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Review Article

Frailty Predicts Clinical Outcomes After Left Atrial Appendage Closure: A Systematic Review and Meta-analysis

Hamzah Pratama Megantara[1,2], Naura Anjanie[3], Joeristanti Soelistyaningroem[4]

Abstract

Frailty is increasingly recognized in older adults referred for percutaneous Left Atrial Appendage Closure (LAAC), yet its prognostic implications remain incompletely defined. We evaluated whether frailty is associated with worse clinical outcomes after LAAC. PubMed, ScienceDirect, Scopus, and Cochrane Library were searched from inception through April 2026. Observational studies evaluating adults undergoing LAAC and reporting outcomes by frailty status were eligible. Three reviewers independently performed study selection and data extraction. Risk of bias was assessed with the Newcastle-Ottawa Scale, and pooled estimates were synthesized using inverse-variance models according to heterogeneity. Six observational study reports were included, comprising five retrospective datasets and one prospective cohort. Across reports, 201,411 procedure records were represented, although one Medicare cohort contributed to two related publications. Frailty prevalence ranged from 5.8% to 49.3%. Frailty was associated with higher all-cause mortality (Odds Ratio [OR] 2.60, 95% Confidence Interval [CI] 1.92-3.51), major adverse cardiovascular events (OR 1.82, 95% CI 1.24-2.68), rehospitalization (OR 1.51, 95% CI 1.17-1.94), ischemic stroke (OR 1.81, 95% CI 1.10-2.96), bleeding events (OR 1.23, 95% CI 1.02-1.49), and vascular or procedure-related complications (OR 1.43, 95% CI 1.23-1.67). Transient ischemic attack and pericardial complications were not statistically significant. Frailty identifies LAAC candidates at higher early and intermediate-term risk despite high procedural success. Because the evidence is mainly observational and heterogeneous, frailty assessment should refine counseling, optimization, and shared decision-making rather than serve as a stand-alone reason to withhold LAAC.

[1]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom.
[2]Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia.
[3]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[4]Mitra Keluarga Cibubur General Hospital, Bekasi, Indonesia.

Correspondence:
Hamzah Pratama Megantara,

Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, United Kingdom/Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia.

Email: hamzahpratama10@gmail.com

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Introduction

Stroke prevention is central to the management of atrial fibrillation, particularly in older adults with multiple comorbidities who are simultaneously vulnerable to thromboembolic and bleeding complications.[1] Percutaneous Left Atrial Appendage Closure or occlusion (LAAC) has become an established alternative for selected patients who are poor candidates for long-term oral anticoagulation or who have a prohibitive bleeding profile.[1-2]

The clinical evidence base for LAAC has been shaped by pivotal trials including PROTECT AF and PREVAIL, which compared the WATCHMAN device with warfarin, and PRAGUE-17, which compared LAAC with direct oral anticoagulants in high-risk patients with atrial fibrillation.[3-5] These trials support the role of LAAC in appropriately selected patients, but they were not included in the present meta-analysis because they did not specifically evaluate frailty-stratified outcomes. Therefore, they do not directly answer whether frailty modifies prognosis after LAAC.

Frailty is a multidimensional syndrome characterized by reduced physiologic reserve and increased vulnerability to internal and external stressors.[6] In cardiovascular medicine, frailty has emerged as a clinically relevant determinant of adverse outcomes after invasive procedures, especially among older adults whose chronological age alone does not fully capture biologic risk.[7] This distinction matters in LAAC because standard thromboembolic and bleeding scores such as CHA2DS2-VASc and HAS-BLED capture key clinical risk factors, but they do not directly measure mobility, disability, cognition, nutrition, functional dependence, or recovery capacity. Frailty may therefore add prognostic information beyond age and conventional risk scores.

Over the last several years, registry-based, claims-based, electronic health record, and prospective studies have evaluated frailty in LAAC using different operational definitions, including the Hospital Frailty Risk Score, the Kim claims-based frailty index, Johns Hopkins Adjusted Clinical Groups frailty-defining diagnoses, diagnosis-based frailty indicators, the Essential Frailty Toolset, and a registry-derived frailty scale.[8-13] These studies have generally suggested worse short-term and intermediate-term outcomes among frail patients, but the magnitude and consistency of association across clinically relevant outcomes have not been synthesized formally.

The primary question of this systematic review and meta-analysis was whether frailty, as defined in each included study, is associated with higher all-cause mortality after percutaneous LAAC. The prespecified primary outcome was all-cause mortality. Secondary outcomes were major adverse cardiovascular events, rehospitalization or readmission, ischemic stroke, transient ischemic attack, bleeding events, vascular or procedure-related complications, and pericardial complications. We hypothesized that frailty would be associated with higher mortality and a broader adverse event burden after LAAC.

