magnitude of the effect size.*

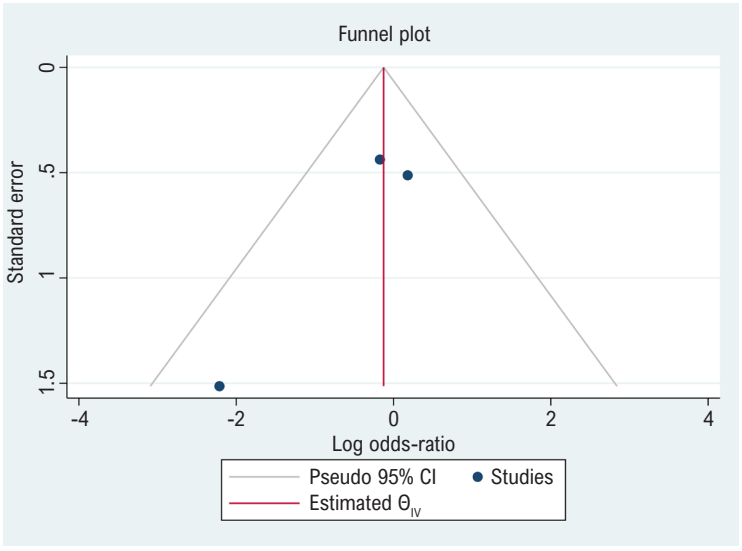


Figure 4 – *The funnel plot for all-cause mortality shows one study with lower precision located on the left, and two studies with higher precision clustered near the pooled effect estimate.*

Random-effects meta-regression
Method: REML
SE adjustment: Knapp-Hartung

Number of obs =	3
Residual heterogeneity:	
tau2 =	3.5e-07
I2 (%) =	0.00
H2 =	1.00
R-squared (%) =	0.00
Model F(1,1) =	3.07
Prob > F =	0.3301

_meta_es	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
meta_se	-1.915326	1.092781	-1.75	0.330	-15.80042	11.96977
_cons	.8656635	.6151863	1.41	0.393	-6.951019	8.682346

Test of residual homogeneity: Q_res = chi2(2) = 0.56 Prob > Q_res = 0.4554

Regression-based Egger test for small-study effects
Random-effects model
Method: REML
SE adjustment: Knapp-Hartung

H0: beta1 = 0; no small-study effects

beta1 =	-1.92
SE of beta1 =	1.093
t =	-1.75
Prob > |t| =	0.3301

Figure 5 – *Small-Study Effects Test for All-Cause Mortality: The heterogeneity statistics (tau² = 3.5e-07 [virtually zero], I² = 0.00%, H² = 1.00) indicated an absence of statistical heterogeneity among the studies. This conclusion was further supported by the residual heterogeneity test (Q_ res = 0.56, p = 0.4554). For the small-study effect test, the regression coefficient was -1.915. However, this association was not statistically significant (P > |t| = 0.330), and the 95% confidence interval [-15.80, 11.97] included zero. This confirmed that there is no significant association between study precision (sample size) and the mortality effect size.*

