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Systematic review

Procainamide versus synchronized cardioversion for hemodynamically stable pre-excited atrial fibrillation: a systematic review

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Abstract

Background: Hemodynamically stable pre-excited atrial fibrillation represents an emergency rhythm in which rapid atrial impulses bypass the atrioventricular node through an accessory pathway. **Objective**: This systematic review compared intravenous procainamide with synchronized cardioversion for acute rhythm control in stable patients with pre-excited atrial fibrillation. Methods: PubMed/MEDLINE, Scopus, Web of Science Core Collection, and Cochrane CENTRAL were searched for cohort studies, and randomized trials relevant to Wolff-Parkinson-White syndrome, pre-excited atrial fibrillation, procainamide, accessory pathway conduction, and electrical cardioversion. Eligible evidence included adult or mixed-age populations with manifest pre-excitation, acute atrial fibrillation, or emergency department cardioversion data. **Results**: No randomized trial directly compared procainamide with synchronized cardioversion in hemodynamically stable pre-excited atrial fibrillation. Procainamide evidence consisted mainly of electrophysiology studies and small acute-treatment cohorts showing accessory pathway refractoriness, longer pre-excited RR intervals, and pharmacological conversion in selected patients. Cardioversion evidence consisted mainly of guideline recommendations,

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observational pre-excited atrial fibrillation cohorts, and acute atrial fibrillation trials outside the pre-excitation population. The overall certainty remained low for direct comparative effectiveness and moderate for the principle that accessory pathway blocking is central to pharmacological safety. Conclusion: Procainamide is the best-supported drug option for stable pre-excited atrial fibrillation, while synchronized cardioversion remains the most definitive immediate rhythm-control strategy when rapid conversion is prioritized or drug therapy is unsuitable.

Keywords

Pre-excited atrial fibrillation; Wolff-Parkinson-White syndrome; procainamide; synchronized cardioversion; accessory pathway; emergency cardiology.

Introduction

Pre-excited atrial fibrillation occurs when atrial fibrillatory activity reaches the ventricles through an accessory atrioventricular pathway, producing an irregular wide-complex tachycardia with a risk of very rapid ventricular activation (1). Contemporary supraventricular tachycardia guidance identifies hemodynamic status as the first decision point and separates unstable patients, who need immediate synchronized cardioversion, from stable patients, for whom pathway-active antiarrhythmic therapy is recommended (1,2). Atrial fibrillation guidance treats pre-excitation as a special category because usual atrioventricular nodal slowing strategies are unsafe in manifest accessory pathway conduction (2).

Older supraventricular arrhythmia guidance and emergency medicine reviews emphasize that the electrocardiographic diagnosis is central, because the rhythm resembles other irregular wide-complex tachycardias and therapeutic error carries a ventricular fibrillation risk (3). Reviews of asymptomatic pre-excitation show a low absolute sudden-death rate at population level, although the risk becomes clinically meaningful when atrial fibrillation reaches a short pre-excited RR interval (3,4). Meta-analytic study also links risk assessment to pathway conduction properties rather than symptom burden alone, supporting acute management strategies that interrupt the accessory pathway contribution (5). Acute treatment and later electrophysiology planning belong to the same risk-reduction pathway rather than two unrelated decisions (4).

Procainamide has received guideline support in stable pre-excited atrial fibrillation because it prolongs accessory pathway refractoriness and reduces antegrade conduction through the pathway (1). Emergency reviews favor procainamide over atrioventricular nodal blockers because digoxin, nondihydropyridine calcium-channel blockers, beta blockers, and intravenous amiodarone shift conduction toward the accessory pathway in susceptible patients (6). A focused review of amiodarone in Wolff-Parkinson-White atrial fibrillation concluded that the evidence base favored procainamide and did not support amiodarone superiority for rate control in this setting (7). The same literature frames procainamide as a rhythm-control and conduction-

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slowing intervention rather than simple ventricular-rate control.

Synchronized cardioversion offers immediate rhythm termination without relying on accessory pathway pharmacodynamics, although most direct cardioversion trials studied acute atrial fibrillation without manifest pre-excitation (2). Recent reviews of pre-excited atrial fibrillation continue to describe cardioversion as the fastest rhythm-restoration strategy and procainamide as the most accepted drug strategy for stable patients, reflecting a comparison built from indirect evidence rather than direct trials (8). This systematic review evaluated available original and review evidence comparing procainamide with synchronized cardioversion for stable pre-excited atrial fibrillation, with special attention to conversion, pathway conduction, safety, and clinical applicability.