Methods

Study Design and Reporting Standard

This systematic review and meta-analysis was prepared in accordance with the PRISMA 2020 statement.[14] The review protocol was registered in PROSPERO (CRD420261360553; registered on 11 April 2026), and the registration record is provided as Supplementary File 1. The PRISMA 2020 checklist was used to guide and evaluate the completeness of reporting for this review, and the completed checklist is provided as Supplementary File 2.

Eligibility Criteria

We included observational studies of adult patients undergoing percutaneous LAAC that assessed frailty before or at the index procedure and reported at least one clinical outcome by frailty status or category. Eligible reports could provide adjusted effect estimates, unadjusted relative effects, or event data from which a study-level effect measure could be derived.

We excluded case reports, narrative reviews, conference abstracts without extractable outcome data, studies of non-LAAC structural heart interventions, and reports that did not separate outcomes according to frailty exposure. Pivotal randomized LAAC trials such as PROTECT AF, PREVAIL, and PRAGUE-17 were reviewed for clinical context but were not eligible for quantitative synthesis because they did not report frailty-stratified outcomes. When multiple publications arose from a related data source, all reports were reviewed carefully, and cohort overlap was documented.

Information Sources and Search Strategy

A systematic search was performed in PubMed, ScienceDirect, Scopus, and Cochrane Library from inception through April 2026 using controlled vocabulary terms and free-text keywords related to frailty, LAAC or occlusion, and atrial fibrillation. Full reproducible search strategies for all four databases

are provided as Supplementary File 3. No restriction on publication year was applied. The PROSPERO registration record for this review is provided as Supplementary File 1.

Study Selection and Data Extraction

Three reviewers independently screened titles and abstracts, reviewed full-text articles for eligibility, and extracted study-level data using a prespecified form. Disagreements were resolved by discussion among three authors. Extracted variables included study design, country and data source, enrollment period, frailty definition, sample size, baseline characteristics, follow-up duration, reported outcomes, adjusted covariates, and effect estimates.

Frailty Exposure and Outcomes

Frailty was accepted as defined by each study. Operational definitions included the Johns Hopkins Adjusted Clinical Groups frailty-defining diagnoses, Hospital Frailty Risk Score, Kim claims-based frailty index, diagnosis-based frailty indicator, Essential Frailty Toolset, and a pragmatic registry-derived 5-point frailty scale.[8-13] Among the included reports, the most commonly recurring administrative models were the Hospital Frailty Risk Score and Kim claims-based frailty index used in Medicare analyses; diagnosis-based frailty indicators and registry-derived scales were also used in large United States datasets, while direct bedside assessment with the Essential Frailty Toolset was available only in the prospective Frail-LAAC cohort.[8-13,15-16]

The primary outcome of this review was all-cause mortality. Secondary outcomes were major adverse cardiovascular events, rehospitalization or readmission, ischemic stroke, transient ischemic attack, bleeding events, vascular or procedure-related complications, and pericardial complications.

Risk of Bias Assessment

Methodological quality of the included cohort studies was assessed using the Newcastle-Ottawa Scale, focusing on selection, comparability, and outcome ascertainment.[17] Studies with higher star ratings were interpreted as having lower risk of bias, although residual confounding remained possible because all included studies were observational.

Statistical Analysis

For quantitative synthesis, study-level effect estimates were log-transformed and pooled using inverse-variance meta-analysis. Because the included literature reported adjusted Odds Ratios (OR) and hazard ratios, published adjusted relative effects were harmonized on a common logarithmic scale and displayed as pooled ORs for consistency of presentation. This approach facilitates prognosis synthesis, but the pooled estimates should be interpreted with appropriate caution because hazard ratios and ORs are not mathematically identical.

Random-effects models were used for outcomes with important between-study heterogeneity, whereas fixed-effect models were used when heterogeneity was low. Statistical heterogeneity was quantified with Cochran's Q test and the I^2 statistic. A two-sided P value < 0.05 was considered statistically significant. Analyses were performed using Review Manager 5.4.

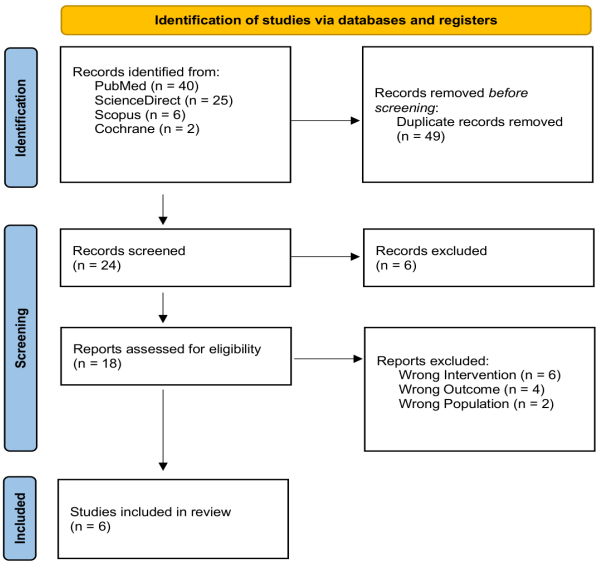


Figure 1. PRISMA 2020 flow diagram of the study selection process for the systematic review and meta-analysis.

