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Research Article

The Effects of Propafenone on Postoperative Atrial Fibrillation in Adult Patients Undergoing Cardiac Surgery: A Meta-Analysis of Randomized Controlled Trials

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Background. Previous research has only conducted a restricted amount of investigations on the effectiveness of propafenone in preventing and treating of atrial fibrillation (AF) after cardiac surgery. Hence, a comprehensive evaluation and meta-analysis were performed to evaluate the effectiveness and safety of propafenone in individuals undergoing cardiac surgery for postoperative atrial fibrillation (POAF). *Methods.* A meta-analysis of randomized controlled trials was conducted. Until September 15th, 2023, various databases were searched. The main focal points consisted of the presence of POAF, transition from AF to sinus rhythm, and reappearance of AF. The odds ratios (ORs) for treatment effects on dichotomous variables were calculated. *Results.* The analysis of data included 9 controlled trials that were randomized and had 1014 patients. The findings indicated that propafenone has a significant impact on reducing the occurrence of POAF in adult patients who undergo cardiac surgery (OR, 0.52; 95% CI: 0.30, 0.89; $P = 0.02$). In addition, it was observed that propafenone significantly increase the rate of conversion to sinus rhythm from AF within 20 min (OR, 5.39; 95% CI: 2.25, 12.91; $P = 0.0002$) and 1 hour (OR, 2.89; 95% CI: 1.50, 5.57; $P = 0.002$) after administration. Surprisingly, the administration of propafenone treatment did not have a significant impact on the rate of conversion to sinus rhythm from AF within 24 hours (OR, 0.63; 95% CI: 0.38, 1.04; $P = 0.07$) after administration. *Conclusions.* The present study suggests that the postoperative administration of propafenone to adult cardiac surgery patients is both safe and effective for preventing and treating POAF.

1. Introduction

Postoperative atrial fibrillation (POAF) is a common perioperative cardiac arrhythmia. Previous studies have reported that patients following cardiac surgery (CS) may have a 10% to 30% risk of POAF [1]. Furthermore, research has indicated that approximately 40% to 60% of individuals encounter POAF following coronary artery bypass grafting (CABG) or cardiac valve surgery [2, 3]. In patients

undergoing cardiac surgery, perioperative arrhythmia, particularly atrial fibrillation (AF), in individuals undergoing CS has been associated with increased rates of morbidities, mortality, duration of hospitalization, and medical costs [4–11]. Hence, it is crucial to address these complications through effective interventions. CS patients are advised to use beta-blocker therapy for the prevention and management of tachyarrhythmias, in accordance with the existing clinical practice standards [6]. According to

multiple studies [12, 13], beta-blockers can decrease the occurrence of AF by up to 61%, when compared to a placebo. Therefore, routine use of beta-blockers after CS should be considered the standard of treatment for preventing AF. In summary, POAF is a major worry for individuals who are having heart surgery, and it is crucial to employ tactics to reduce its incidence. It has been demonstrated that beta-blocker medication effectively lowers the risk of AF and its associated complications. Thus, incorporating routine beta-blocker administration after CS is crucial in the management of POAF.

Propafenone, a popular class Ic antiarrhythmic medication that has been widely used for several decades, serves as a strong sodium channel blocker. In addition, it exhibits modest blockage of calcium channels and beta-adrenergic receptors, resulting in significant reductions in conduction velocity across all cardiac tissues. One distinct advantage of propafenone, as a class Ic agent, is its dose-dependent property, offering the convenience of single-loading dose administration with minimal side effects [14]. Several other research studies have demonstrated the effectiveness of propafenone treatment in the prevention of atrial tachyarrhythmia and the reduction of POAF occurrence following CS [15–17]. Moreover, multiple studies have shown that propafenone effectively manages AF following CS by controlling rapid ventricular response and facilitating the conversion to sinus rhythm [18–22]. Despite these findings, there remains a scarcity of studies investigating propafenone's effectiveness in treating and preventing AF and other atrial tachyarrhythmias following CS. More well-designed clinical trials are still required to comprehensively evaluate the role of propafenone in managing and preventing these conditions effectively.