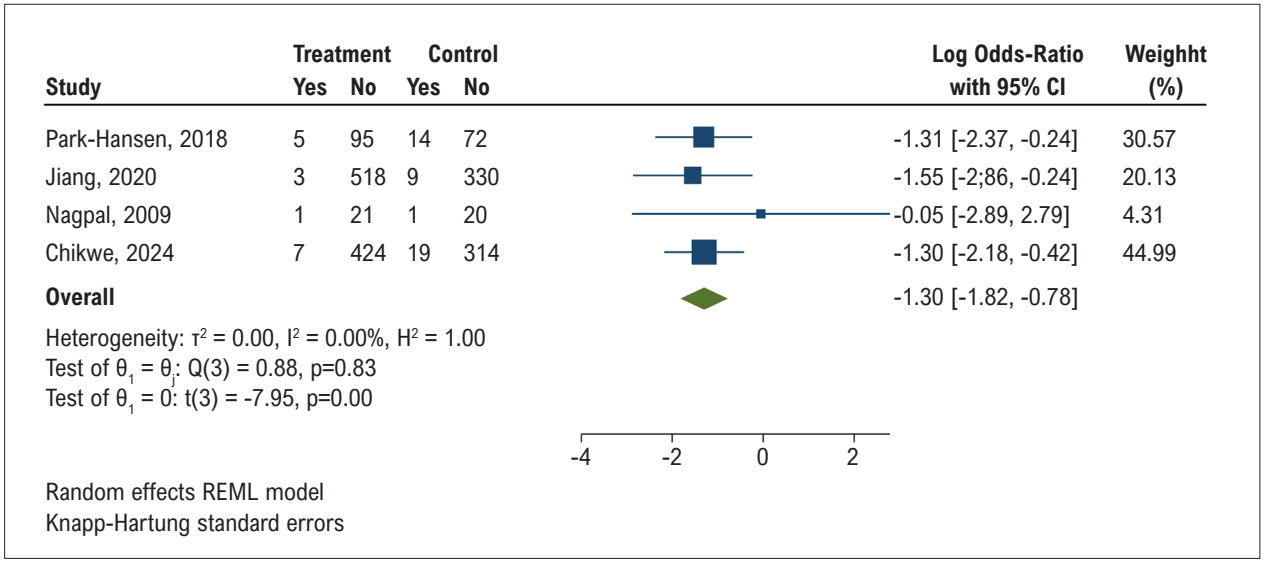


Figure 6 – *Forest plot of the comparative meta-analysis: stroke event incidence in endocardial left atrial appendage closure group versus no left atrial appendage closure group.*

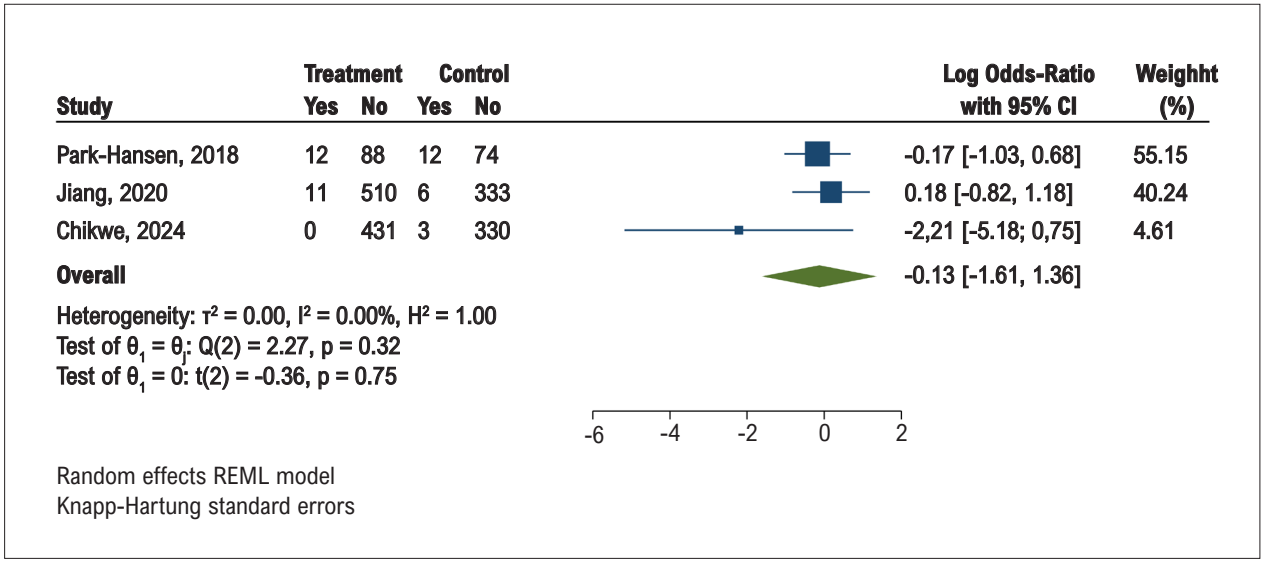


Figure 7 – *Forest plot of the meta-analysis comparing all-cause mortality between endocardial left atrial appendage closure and no left atrial appendage closure groups.*

This study focused on the efficacy of a specific surgical technique: transendocardial suture closure of the LAA for stroke prevention. This approach is frequently employed, particularly in procedures requiring access to the left atrium, such as mitral valve surgery. It can also be utilized in right-sided minimally invasive procedures (e.g., mini-thoracotomy or minimally invasive mitral valve surgery). Our previous study identified a specific rate of long-term recanalization with transendocardial suture closure.[17] The present study aimed to further clarify its efficacy and safety. Previous studies have indicated that surgical LAA closure is clinically effective for stroke prevention in patients with AF, with some evidence suggesting potential cost-effectiveness in certain contexts.[15] This meta-analysis found that transendocardial LAAC was associated with a substantial reduction in stroke risk. These findings support the stroke-preventive potential of surgical LAA closure. Therefore, in patients already undergoing cardiac procedures that involve left atrial access, concomitant transendocardial suture closure may offer a convenient opportunity for LAA occlusion without the need for an additional incision.