Results

Study Selection

The electronic search identified 73 records. After duplicate removal, 24 records underwent title and abstract screening, and 18 full-text articles were assessed for eligibility. Six study reports met the inclusion criteria for qualitative synthesis, and outcome-specific meta-analyses included three to seven cohort-level estimates depending on the endpoint. Figure 1 presents the PRISMA 2020 flow diagram.

Study Characteristics

The included literature comprised six study reports published between 2022 and 2026, representing 201,411 reported procedure records across administrative claims, national registry, electronic health record, and prospective multicenter cohort data sources.[8-13] One Medicare fee-for-service cohort appeared in two related publications that evaluated different frailty instruments and outcomes.[9-10] Accordingly, the total number of unique participants across all reports is lower than the simple summed total, and overlap should be considered when interpreting pooled estimates.

Five reports were from the United States, and one prospective cohort was conducted across university centers in Canada and Spain.[12] Sample size ranged from 452 in the Frail-LAAC study to 62,980 in a weighted national inpatient sample analysis.[8,12] Table 1 summarizes the design, frailty definitions, baseline profile, follow-up, and reported outcomes of the included studies.

Table 1. Characteristics and baseline profile of included studies.

Study	Setting and design	Sample size / frailty prevalence	Frailty measure	Key baseline profile	Follow-up	Reported outcomes
Agarwal 2023	United States; retrospective weighted National Inpatient Sample, 2015-2019	62,980; frailty 3,670 (5.8%)	Johns Hopkins ACG frailty-defining diagnoses	Frail vs non-frail: age 78.9 vs 75.8 years; women 46.9% vs 41.2%; higher burden of heart failure, hypertension, and valvular disease in frail patients	In-hospital	Overall complications, major complications, peripheral vascular complications, length of stay >1 day, routine home discharge, in-hospital mortality
Wang 2022	United States; Medicare fee-for-service claims, 2016-2019	21,787; frail by HFRS >=5 in 10,740 (49.3%)	Hospital Frailty Risk Score	Overall cohort age 77.5 +/- 6.7 years; frailty associated with more heart failure, chronic kidney disease, chronic obstructive pulmonary disease, anemia, dementia, diabetes, and prior stroke/TIA	30 days to 3 years	Long hospital stay, 30-day readmission, 30-day mortality, 1-year mortality
Wang 2023	United States; Medicare fee-for-service claims, 2016-2019	21,787; frail 45.6% by HFRS and 15.4% by Kim CFI	HFRS and Kim claims-based frailty index	Overall cohort age 77.5 +/- 6.7 years; women 43.8%; study focused on comparative performance of distinct claims-based frailty measures	30 days and 1 year	30-day mortality, 1-year mortality, readmission, long hospital stay, days at home
Darden 2024	United States; NCDR LAAO Registry, 2016-2021	57,728; frail 7,693 (13.3%); pre-frail 44,360 (76.8%)	Novel 5-point registry frailty scale	Overall cohort age 78.0 +/- 7.9 years; women 41.2%; frail and pre-frail groups were older, more comorbid, and more disabled	In-hospital and 45 days	In-hospital mortality, major complications, any complications, respiratory failure, pericardial effusion, cardiac arrest, prolonged hospitalization, 45-day mortality

Table 1. (continued)

Study	Setting and design	Sample size / frailty prevalence	Frailty measure	Key baseline profile	Follow-up	Reported outcomes
Cepas-Guillén 2026	Canada and Spain; prospective multicenter Frail-LAAC cohort, 2022-2024	452; frail 101 (22.4%)	Essential Frailty Toolset	Frail vs non-frail: age 79.9 +/- 6.3 vs 75.4 +/- 7.8 years; women 43.6% vs 30.8%; higher comorbidity burden in frail patients	Median 12 (4-22) months	Composite of all-cause mortality or ischemic events, all-cause mortality, ischemic events, major bleeding, rehospitalization, quality of life
Jain 2026	United States; TriNetX collaborative network, propensity-score matched analysis, 2015-2025	36,677 before matching; frail 8,384 (22.9%); 8,051 matched pairs	Diagnosis-based frailty indicator	Before matching, frail patients were older (79.8 vs 77.7 years) and more often female (44.2% vs 38.6%)	Time-to-event follow-up after matching	All-cause mortality, MACCE, major bleeding, major vascular complications, all-cause readmission, pericardial complications

Abbreviations: ACG, Adjusted Clinical Groups; CFI, claims-based frailty index; EHR, electronic health record; HFRS, Hospital Frailty Risk Score; LAAC, left atrial appendage closure; LAAO, left atrial appendage occlusion; MACCE, major adverse cardiac and cerebrovascular events; NCDR, National Cardiovascular Data Registry; TIA, transient ischemic attack.