This study aims to evaluate the clinical efficacy and safety of propafenone in preventing and treating POAF in patients with CS, considering the scarce evidence available on its routine use. The findings of this study may facilitate evidence-based decision-making regarding the use of propafenone within this specific patient cohort, ultimately improving patient outcomes and guiding future research in this field.

2. Methods

It is important to mention that our meta-analysis protocol has been properly registered in the PROSPERO (CRD42022391755). By adhering to these rigorous guidelines and protocols (PRISMA) [23], we aimed to ensure the highest standards of research quality and reporting transparency.

2.1. Search Strategy. In order to find potential relevant randomized controlled trials (RCTs) for our comprehensive review and meta-analysis, we performed an extensive search across various databases. We conducted a thorough search of various databases including PubMed, Cochrane Library, Embase, Medline, China National Knowledge Infrastructure (CNKI), and Wan Fang database up until September 15th, 2023.

The search strategy included employing different combinations of search terms, as outlined in Supplement Table 1. The included terms encompassed CS-related keywords such as cardiac surgery, coronary artery bypass grafting, cardiopulmonary bypass, valve surgery, and aortic surgery, along with propafenone and study design terms such as RCTs, controlled clinical trials, randomized, and random selection. Furthermore, we applied an English language restriction to the search.

2.2. Inclusion Criteria and Exclusion Criteria. We included all RCTs that compared the effectiveness and safety of propafenone with CG (amiodarone/procainamide/ibutilide/ saline) on adults undergoing CS. The main outcomes of concern comprised the occurrence of POAF. Additional outcomes of concern comprised the rate of transition from AF to normal heart rhythm, the reappearance of AF, and any negative events following the surgery. Exclusion criteria encompassed the research published as review articles, case reports, or abstracts and non-English language literature. In order to choose suitable studies for inclusion, two investigators (JHD and JL) independently assessed the titles and abstracts of all studies that were included. Any studies that were deemed ineligible based on this initial assessment were excluded. The remaining studies underwent a thorough analysis of the complete text to confirm their eligibility for eventual inclusion.

2.3. Literature Selection and Data Abstraction. Two researchers (JHD and JL) managed the literature using Endnote X9 [24] and autonomously performed the extraction of data. The extraction process entailed gathering information such as the author, publication year, journal, overall patient count, patient count in the propafenone group (PG) and control group (CG), gender, age, surgical procedure, and relevant outcome data. All authors were engaged in discussion to resolve any discrepancies that arose during the extraction process.

2.4. Quality Assessment. The evaluation of these criteria encompassed different factors, such as the generation of sequences, concealment of allocation, participant and outcome assessor blinding, completeness of outcome data, reporting bias, and other potential sources of bias. The evaluation procedure adhered to the prescribed instructions [25]. Furthermore, the methodological rigor was independently evaluated using a modified version of the Jadad score [26]. By conducting a comprehensive and standardized assessment, we were able to thoroughly evaluate the potential bias and the overall quality of the RCTs included in this study.

2.5. Data Analysis and Statistical Methods. The analysis of data was performed using RevMan 5.3 (Oxford, UK). The Mantel Haenszel method was utilized to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for binary data. When considered suitable, we performed subgroup analyses to explore the potential impact of patient attributes and control substances on the results. To explore potential publication bias, funnel plots of the data were visually inspected. Two-sided tests were used for all statistical analyses, with a significance threshold of $P < 0.05$.

2.6. Subgroup Analysis and Heterogeneity. Those included studies were categorized into two subgroups based on whether they focused on the prevention or treatment of AF. Within the prevention subgroup, the use of prophylactic propafenone was further divided into four subgroups based on the specific postoperative atrial arrhythmias being targeted: postoperative atrial arrhythmia, POAF, postoperative atrial flutter, and postoperative supraventricular tachyarrhythmia. The trials investigating the utilization of propafenone for treating AF to restore sinus rhythm were categorized into three subgroups according to various time intervals following administration: 20 minutes, 1 hour, and 24 hours. This categorization allowed for a more detailed analysis and examination of the effects of propafenone in various clinical scenarios related to both the prevention and treatment of AF.

