INPLASY

INPLASY202630021

doi: 10.37766/inplasy2026.3.0021

Received: 6 March 2026

Published: 6 March 2026

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Management Strategies for Right-to-Left Intraatrial Shunt with Thrombus in Transit: A Systematic Review of 297 Patients and Associated Mortality Outcomes

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ADMINISTRATIVE INFORMATION

Support - Not applicable.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202630021

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 6 March 2026 and was last updated on 6 March 2026.

INTRODUCTION

Review question / Objective Population: Adult patients diagnosed with thrombus in transit across a patent foramen ovale or atrial septal defect.
Intervention/Exposure: Therapeutic strategies including surgical embolectomy, anticoagulation, thrombolysis, and percutaneous aspiration, with or without PFO/ASD closure.
Comparator: Comparison of outcomes across different treatment strategies.
Outcomes: Mortality, short-term clinical improvement, and survival outcomes.
Study design: Case reports, case series, and observational studies describing thrombus in transit visualized by transthoracic or transesophageal echocardiography.

Rationale Thrombus in transit (TIT) across a patent foramen ovale (PFO) or atrial septal defect (ASD) is a rare but potentially life-threatening clinical condition associated with paradoxical embolism and high mortality risk. Although advances in echocardiography and interventional techniques have improved the detection and management of this condition, optimal treatment strategies remain uncertain due to the rarity of cases and the lack of prospective studies or established guidelines. Most of the available evidence consists of case reports and small case series describing various management approaches, including surgical embolectomy, anticoagulation, thrombolysis, and percutaneous aspiration, with or without closure of the intra-atrial shunt. Because individual reports provide limited insight into overall outcomes, a systematic synthesis of the available literature is necessary to better characterize clinical presentations, diagnostic modalities, management strategies, and outcomes. Therefore, this systematic review was conducted to summarize the existing evidence and provide a comprehensive overview of treatment approaches and survival outcomes in adult patients with thrombus in transit across right-to-left intra-atrial shunts.

Condition being studied The condition of interest is thrombus in transit (TIT) across a right-to-left intra-atrial shunt, most commonly a patent foramen ovale (PFO) or atrial septal defect (ASD). This phenomenon occurs when a thrombus originating from the venous circulation becomes temporarily lodged within the interatrial septum while passing from the right atrium to the left atrium. This situation carries a high risk of paradoxical embolism, which can result in systemic complications such as stroke, myocardial infarction, or peripheral arterial embolism. TIT is typically diagnosed using transthoracic or transesophageal echocardiography and is often identified in the context of pulmonary embolism or deep venous thrombosis. Due to the rarity of this condition and the absence of standardized management guidelines, treatment approaches vary widely and may include surgical thrombectomy, anticoagulation therapy, thrombolysis, percutaneous aspiration, and closure of the underlying atrial shunt.

METHODS

Search strategy The search was conducted following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. We systematically searched the PubMed/MEDLINE database from its inception through March 2025, and cases were included from 1987 up to 2025. The search terms included combinations of controlled vocabulary and keywords such as "thrombus in transit," "paradoxical embolism," "right-to-left shunt," "patent foramen ovale," "atrial septal defect," "trapped thrombus," "intracardiac thrombus," "pulmonary embolism," "stroke," "anticoagulation," "thrombolysis," "cardiac surgery," and "PFO/ASD closure." Boolean operators (AND, OR) and truncation techniques were used to maximize sensitivity and capture a wide range of study types. We also manually screened the reference lists of eligible articles to identify additional studies that were not retrieved through the electronic search. Only articles published in English were considered. Other studies, including conference proceedings, unpublished manuscripts, or non-peer-reviewed sources, were not included in this review. To date, there are no randomized trials or large prospective studies specifically evaluating thrombus in transit or directly comparing treatment strategies and outcomes in this population.

Participant or population Adult patients diagnosed with thrombus in transit (TIT) across a right-to-left intra-atrial shunt, most commonly patent foramen ovale (PFO) or atrial septal defect (ASD), identified by transthoracic or transesophageal echocardiography. Cases reported in the context of pulmonary embolism, deep venous thrombosis, or paradoxical embolic events were included. Pediatric cases and reports without clear echocardiographic visualization of thrombus in transit were excluded.

Intervention Therapeutic strategies used in the management of thrombus in transit, including surgical embolectomy, anticoagulation therapy, systemic thrombolysis, and percutaneous aspiration or thrombectomy. Closure of the interatrial shunt (PFO or ASD), when reported, was also evaluated as part of the management strategy.

Comparator Comparisons were made between different management strategies, including surgical treatment, anticoagulation therapy, thrombolysis, and percutaneous aspiration. Outcomes were also compared between patients who underwent closure of the interatrial shunt and those managed without closure.

Study designs to be included Case reports, case series, and observational studies describing adult patients with thrombus in transit across a patent foramen ovale or atrial septal defect confirmed by echocardiographic imaging.