Baseline Profile of Frail Patients

Frailty prevalence varied widely according to the instrument used and the underlying data source. In Agarwal et al., frailty prevalence was 5.8% using Johns Hopkins Adjusted Clinical Groups frailty-defining diagnoses within the National Inpatient Sample.[8] In the Medicare cohort analyzed by Wang et al., frailty prevalence was 49.3% using the Hospital Frailty Risk Score and 15.4% using the Kim claims-based frailty index.[9-10] In the prospective Frail-LAAC study, 22.4% of patients were classified as frail using the Essential Frailty Toolset, while the NCDR LAAO Registry analysis classified 13.3% as frail and 76.8% as pre-frail using a pragmatic 5-point registry scale.[11-12] In the TriNetX cohort, 22.9% of patients were frail before propensity matching.[13]

Across studies, frail patients were consistently older, more often female, and carried a greater burden of comorbid disease. Frail strata had higher frequencies of heart failure, chronic kidney disease, chronic obstructive pulmonary disease, anemia, diabetes, dementia, prior stroke or transient ischemic attack, and disability-related markers.[8-13] In the prospective Frail-LAAC study, frail patients had a mean age of 79.9 years versus 75.4 years among non-frail patients, and women represented 43.6% versus 30.8%, respectively.[12] Similar gradients were evident in claims-based and registry analyses.

Procedural Profile and Risk of Bias

Despite clinically worse baseline risk, procedural success remained high in contemporary cohorts. In the Frail-LAAC study, device success was 99.6% and procedural success was 97.3%, without a statistically significant difference in procedure-related complications among frailty groups.[12] This pattern suggests that the adverse prognostic effect of frailty is not explained solely by immediate technical failure.

Risk of bias assessment using the Newcastle-Ottawa Scale is shown in Table 2. Five studies received 8 of 9 stars, and one study received 7 of 9 stars.[8-13] Common limitations included observational design, reliance on diagnosis-based or claims-based frailty measures, heterogeneity in endpoint definitions, and the possibility of partial cohort overlap between related Medicare reports.

Table 2. Risk of bias assessment using the Newcastle-Ottawa Scale.

Study	NOS score	Main limitation or note
Agarwal 2023	7/9	Inpatient-only follow-up and diagnosis-based frailty ascertainment
Wang 2022	8/9	Claims-based frailty assessment and residual confounding despite large cohort
Wang 2023	8/9	Likely overlap with the Wang 2022 Medicare cohort; distinct frailty instruments assessed
Darden 2024	8/9	Registry analysis with limited extractable subgroup-level baseline detail
Cepas-Guillén 2026	8/9	Prospective design but modest sample size
Jain 2026	8/9	Retrospective EHR coding and residual unmeasured confounding

Abbreviation: NOS, Newcastle-Ottawa Scale.

Pooled Clinical Outcomes

Outcome-specific pooled analyses are summarized in Table 3 and displayed in Figure 2, which presents updated forest plots of pooled clinical outcomes in frail versus non-frail patients undergoing LAAC. The statistical model used for each endpoint is indicated in Table 3 and in each corresponding forest plot panel.

Frailty was associated with significantly higher all-cause mortality (OR 2.60, 95% Confidence Interval [CI] 1.92-3.51; I^2 = 91%; Figure 2A). The direction of association was generally consistent across large registry, claims-based, and prospective cohort data, although heterogeneity was substantial and the pooled effect should be interpreted as an overall prognostic signal rather than a precise uniform effect size.

Table 3. Pooled outcome estimates according to frailty status.

Outcome	Figure panel	No. of study estimates	Model used in Figure 2	Pooled OR (95% CI)	I^2	Interpretation
All-cause mortality	A	7	Random-effects	2.60 (1.92-3.51)	91%	Higher mortality in frail patients; high heterogeneity
Major adverse cardiovascular events	B	3	Random-effects	1.82 (1.24-2.68)	93%	Higher event burden in frail patients; high heterogeneity
Rehospitalization or readmission	C	4	Random-effects	1.51 (1.17-1.94)	95%	Higher readmission risk in frail patients; high heterogeneity
Ischemic stroke	D	3	Fixed-effect	1.81 (1.10-2.96)	0%	Higher ischemic stroke risk
Transient ischemic attack	E	3	Fixed-effect	1.72 (0.87-3.42)	14%	Not statistically significant
Bleeding events	F	4	Random-effects	1.23 (1.02-1.49)	57%	Higher bleeding risk
Vascular or procedure-related complications	G	4	Random-effects	1.43 (1.23-1.67)	59%	Higher complication risk
Pericardial complications	H	3	Fixed-effect	1.12 (0.84-1.49)	12%	Not statistically significant

Abbreviations: CI, confidence interval; I^2, I-squared statistic; OR, odds ratio.