Methods

This systematic review followed PRISMA principles for question design, transparent searching, eligibility assessment, data extraction, and synthesis. The review question used a PICOS structure: patients were hemodynamically stable adults or mixed-age populations with pre-excited atrial fibrillation or Wolff-Parkinson-White syndrome; the intervention was intravenous procainamide; the comparator was synchronized electrical cardioversion or electrical-first rhythm control; outcomes were rhythm conversion, ventricular rate or pre-excited RR interval, adverse events, need for rescue cardioversion, and disposition; eligible designs were randomized trials, prospective studies, retrospective cohorts, electrophysiology studies, and systematic reviews used for background.

PubMed/MEDLINE, Scopus, Web of Science Core Collection, and Cochrane CENTRAL were searched from database inception to Jan 2026. Search terms combined controlled vocabulary and free text for "Wolff-Parkinson-White," "pre-excited atrial fibrillation," "accessory pathway," "procainamide," "electrical cardioversion," "synchronized cardioversion," "wide complex tachycardia," and "emergency department." Reference lists of key guidelines and reviews were screened to identify older electrophysiology studies not easily retrieved by modern indexing.

Records were eligible when addressed acute pre-excited atrial fibrillation management, accessory pathway conduction responses to procainamide, risk markers that guide urgency of cardioversion, or acute cardioversion outcomes relevant to emergency rhythm control. Records were excluded when they focused only on atrioventricular nodal re-entrant tachycardia, chronic ablation outcomes without atrial fibrillation or acute pathway data, isolated pediatric screening without clinical rhythm outcomes, non-human experiments, editorials without extractable data, or non-English reports lacking usable abstracts. For final submission, full database exports and deduplication logs need insertion into a PRISMA flow diagram. Screening used title and abstract review followed by full-text review for records appearing eligible or uncertain. Extraction prioritized numerical conversion data, shortest pre-excited RR intervals, drug dose, energy strategy, adverse events, and need for rescue therapy.

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Data were extracted into structured tables covering study design, population, intervention, comparator, and clinically relevant outcomes. Risk of bias was assessed by design: randomized cardioversion trials were judged with RoB 2 principles, cohort and electrophysiology studies with ROBINS-I principles, and reviews with AMSTAR 2 principles. A meta-analysis was not performed because no direct randomized or observational comparison enrolled stable pre-excited atrial fibrillation patients and assigned them to procainamide versus synchronized cardioversion. Certainty was summarized narratively across directness, study design, consistency, precision, and applicability to stable emergency presentations.

