International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

PRECIPitating causes of Atrial Fibrillation with rapid ventricular response: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 April 2026 and was last updated on 20 April 2026.

INTRODUCTION

Review question / Objective Population: Patients presenting to the emergency department
Exposure: Atrial fibrillation with rapid ventricular response
Outcome: Underlying cause or exacerbating cause of atrial fibrillation.

Rationale In the ED, AF with RVR is often treated as a rhythm management problem, but optimal care requires attention to the precipitating cause. A better understanding of the distribution of underlying aetiologies may improve diagnostic prioritisation, guide investigations, and support more targeted management strategies. At present, no comprehensive synthesis appears to have specifically examined the underlying causes of AF with RVR in ED populations. This review will address that gap by collating and quantitatively summarising evidence from observational and interventional studies where relevant.

Condition being studied The condition under study is atrial fibrillation with rapid ventricular response (AF with RVR) presenting in the emergency department. This review will examine the underlying acute or chronic causes that precipitate or exacerbate AF with RVR, such as infection, myocardial ischaemia, heart failure, electrolyte abnormalities, pulmonary embolism, thyrotoxicosis, dehydration, medication-related factors, and other systemic triggers.

METHODS

Search strategy A comprehensive literature search will be undertaken in the following electronic databases:
• MEDLINE
• Embase
• CINAHL
• CENTRAL
• Google scholar
The search strategy will combine controlled vocabulary terms and free-text keywords related to:

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• atrial fibrillation;
• rapid ventricular response;
• emergency department or emergency service;
• cause, precipitant, trigger, aetiology, exacerbation, or underlying condition.
An example search strategy for MEDLINE will include combinations of terms such as:
• "atrial fibrillation" OR "AF"
• "rapid ventricular response" OR "RVR" OR "tachycardia"
• "emergency department" OR "emergency service" OR "emergency room"
• "cause" OR "aetiology" OR "etiology" OR "precipitant" OR "trigger" OR "underlying cause"
Reference lists of included studies and relevant reviews will also be hand-searched to identify additional eligible studies. Grey literature may be considered if it provides sufficient data and methodological detail.

Participant or population The review will include adult (>17 yrs) patients presenting to the ED with AF and rapid ventricular response. Where definitions vary between studies, the authors' diagnostic definitions will be recorded. If possible, the threshold used for rapid ventricular response, such as ventricular rate above 110 beats per minute or another study-specific definition, will be extracted and considered in the analysis.

Intervention The exposure of interest is presentation to the ED with atrial fibrillation with rapid ventricular response. Studies using synonymous terms such as "AF with RVR," "rapid AF," or "atrial fibrillation with tachycardia" will be considered if clinically comparable.

Comparator Outcome
The primary outcome is the reported underlying, precipitating, associated, or exacerbating cause of AF with RVR. Causes may include, but are not limited to:
• infection or sepsis;
• acute coronary syndrome or myocardial ischaemia;
• heart failure or fluid overload;
• electrolyte disturbance;
• pulmonary embolism;
• thyrotoxicosis;
• dehydration or hypovolaemia;
• medication non-adherence or withdrawal;
• alcohol or substance-related triggers;
• postoperative or procedural states;
• idiopathic or no clear cause identified.

Study designs to be included • use observational or interventional study designs, including prospective cohort studies, retrospective cohort studies, cross-sectional studies, case-control studies, or relevant trial baseline data.

Eligibility criteria Inclusion Criteria
Studies will be included if they:
• involve adult or mixed adult populations presenting to an emergency department;
• include patients diagnosed with atrial fibrillation with rapid ventricular response, or clearly report a subgroup consistent with AF with RVR;
• report at least one underlying, precipitating, associated, or exacerbating cause of AF with RVR;
• use observational or interventional study designs, including prospective cohort studies, retrospective cohort studies, cross-sectional studies, case-control studies, or relevant trial baseline data
• are published in peer-reviewed journals.

Information sources A comprehensive literature search will be undertaken in the following electronic databases:
• MEDLINE
• Embase
• CINAHL
• Scopus
• CENTRAL
• Google Scholar
Reference lists of included studies and relevant reviews will also be hand-searched to identify additional eligible studies. Grey literature may be considered if it provides sufficient data and methodological detail.

Main outcome(s) To identify studies reporting the underlying or precipitating causes of AF with RVR in ED patients.

To describe the range of underlying causes reported across studies.

To estimate the pooled proportion of major underlying causes of AF with RVR, where sufficient homogeneous data are available.

To explore variation in reported causes according to study design, setting, patient characteristics, and geographic region.

To assess the quality of the included studies and the certainty of the evidence.

Data management A standardised data extraction form will be developed and piloted. The following data will be extracted:
• study characteristics: author, year, country, study design, setting;
• participant characteristics: sample size, age, sex, comorbidities;

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• AF with RVR definition and diagnostic criteria;
• ED presentation characteristics;
• reported underlying or precipitating causes;
• frequency or proportion of each cause;
• methods used to determine the underlying cause;
• secondary outcomes where reported, such as admission, length of stay, or mortality.
Data extraction will be performed independently by two reviewers.