Frailty was also associated with higher major adverse cardiovascular events (OR 1.82, 95% CI 1.24-2.68; I^2 = 93%; Figure 2B) and rehospitalization or readmission (OR 1.51, 95% CI 1.17-1.94; I^2 = 95%; Figure 2C). These endpoints also showed substantial heterogeneity, consistent with differences in frailty definitions, follow-up periods, event definitions, and adjustment strategies across the included studies.

For cerebrovascular outcomes, frailty was associated with ischemic stroke (OR 1.81, 95% CI 1.10-2.96; I^2 = 0%; Figure 2D), whereas the association with transient ischemic attack did not reach statistical significance (OR 1.72, 95% CI 0.87-3.42; I^2 = 14%; Figure 2E).

Frailty was associated with bleeding events (OR 1.23, 95% CI 1.02-1.49; I^2 = 57%; Figure 2F) and vascular or procedure-related complications (OR 1.43, 95% CI 1.23-1.67; I^2 = 59%; Figure 2G). In contrast, pericardial complications were not significantly different according to frailty status (OR 1.12, 95% CI 0.84-1.49; I^2 = 12%; Figure 2H).

Study-Level Interpretation

The association between frailty and mortality was particularly pronounced in several individual studies. In the NCDR LAAO Registry, frailty was associated with higher adjusted odds of in-hospital death and 45-day mortality, while in the prospective Frail-LAAC cohort frailty was associated with substantially higher risks of the composite of death or ischemic events and of all-cause mortality during follow-up.[11-12] In the propensity-matched TriNetX cohort, frailty remained associated with all-cause mortality and all-cause readmission after matching.[13]

Not every endpoint was uniformly increased in every individual study. For example, Agarwal et al. reported higher in-hospital complications and vascular complications among frail patients but did not observe a significant difference in crude in-hospital mortality.[8] Similarly, the prospective Frail-LAAC study demonstrated high procedural success across groups despite markedly worse longer-term outcomes in frail patients.[12] These data suggest that frailty may be more strongly related to overall postprocedural clinical vulnerability than to immediate device deployment success.