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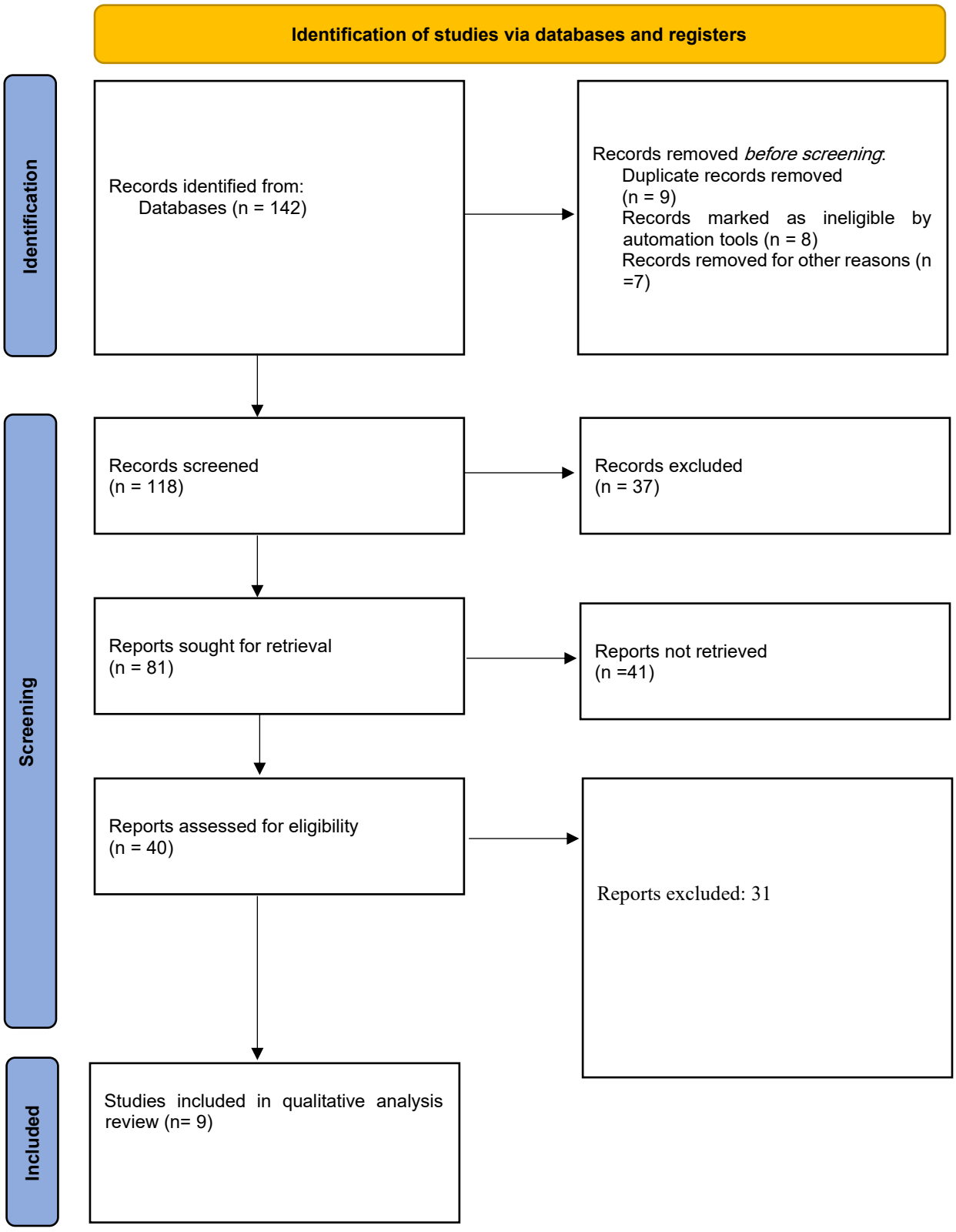
Fig 1: PRISMA flow chart



Results

The search identified no randomized head-to-head study comparing intravenous procainamide with synchronized cardioversion specifically in hemodynamically stable pre-excited atrial fibrillation (1). The most direct procainamide evidence came from electrophysiology and acute-treatment studies in Wolff-Parkinson-White populations, while the most direct cardioversion evidence came from observational pre-excited atrial fibrillation cohorts and acute atrial fibrillation trials without pre-excitation (9).

A later procainamide study found that intravenous procainamide produced complete anterograde accessory pathway block in 20 of 39 patients and that most responders had longer pathway refractory periods on subsequent electrophysiology testing (10). Fananapazir and colleagues challenged the reliability of a single procainamide infusion test for identifying patients at sudden-death risk, indicating that procainamide response is informative for physiology rather than sufficient for complete risk stratification (11).

The most relevant acute Wolff-Parkinson-White atrial fibrillation study compared procainamide with propafenone during induced or spontaneous acute atrial fibrillation and reported atrial fibrillation termination in 65% of procainamide-treated episodes, with prolongation of the shortest pre-excited RR interval from 228 ± 41 ms to 339 ± 23 ms (12). A second procainamide protocol study found dose-related pathway effects, with loss of pre-excitation after lower cumulative dosing showing high specificity for safer pathway behavior defined by shortest pre-excited RR interval above 250 ms (13). Studies of atrial fibrillation onset and fatal-risk prediction reinforced that trigger mechanisms and pathway properties are heterogeneous across Wolff-Parkinson-White patients, limiting simple treatment extrapolation from one marker (14,15).