All-cause mortality was 2.5% in the LAAC group and 3.4% in the control group, a difference that was not statistically significant. Similarly, the LAAOS-III trial and other studies

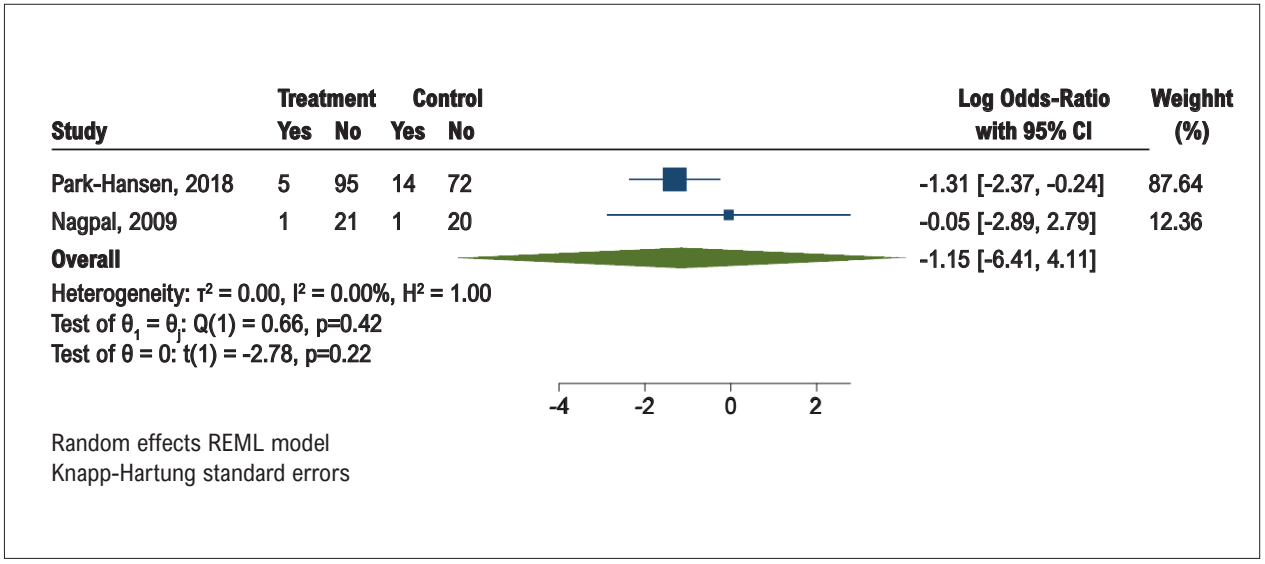


Figure 8 – *Sensitivity analysis: Forest plot of the association between surgical left atrial appendage closure and stroke prevention in RCTs.*