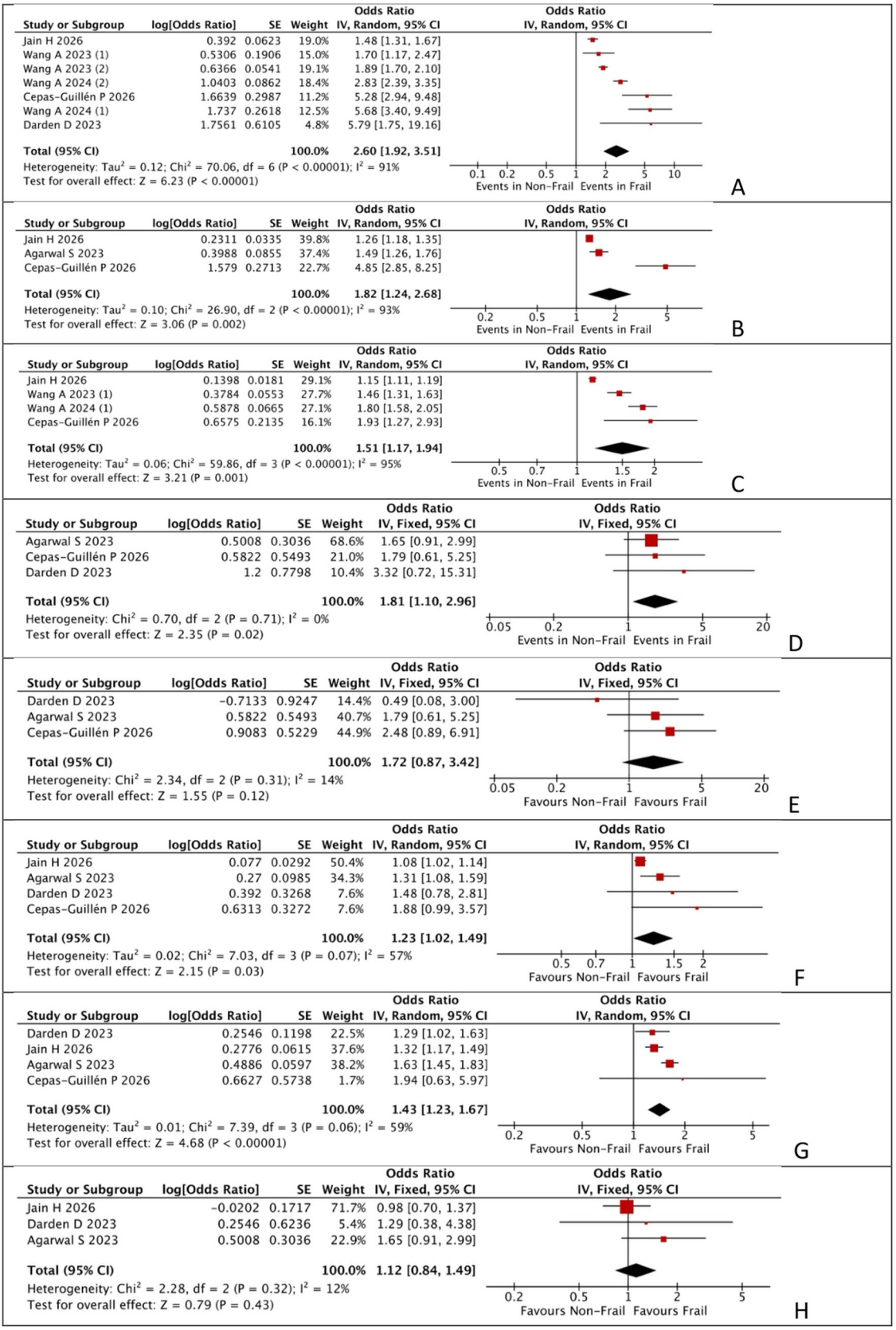


Figure 2. Forest plots of pooled clinical outcomes comparing frail versus non-frail patients undergoing percutaneous left atrial appendage closure. Panel A, all-cause mortality; Panel B, major adverse cardiovascular events; Panel C, rehospitalization or readmission; Panel D, ischemic stroke; Panel E, transient ischemic attack; Panel F, bleeding events; Panel G, vascular or procedure-related complications; and Panel H, pericardial complications.

Discussion

Principal Findings

This systematic review and meta-analysis shows that frailty is consistently associated with poorer prognosis among patients undergoing percutaneous LAAC. Across contemporary observational datasets and one prospective multicenter cohort, frailty was associated with higher mortality, major adverse cardiovascular events, rehospitalization, bleeding, and vascular or procedure-related complications. By contrast, the pooled associations for transient ischemic attack and pericardial complications were not statistically significant.

These findings are clinically important because LAAC is often considered for patients who are older, medically complex, and judged to be poor candidates for long-term anticoagulation. In that setting, frailty appears to capture a domain of risk that is not fully represented by age alone or by standard thromboembolic and bleeding scores.

Why frailty matters in older LAAC populations

The observed pattern of results is biologically and clinically plausible. Frailty reflects diminished physiologic reserve across multiple systems, including mobility, nutrition, renal function, cognition, and recovery capacity. A patient may undergo technically successful LAAC, yet still remain vulnerable to decompensation, reduced resilience after hospitalization, difficulty recovering from procedural stress, medication-related complications, falls, recurrent admissions, or competing noncardiovascular illness.

The consistently elevated risks of mortality and rehospitalization likely reflect this broader vulnerability rather than a single device-specific mechanism. Similarly, the higher pooled odds of bleeding and vascular or procedure-related complications may be influenced by frailty-associated features such as impaired tissue reserve, anemia, vascular fragility, chronic kidney disease, malnutrition, disability, and greater overall care complexity.

Heterogeneity and interpretation of pooled estimates

Several pooled endpoints showed substantial heterogeneity, particularly all-cause mortality, major adverse cardiovascular events, and rehospitalization. This heterogeneity is likely multifactorial. The included studies differed in frailty instruments and thresholds, ranging from claims-based scores to direct bedside assessment; data sources, ranging from inpatient administrative data to longitudinal registries and electronic health records; outcome definitions and follow-up duration; adjustment strategies; and whether estimates reflected early procedural outcomes or intermediate-term clinical events.

This heterogeneity affects interpretation. The pooled estimates should not be read as a single precise treatment-effect estimate applicable to every LAAC population. Rather, they indicate that frailty is a reproducible marker of adverse prognosis across heterogeneous real-world cohorts. Consequently, the direction and consistency of association are more clinically informative than the exact magnitude of each pooled OR. This also reinforces the need for prospective studies using standardized frailty instruments and harmonized endpoint definitions.

Residual confounding and baseline risk

Frailty was consistently accompanied by older age and higher comorbidity burden. Therefore, worse outcomes among frail patients cannot be attributed solely to periprocedural effects or to LAAC itself. Although several included studies adjusted for measured comorbidities or used propensity matching, residual and unmeasured confounding remain plausible. Frailty may partly reflect the cumulative effect of disease burden, disability, functional limitation, and competing noncardiovascular mortality risk. The findings should therefore be interpreted as prognostic associations rather than proof that frailty directly causes post-LAAC complications.