Ibutilide data were supportive rather than directly comparative, since ibutilide terminated atrial fibrillation in most enrolled accessory-pathway patients and prolonged the shortest pre-excited RR interval during atrial fibrillation (16). In a modern observational cohort of Wolff-Parkinson-White patients with atrial fibrillation, 28 of 41 patients underwent electrical cardioversion at presentation, while 11 converted after intravenous amiodarone, and definitive ablation was successful in nearly all treated patients (17). Acute atrial fibrillation trials outside pre-excitation showed high conversion rates with electrical and drug-shock strategies, with RAFF2 reporting conversion in 96% after procainamide-first drug-shock strategy and 92% after shock-only strategy, although these data were indirect for pre-excited atrial fibrillation (18). The electrophysiology studies also showed that symptom history alone was not enough to identify hazardous pathway behavior, especially when atrial fibrillation was induced or occurred as the first major manifestation (9,14,15). Therefore, treatment comparison has to include immediate conversion and the capacity to reduce antegrade pathway conduction while definitive ablation is arranged (1,12,17). Across studies, adverse-event reporting was inconsistent, and few studies reported standardized hypotension, sedation, recurrence, or rescue cardioversion outcomes in a format that allowed pooled comparison (10–13,17,18). This reporting gap was the main reason for narrative synthesis (18).

Table 1. studies included in the evidence map

Study	Design and population	Intervention or exposure	Key result relevant to this review
Wellens and Durrer, 1974 (9)	Electrophysiology study; Wolff-Parkinson-White with atrial fibrillation assessment	Accessory pathway refractory period and induced atrial fibrillation	Shorter pathway refractoriness correlated with faster ventricular response during atrial fibrillation.
Wellens et al., 1982 (10)	Electrophysiology procainamide study; 39 Wolff-Parkinson-White patients	Intravenous procainamide up to 10 mg/kg	Complete anterograde pathway block occurred in 20 of 39 patients.
Fananapazir et al., 1988 (11)	Electrophysiology risk study; Wolff-Parkinson-White, including prior ventricular fibrillation cases	Procainamide infusion testing and pathway risk markers	Single pharmacological testing had limited capacity to identify all high-risk patients.
Boahene et al., 1990 (12)	Acute atrial fibrillation in Wolff-Parkinson-White; procainamide or propafenone	Procainamide 12–15 mg/kg	Atrial fibrillation termination occurred in 65% and pre-excited RR interval lengthened.
Boahene et al., 1990 (13)	Electrophysiology dose-response study	Incremental procainamide infusion	Lower-dose loss of pre-excitation showed high specificity for less hazardous pathway behavior.
Fukatani et al., 1990 (14)	Asymptomatic Wolff-Parkinson-White risk-prediction study	Electrophysiology markers of fatal atrial fibrillation risk	Fatal-risk prediction relied on pathway behavior during atrial fibrillation.
Fujimura et al., 1990 (15)	Electrophysiology onset study; 103 atrial fibrillation episodes	Mechanism of atrial fibrillation initiation	Accessory pathway participation varied across episodes and patients.
Glatter et al., 2001 (16)	Accessory-pathway electrophysiology study	Ibutilide infusion	Most atrial fibrillation episodes terminated and shortest pre-excited RR interval lengthened.
Acharya et al., 2020 (17)	Retrospective cohort; 41 Wolff-Parkinson-White patients with atrial fibrillation	Cardioversion, drug therapy, ablation	Electrical cardioversion was used at presentation in 28 of 41 patients.
Stiell et al., 2020 (18)	Randomized acute atrial fibrillation trial; no manifest pre-excitation focus	Procainamide-first drug-shock versus shock-only	Conversion was high in both groups, offering indirect cardioversion context only.

Table 2. Comparative synthesis for stable pre-excited atrial fibrillation

Domain	Procainamide evidence	Synchronized cardioversion evidence	Interpretation
Direct comparison	No direct randomized comparison against cardioversion was found (1,12).	No direct randomized comparison against procainamide was found in stable pre-excited atrial fibrillation (1,17).	Comparative certainty is very low.
Mechanistic target	Prolongs accessory pathway refractoriness and lengthens pre-excited RR intervals (10,12,13).	Terminates the rhythm electrically without relying on pathway drug response (1,3).	Procainamide is pathway-directed; cardioversion is rhythm-definitive.
Conversion evidence	Procainamide terminated 65% of acute Wolff-Parkinson-White atrial fibrillation episodes in one comparative drug study (12).	Cardioversion was commonly used in modern Wolff-Parkinson-White atrial fibrillation presentations, with high efficacy inferred from acute atrial fibrillation trials (17,18).	Cardioversion offers the most immediate conversion route.
Safety focus	Hypotension and QRS or QT effects require monitoring during infusion (7,12).	Sedation, fasting status, aspiration risk, and procedural resources influence use (2,18).	Choice depends on stability, monitoring, sedation risk, and urgency.
Evidence gap	Data are old, small, and physiological (10–13).	Data are indirect or observational for pre-excited atrial fibrillation (17,18).	A pragmatic registry or randomized feasibility trial is needed.