3. Results

3.1. Search Results. Initially, 102 pertinent studies were identified through thorough searches across various databases, encompassing PubMed, Cochrane Library, Embase, Medline, CNKI, and Wan Fang. Additional records ($n = 10$) were also found through other sources, such as reference lists. Duplicate studies ($n = 12$) were removed using Endnote Software (Version X9, Thompson Reuters, CA). Based on the title and abstract screening, 79 studies were deemed irrelevant and subsequently excluded. An additional 11 studies were excluded after a thorough review of the full text. Ultimately, nine studies [12, 15–22] fulfilled the pre-established inclusion criteria and were incorporated into this meta-analysis (Figure 1).

3.2. Characteristics of Included Trials. Table 1 presents the main characteristics of the nine included studies, comprising a total of 1,014 patients, which investigated the effectiveness of propafenone in both preventing and treating AF during CS. In the intention to treat population, Mörike 2008 (2) was incorporated, while Mörike 2008 (1) consisted of the participants who successfully finished the final study. These randomized double-blind studies were published between 1987 and 2008 and enrolled adult patients undergoing CS. Out of the various studies conducted, four administered propafenone through oral means, four utilized intravenous injection, and one employed a combination of intravenous and oral administration. The research was carried out in

diverse countries, such as the USA, Canada, Germany, the UK, Iran, Belgium, and Italy. All the included studies focused on patients undergoing CABG or valve surgery. Specifically, three studies investigated the preventive effects of propafenone for POAF, while the remaining six studies assessed the treatment effects of propafenone for POAF. The patients included in this study were all adults.

3.3. Potential for Prejudice in the Studies That Were Included. Out of the nine RCTs, one study failed to disclose allocation concealment, leading to an unclear risk of bias. Furthermore, there was a study that did not have reported blinding of participants and personnel, which suggests an unclear risk of bias. A different study failed to mention the blinding of outcome evaluation and should be categorized as having an unclear risk of bias. Moreover, incomplete outcome data were not reported in two studies, and selective reporting was not reported in two studies, resulting in unclear risk of bias assessments (Figure 2). Among nine included trials, eight [12, 15–18, 20–22] attained Jadad scores ≥5, indicating high quality, while one trial [19] received a Jadad score of 4 (Table 2).

3.4. Preventive Effects on Postoperative Arrhythmia. The clinical outcomes of POAF were derived from two studies, which included three treatment groups consisting of propafenone and saline. A meta-analysis demonstrated that propafenone can significantly reduce the occurrence of POAF in adult patients undergoing CS (OR, 0.52; 95%CI: 0.30, 0.89; $P = 0.02$) with heterogeneity ($I^2 = 0\%$, $P = 0.41$). However, propafenone achieved no statistically significant influence in the postoperative atrial flutter, postoperative atrial arrhythmia, and postoperative supraventricular tachyarrhythmia (Figure 3).

3.5. Frequency of Transition from AF to Normal Sinus Rhythm. Six studies, including eleven treatments (propafenone, amiodarone, procainamide, ibutilide, and saline), contributed to the clinical outcome of 20 minutes, 1 hour, and 24 hours after administration in POAF patients. The meta-analysis revealed that propafenone significantly increased the occurrence of conversion from AF to normal sinus rhythm in 20 minutes after being given (OR, 5.39; 95% CI: 2.25, 12.91; $P = 0.0002$) with heterogeneity ($I^2 = 0\%$, $P = 0.46$), as well as within 1 hour after administration. Nevertheless, propafenone did not have a significant impact on the rate of conversion to sinus rhythm from AF in 24 hours after being administered (Figure 4).