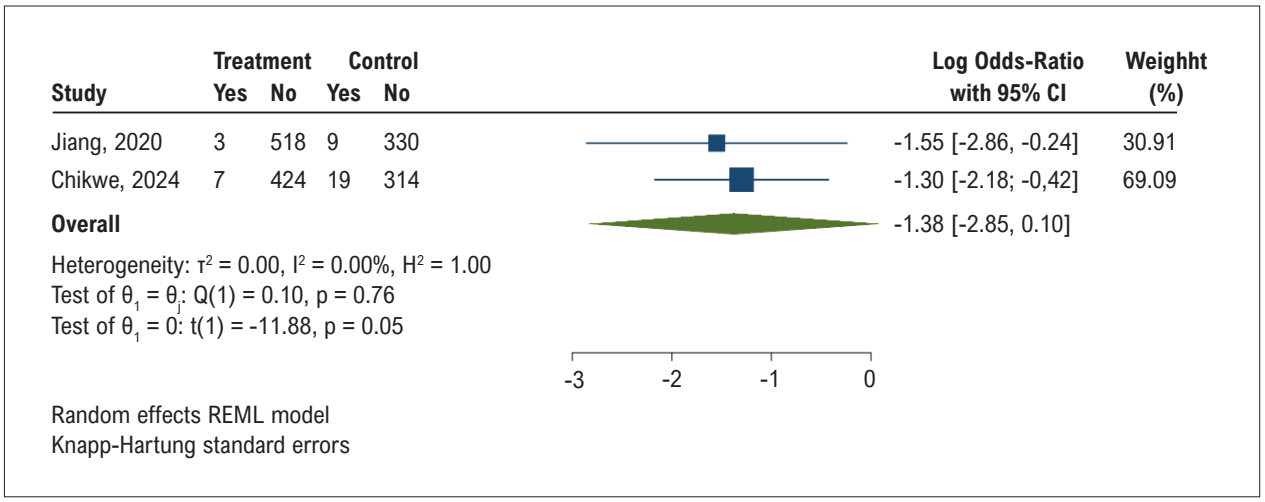


Figure 9 – *Sensitivity analysis: Forest plot of the association between surgical left atrial appendage closure and stroke prevention in RCSs..*

also reported limited survival benefit when comparing AF patients with or without LAAC. This observation may be attributable to the fact that mortality in AF patients typically results from composite factors such as heart failure and non-stroke cardiovascular events, with stroke-related deaths comprising a relatively low proportion. The primary analysis showed a significant association between LAAC and reduced stroke risk ($p < 0.01$). To assess the robustness of this finding, we performed a subgroup analysis stratified by study design (RCTs vs. RCSs) using a random-effects REML model with Knapp-Hartung adjustment.

In the RCTs subgroup, the pooled effect was not significant. This is likely due to the small number of studies and the limited sample size in Nagpal 2009, which had wide confidence intervals.[15] Notably, Park-Hansen 2018, a high-quality RCT with the largest weight (87.6%), showed a significant protective effect.[16] This suggests that prospective evidence, though limited, is consistent with a benefit of the intervention.

In the RCSs subgroup, both studies individually showed significant protective effects. The pooled point estimate (Log OR = –1.38) was similar to that of the RCTs subgroup. However, the 95% CI crossed the null (upper limit 0.10), so the pooled effect was not statistically significant. Retrospective studies are subject to confounding and selection bias, which may affect the precision of estimates.

Although neither subgroup independently reached significance, the overall analysis (all four studies) was significant ($p < 0.01$). This is not uncommon in meta-analyses. When study effects are consistent in direction, but individual studies are small, pooling increases statistical power and may

detect a true effect not seen in underpowered subgroup analyses. Clinically, the consistent direction of benefit across all studies, along with significant results from the two larger studies (Park-Hansen 2018 and Chikwe 2024),[13,16] suggests that endocardial LAAC may be a valuable option for stroke prevention in appropriately selected cardiac surgery patients.

This study had several limitations: (1) The evidence was limited, as it included only four studies, had a small sample size (n=1853), and reported varying procedural details for LAAC; (2) Differences in AF status, anticoagulation strategies, and follow-up duration might influence the interpretation of the results; (3) The short follow-up resulted in few hard endpoints, limiting conclusions about long-term LAAC benefits.

Conclusion

In summary, the current evidence suggests that endocardial suture closure of the left atrial appendage is associated with a significantly lower risk of stroke compared with no closure, without a significant difference in all-cause mortality. However, these findings are based on a limited number of studies with small sample sizes, variable procedural details, and relatively short follow-up. While the technique may be considered in appropriately selected patients undergoing cardiac surgery with left atrial access, routine use cannot be recommended based on the available evidence. Future well-designed, large-scale prospective studies or RCTs with standardized protocols and longer follow-up are warranted to further validate the efficacy and safety of this procedure.

Author Contributions

Conception and design of the research and Funding acquisition: Huang C; Acquisition of data and Writing of the manuscript: Huang C, Deng L; Analysis and interpretation of the data: Huang C, Huang Y; Statistical analysis: Huang Y; Critical revision of the manuscript for intellectual content: Zhang X.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This article is part of the thesis of Doctoral submitted by Chengfeng Huang, from Jinan University.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Use of Artificial Intelligence

During the preparation of this work, the author(s) used DeepSeek for language polishing, grammar correction, and translation of non-English references. After using this tool/service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the published article.

Availability of Research Data

The underlying content of the research text is contained within the manuscript.

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