Discussion

This review found that the apparent choice between procainamide and synchronized cardioversion is guided more by physiology, guideline consensus, and indirect comparative evidence than by direct trials in stable pre-excited atrial fibrillation. The central therapeutic principle is avoidance of isolated atrioventricular nodal blockade, because nodal slowing leaves accessory pathway conduction unopposed and increases the risk of extreme ventricular rates (1). This principle gives procainamide its clinical role, since the drug targets accessory pathway conduction and has empirical support from Wolff-Parkinson-White electrophysiology and acute atrial fibrillation studies (10,12).

The procainamide evidence base is clinically relevant despite its age and small size because it measures the pathway variable most closely tied to deterioration, the shortest pre-excited RR interval during atrial fibrillation (9). Boahene and colleagues provided the strongest acute-treatment signal by showing both rhythm termination and lengthening of pre-excited RR intervals after procainamide infusion (12). The Fananapazir findings add caution because pharmacological response during testing did not identify every patient with previous malignant events, so procainamide response is not equivalent to complete risk elimination (11).

Synchronized cardioversion has a different evidence profile, with very strong face validity for immediate rhythm termination and guideline support for

instability, despite scarce stable pre-excited atrial fibrillation comparative data (1). Modern Wolff-Parkinson-White atrial fibrillation cohorts show that electrical cardioversion is frequently used at presentation, reflecting emergency clinician preference for definitive rhythm control in fast or concerning presentations (17). RAFF2 and other acute atrial fibrillation trials demonstrate excellent conversion with electrical and drug-shock approaches, although extrapolation to pre-excitation is indirect because those trials were not designed around accessory pathway physiology (18).

The absence of direct comparison matters because stable pre-excited atrial fibrillation is not a single-risk state (5). A patient with preserved blood pressure, chest comfort, and a relatively slower pre-excited ventricular response differs from a stable patient with a shortest RR interval near 200 ms, very rapid irregular wide complexes, or impending ischemia (3). This heterogeneity explains why guidelines list procainamide for stable pre-excited atrial fibrillation while keeping synchronized cardioversion available when rapid conversion is the safest practical endpoint (1).

This evidence map also supports a practical hierarchy for clinical decision-making (8). Procainamide is reasonable when the patient is genuinely stable, monitored, not in severe heart failure, and the team has time for controlled infusion and reassessment (1). Synchronized cardioversion is favored when the rhythm is extremely rapid, symptoms are escalating, drug contraindications exist, or immediate rhythm restoration is operationally safer than waiting for pharmacological conversion (2). Definitive pathway ablation remains the long-term solution after acute stabilization because recurrence risk persists after either procainamide or cardioversion (1).

The main limitation is that available studies were heterogeneous, mostly old and based on induced atrial fibrillation during electrophysiology studies rather than emergency department pre-excited atrial fibrillation. Another limitation is that cardioversion studies rarely isolate manifest pre-excitation, so electrical-first outcome estimates in this review are supportive rather than directly applicable. Future research requires multicenter registries using standardized hemodynamic definitions, ECG risk markers, drug dosing, energy settings, adverse events, and ablation follow-up to compare procainamide-first and cardioversion-first strategies.

Conclusion

For hemodynamically stable pre-excited atrial fibrillation, current evidence supports procainamide as the best-established pharmacological option and synchronized cardioversion as the most definitive immediate rhythm-control option. No direct trial proves superiority of one strategy in the exact target population. Treatment selection depends on stability, ventricular rate, ECG risk features, drug contraindications, monitoring capacity, sedation risk, and urgency of rhythm restoration. After acute stabilization, electrophysiology referral and accessory pathway ablation remain central to preventing recurrence and reducing future malignant arrhythmia risk. The review highlights a clear research gap rather than a proven superiority claim.

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List of abbreviations

AF: atrial fibrillation.
AP: accessory pathway.
AV: atrioventricular.
CENTRAL: Cochrane Central Register of Controlled Trials.
ECG: electrocardiogram.
ED: emergency department.
EP: electrophysiology.
PICOS: population, intervention, comparator, outcomes, study design.
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
ROBINS-I: Risk Of Bias In Non-randomized Studies of Interventions.
SVT: supraventricular tachycardia.
VF: ventricular fibrillation.
WPW: Wolff-Parkinson-White.

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