Relationship to prior cardiovascular frailty literature

The present synthesis extends prior evidence showing that frailty is prognostically important across invasive cardiovascular care, including transcatheter and surgical aortic valve replacement.[7] In contrast to the more mature transcatheter aortic valve replacement literature, the LAAC field has only recently begun to examine frailty explicitly. The studies included in this review used different frailty instruments, yet the direction of association was generally concordant across claims-based, registry-based, and prospective measurements.[8-13]

This convergence is important. It suggests that frailty is not merely a surrogate for chronological age or case mix, but rather a clinically meaningful vulnerability construct that remains relevant even when procedural success is high. At the same time, the heterogeneity of instruments also highlights an unresolved practical question: which frailty tool is most feasible, reproducible, and actionable in routine LAAC evaluation.

Implications for clinical practice

Frailty assessment should not be used as an automatic exclusion criterion for LAAC. Instead, frailty should be considered an adjunctive risk marker that improves preprocedural counseling, expectation setting, and individualized care planning. In most patients, frailty assessment is best used to clarify risk, identify modifiable vulnerabilities, and guide supportive measures rather than to deny an otherwise indicated procedure.

In practical terms, frail patients being considered for LAAC may benefit from medication reconciliation, fall-risk assessment, nutritional assessment, anemia and renal optimization, discharge planning, and earlier multidisciplinary follow-up. Frailty assessment may also help clinicians identify patients in whom severe disability, advanced frailty, or limited life expectancy could reduce the net clinical benefit of a technically feasible procedure. Thus, frailty should primarily improve shared decision-making and perioperative planning, while patient selection should remain individualized and integrated with stroke risk, bleeding risk, procedural feasibility, patient goals, and expected longevity.

Strengths and limitations

This review has several strengths. To our knowledge, it is among the first dedicated evidence syntheses focused specifically on frailty in the LAAC population. It integrates contemporary data from complementary sources, including national claims, national registries, electronic health records, and prospective cohort studies. It also evaluates a broad range of clinically relevant outcomes rather than focusing exclusively on mortality or technical success.

This study also has important limitations. First, all included reports were observational, and only one was a prospective cohort. Causal interpretation is therefore limited. Second, frailty definitions were heterogeneous, ranging from diagnosis-based and claims-based instruments to direct bedside assessment, reducing comparability between studies. Third, frail patients were older and had more comorbidities than non-frail patients, so residual confounding by baseline illness severity, disability, and competing mortality risk cannot be excluded. Fourth, several outcomes showed substantial statistical heterogeneity, likely related to differences in frailty thresholds, endpoint definitions, follow-up duration, adjustment strategies, and data source characteristics.

Fifth, one Medicare fee-for-service cohort contributed to two related publications using different frailty measures.[9-10] Although the overlap was handled cautiously and interpreted transparently, some pooled analyses may still have been influenced by partial non-independence of observations. Sixth, the quantitative synthesis harmonized different relative effect measures onto a common log effect scale for pooled display. This approach is practical for prognosis meta-analysis, but it remains an approximation and should be interpreted accordingly. Seventh, prior atrial fibrillation ablation history was not consistently reported or analyzable in the included datasets. Some patients in large registry or claims cohorts may have had previous ablation, but this exposure could not be incorporated into subgroup or meta-regression analyses. Finally, some study reports, particularly large registry analyses, provided limited extractable baseline detail for all subgroup-level characteristics.[11]

Recommendations for future work

Future prospective studies should compare pragmatic bedside frailty instruments with claims-based or registry-based tools in the same LAAC population to determine which measures are most informative for real-time clinical decision-making. Standardization of frailty reporting would also improve comparability across studies and reduce heterogeneity in future evidence syntheses.

Researchers should move beyond procedural success alone and report patient-centered outcomes that matter for older adults, including functional recovery, time at home, quality of life, dependency, institutionalization, and treatment burden. Where feasible, individual participant data meta-analysis or carefully designed registry studies could help clarify whether frailty provides incremental prognostic value beyond existing clinical scores and whether specific frailty domains, such as malnutrition, falls, or mobility limitation, drive risk more strongly than others.

Conclusion

Frailty is associated with worse clinical outcomes after percutaneous LAAC, particularly all-cause mortality, major adverse cardiovascular events, rehospitalization, bleeding, and vascular or procedure-related complications. These findings indicate potential incorporation of frailty assessment into preprocedural risk stratification and shared decision-making for older adults being considered for LAAC. However, the evidence remains mainly observational and heterogeneous; hence, frailty should be used to refine counseling, optimization,

and individualized decision-making rather than as a stand-alone exclusion criterion. Additional prospective studies are needed to determine which frailty instruments are most actionable and whether frailty-informed care pathways can improve outcomes.