Eligibility criteria The search was limited to human studies involving adults. Only case reports, case series, and letters to the editor that provided sufficient clinical details were included. Studies were required to describe patients with TIT visualized through TTE or TEE and to report one relevant clinical variable, such as etiology (provoked or unprovoked), comorbidities, imaging findings, or outcomes (e.g., survival time, mortality). Therapeutic strategy was mandatory to be included (e.g., anticoagulation, thrombolysis, surgical embolectomy, percutaneous aspiration). The final dataset included only studies with full-text availability to ensure complete data extraction. Duplicate publications, non-clinical experimental studies, review articles, abstracts without detailed individual patient data, postmortem-only reports, and studies in languages other than English were excluded. The systematic search strategy was designed to ensure an image describing the thrombus in the defect and focused review of treatment strategies and outcomes for thrombus in transit in patients with right-to-left intraatrial shunting.

Information sources A systematic literature search was conducted in PubMed, Embase, and

Scopus from database inception through March 2025. Reference lists of relevant articles and previously published reviews were also screened to identify additional eligible studies. Only peer-reviewed publications were included in the review.

Main outcome(s) The primary outcome of interest was all-cause mortality associated with thrombus in transit across a right-to-left intra-atrial shunt. Secondary outcomes included short-term clinical improvement and survival outcomes according to different treatment strategies, including surgical embolectomy, anticoagulation therapy, thrombolysis, and percutaneous aspiration, as well as the impact of PFO or ASD closure on patient outcomes. Survival analysis was performed to evaluate differences in outcomes across treatment modalities.

Additional outcome(s) Additional outcomes included the frequency of different clinical presentations (respiratory, cardiac, and neurological symptoms), the prevalence of provoked versus unprovoked events, diagnostic modalities used for thrombus detection, and the distribution of treatment strategies. We also evaluated the proportion of patients undergoing closure of the intra-atrial shunt (PFO or ASD) and examined survival differences across treatment modalities using Kaplan–Meier analysis.

Data management All records identified through database searches were exported and managed using reference management software to remove duplicate citations. Titles and abstracts were screened independently by two reviewers, followed by full-text assessment of potentially eligible studies. Data from included studies were extracted using a standardized data collection form capturing demographic characteristics, clinical presentation, diagnostic methods, treatment strategies, and outcomes. Discrepancies during screening or data extraction were resolved through discussion and, when necessary, consultation with a third reviewer. Extracted data were organized in a structured dataset for subsequent statistical analysis.

Quality assessment / Risk of bias analysis Risk of bias was evaluated for each included case report and case series using the validated Murad et al. checklist. This tool assesses eight domains: clarity of case selection, exposure ascertainment, outcome measurement, alternative cause exclusion, follow-up adequacy, timeline clarity, response to intervention, and overall detail for clinical applicability.

The quality assessment was performed by two sets of two reviewers, where each article was assessed. Any differences between reviewers were solved by discussion, and third author was consulted to give a final decision regarding any unsolved disputes. Each study was rated as Good, Fair, or Poor quality based on the number of "Yes" responses (6-8 = Good, 4-5 = Fair, 0-3 = Poor). A full summary of the risk of bias assessments and studies included is provided in supplemental table.

Strategy of data synthesis Statistical analysis was performed using SPSS version 25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY). Descriptive statistics summarized patient demographics, clinical features, diagnostic methods, treatments, and outcomes. Chi-squared tests were used to compare treatment types with key categorical outcomes, including mortality, symptom resolution, and cause of death. The Mann-Whitney U test assessed associations between non-parametric variables such as symptom severity, comorbidities, provoked vs. unprovoked causes, and embolization sites with outcomes. Survival analysis was conducted using Kaplan-Meier curves to evaluate 120-day survival across treatment strategies, PFO/ASD closure, and their combinations. Differences in survival were assessed using the log-rank test. Multivariable Cox regression identified independent predictors of mortality, including treatment type, IVC filter placement, embolization sites, etiology (provoked vs. unprovoked), age, and sex. A p-value <0.05 was considered statistically significant.

Subgroup analysis Subgroup analyses were performed to evaluate outcomes according to different treatment strategies, including surgical embolectomy, anticoagulation therapy, thrombolysis, and percutaneous aspiration. Additional subgroup analyses examined outcomes among patients who underwent closure of the interatrial shunt (PFO or ASD) compared with those managed without closure. Survival differences across treatment groups were explored using Kaplan–Meier survival analysis.

Sensitivity analysis Formal sensitivity analyses were limited due to the observational nature of the included evidence, which primarily consisted of case reports and case series. However, analyses were repeated after stratifying patients according to treatment strategy and shunt closure status to evaluate the consistency of observed outcomes across subgroups.

Language restriction Only studies published in English were included in the review.

Country(ies) involved United States.

Keywords Thrombus in transit;Impending paradoxical embolism;Right-to-left intraatrial shunt;Surgical embolectomyTranscatheter closure.

Contributions of each author

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