Quality assessment / Risk of bias analysis As most eligible studies are expected to be observational, methodological quality will be assessed using an appropriate tool such as the Joanna Briggs Institute critical appraisal checklist for prevalence studies or cohort studies, depending on study design. If substantial diagnostic classification issues are present, an alternative appraisal approach may be considered. Two reviewers will independently assess risk of bias, with disagreements resolved through consensus.

Strategy of data synthesis Initially, findings from all included studies will be summarised descriptively. Study characteristics will be tabulated, including author, year, country, study design, emergency department setting, sample size, patient demographics, definition of atrial fibrillation with rapid ventricular response (AF with RVR), and method used to identify the underlying cause. Reported causes of AF with RVR will be extracted and grouped into clinically meaningful categories. These categories may include infection or sepsis, myocardial ischaemia or acute coronary syndrome, heart failure, electrolyte disturbances, pulmonary embolism, thyrotoxicosis, dehydration or hypovolaemia, medication-related causes, alcohol or substance use, postoperative causes, and cases with no identifiable cause.

The descriptive analysis will report the range and frequency of these underlying causes across studies. If substantial variation exists in terminology, similar causes will be harmonised into standardised categories before analysis. For example, "chest sepsis," "pneumonia," and "systemic infection" may be grouped under infection, while "acute coronary syndrome" and "myocardial infarction" may be grouped under myocardial ischaemia. This process will improve comparability across studies while preserving the original reported data.

Quantitative Synthesis and Meta-analysis

Where studies are sufficiently similar in population, outcome definition, and reporting format, a meta-analysis will be performed. The principal quantitative outcome will be the pooled proportion of each reported underlying cause among ED patients presenting with AF with RVR.

Because the outcome of interest is a proportion rather than a treatment effect, a meta-analysis of proportions will be conducted. For each study, the numerator will be the number of patients reported to have a specific underlying cause, and the denominator will be the total number of patients with AF with RVR assessed in that study. Separate pooled estimates will be calculated for each major cause category.

A random-effects model will be used for all meta-analyses because clinical and methodological heterogeneity between studies is expected. Differences may arise from study setting, patient selection, diagnostic thresholds, definition of AF with RVR, and methods used to determine the underlying cause. A random-effects model is therefore more appropriate than a fixed-effect model, as it assumes that the true effect size may vary across studies.

If raw proportions are highly skewed, a variance-stabilising transformation, such as the Freeman–Tukey double arcsine transformation or logit transformation, may be used prior to pooling. Back-transformed pooled estimates will then be presented as percentages with 95% confidence intervals. Forest plots will be generated for each major cause category to visually display individual study estimates and pooled results.Assessment of Heterogeneity

Statistical heterogeneity across studies will be assessed using the I^2 statistic, tau-squared (τ^2), and the chi-square test for heterogeneity. The I^2 statistic will be used to estimate the proportion of total variability attributable to between-study heterogeneity rather than chance. Although thresholds are only approximate, I^2 values of around 25%, 50%, and 75% may be interpreted as low, moderate, and high heterogeneity, respectively. Tau-squared will provide an estimate of the between-study variance.

Where substantial heterogeneity is observed, possible sources will be explored through subgroup analysis or sensitivity analysis, provided sufficient studies are available.

Subgroup analysis If enough data are available, subgroup analyses will be undertaken to explore differences in the distribution of underlying causes according to:

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geographic region or country;

study design, such as prospective versus retrospective studies;

type of hospital or emergency department setting;

patient age group;

proportion of patients with known previous atrial fibrillation versus new-onset AF;

definition of rapid ventricular response used in the study;

method used to establish the underlying cause, such as clinician diagnosis, discharge diagnosis, or predefined diagnostic criteria.

These subgroup analyses will help determine whether variations in reported causes reflect genuine clinical differences or methodological inconsistency.

Sensitivity analysis Sensitivity analyses will be performed to assess the robustness of the pooled findings. These may include:

excluding studies judged to be at high risk of bias;

excluding studies with unclear or non-standard definitions of AF with RVR;

excluding studies with very small sample sizes;

comparing transformed versus untransformed proportion estimates where relevant;

excluding studies in which the underlying cause was not clearly defined or categorised.

These analyses will help determine whether the main findings are stable and not driven by low-quality or methodologically heterogeneous studies.

Language restriction No.

Country(ies) involved Australia.

Keywords Atrial fibrillation; emergency department; aetiology; rapid ventricular response.

Dissemination plans The findings will be submitted for publication in a peer-reviewed journal relevant to emergency medicine or cardiology and may also be presented at national or international conferences.

Contributions of each author

Author 1 - Salman Naeem - Author 1 conceived the study and was responsible for drafting the protocol, including development of the review question, eligibility criteria, search strategy, and planned methods of synthesis and analysis.
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