List of Abbreviations

CI Confidence Interval
LAAC Left Atrial Appendage Closure
OR Odds Ratio

Ethical Clearance

This study is a systematic review and meta-analysis of previously published aggregate data. New participant recruitment, direct patient contact, and access to identifiable individual-level data were not involved. Accordingly, formal ethics committee approval and written informed consent were not required for the present analysis.

Publication Approval

All authors consent to the publication of this manuscript.

Authors' Contributions

HPM conceived the study, performed study selection, data extraction, and drafting; NA participated in screening, data extraction, and manuscript review; JS supervised the project, interpreted data, and critically revised the manuscript; all authors approved the final version.

Acknowledgments

None.

Conflict of Interest

The authors declare no conflict of interest.

Availability of Data and Materials

All data analyzed in this study were extracted from published articles cited in the manuscript. The study-level extraction sheet and meta-analytic dataset are available from the corresponding author upon reasonable request.

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Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the authors used ChatGPT (GPT-5.6 Sol, OpenAI) solely to assist with language editing, including improvements in grammar, clarity, readability, and academic phrasing. The AI tool was not used to generate or alter the scientific content, study methodology, data, statistical analyses, interpretation of results, or conclusions presented in this manuscript. All AI-assisted language edits were subsequently reviewed, verified, and approved by the authors. The authors take full responsibility for the accuracy, integrity, and final content of the manuscript.

References

1. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024;149:e1-e156. https://doi.org/10.1161/CIR.0000000000001193
2. Glikson M, Wolff R, Hindricks G, et al. EHRA/EAPCI expert consensus statement on catheter-based left atrial appendage occlusion - an update. EuroIntervention. 2020;15:1133-80. https://doi.org/10.4244/EIJY19M08_01
3. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet. 2009;374:534-42. https://doi.org/10.1016/S0140-6736(09)61343-X
4. Holmes DR Jr, Kar S, Price MJ, et al. Prospective randomized evaluation of the WATCHMAN left atrial appendage closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol. 2014;64:1-12. https://doi.org/10.1016/j.jacc.2014.04.029
5. Osmancik P, Herman D, Neuzil P, et al. Left

atrial appendage closure versus direct oral anticoagulants in high-risk patients with atrial fibrillation. J Am Coll Cardiol. 2020;75:3122-35. https://doi.org/10.1016/j.jacc.2020.04.067
6. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56:M146-M56. https://doi.org/10.1093/gerona/56.3.M146
7. Afilalo J, Lauck S, Kim DH, et al. Frailty in older adults undergoing aortic valve replacement: the FRAILTY-AVR study. J Am Coll Cardiol. 2017;70:689-700. https://doi.org/10.1016/j.jacc.2017.06.024
8. Agarwal S, Munir MB, Bansal A, et al. Impact of frailty on in-hospital outcomes in patients who underwent percutaneous left atrial appendage occlusion. Am J Cardiol. 2023;196:19-21. https://doi.org/10.1016/j.amjcard.2023.03.015
9. Wang A, Ferro EG, Song Y, et al. Frailty in patients undergoing percutaneous left atrial appendage closure. Heart Rhythm. 2022;19:814-21. https://doi.org/10.1016/j.hrthm.2022.01.007
10. Wang A, Ferro EG, Xu J, et al. Comparative performance of distinct frailty measures among patients undergoing percutaneous left atrial appendage closure. Pacing Clin Electrophysiol. 2023;46:242-50. https://doi.org/10.1111/pace.14649
11. Darden D, Munir MB, Zimmerman S, et al. Frailty and associated outcomes in patients undergoing percutaneous left atrial appendage occlusion: findings from the NCDR LAAO registry. J Interv Card Electrophysiol. 2024;67:625-35. https://doi.org/10.1007/s10840-023-01662-1
12. Cepas-Guillen P, Vidal-Cales P, Nombela-Franco L, et al. Frailty in patients undergoing percutaneous left atrial appendage closure: the Frail-LAAC study. Heart Rhythm. Published online 2026. https://doi.org/10.1016/j.hrthm.2026.01.041
13. Jain H, Soni K, Odat RM, et al. Impact of frailty on outcomes following percutaneous left atrial appendage occlusion: a propensity-score matched analysis. Am J Cardiol. 2026;265:22-6. https://doi.org/10.1016/j.amjcard.2026.02.006
14. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71
15. Gilbert T, Neuburger J, Kraindler J, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet. 2018;391:1775-82. https://doi.org/10.1016/S0140-6736(18)30668-8
16. Kim DH, Schneeweiss S, Glynn RJ, Lipsitz LA, Rockwood K, Avorn J. Measuring frailty in Medicare data: development and validation of a claims-based frailty index. J Gerontol A Biol Sci Med Sci. 2018;73:980-7. https://doi.org/10.1093/gerona/glx229
17. Stang A. Critical evaluation of the Newcastle-Ottawa Scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25:603-5. https://doi.org/10.1007/s10654-010-9491-z