3.6. Recurrence of AF. The study, which involved three trials with 245 patients and four comparisons, concluded that propafenone had no statistically significant effect on the recurrence of AF compared to the CG. Low heterogeneity was noted among the studies included (Figure 4).
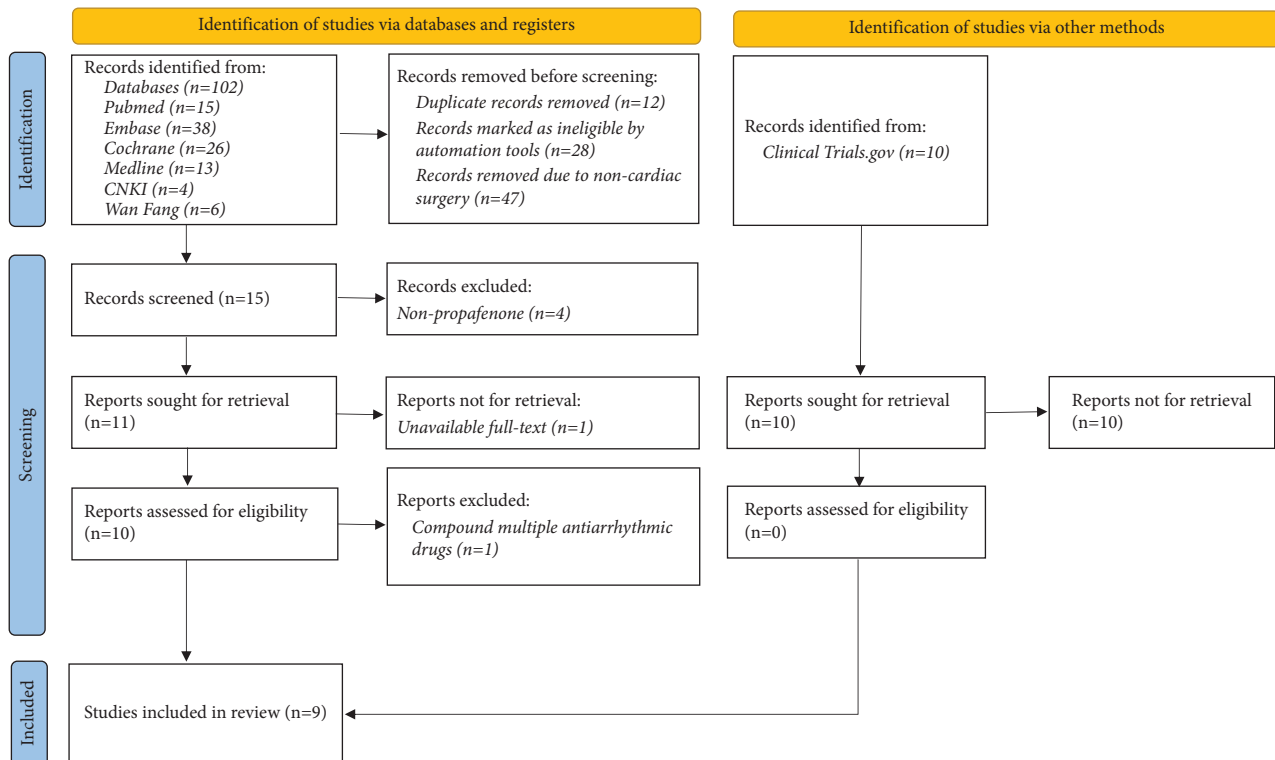
Figure 1: Flowchart.

3.7. Postoperative Adverse Events. Postoperative total adverse effects, postoperative hypotension, and postoperative bradycardia in the hospital were reported in six trials (eight comparisons, 661 patients), two trials (two comparisons, 146 patients), and three trials (four comparisons, 276 patients), respectively (Table 1). The meta-analysis demonstrated that propafenone achieved no statistically significant influence on postoperative total adverse effects with control. However, propafenone exhibited a significant decrease in the occurrence of postoperative hypotension. In contrast, PG showed similar postoperative bradycardia compared to CG (Figure 5).

3.8. Discontinuation due to Adverse Events. The adverse events observed in the studies included POAF, atrial flutter, supraventricular tachyarrhythmia, bradycardia, ventricular tachyarrhythmia, and atrioventricular block. The study, which included 483 patients and four comparisons, found that propafenone did not have a statistically significant effect on discontinuation due to adverse events compared to the CG. Moderate heterogeneity was noted among the included studies (Figure 5).

3.9. Sensitivity Testing and Publication Bias. The sensitivity analysis table indicated that different statistical models did not influence the results (Tables 3 and 4). Moreover, the exclusion of certain studies from outcome measures with high heterogeneity revealed no significant change in overall treatment effects (Table 5). However, it should be noted that there might be a small sample size effect or potential

publication bias (Figure 2). No significant publication bias was found in the assessment of funnel visualizations for the preventative effect on postoperative arrhythmia and the treatment effect on the occurrence of conversion from AF to sinus rhythm, as indicated by Egger's test ($P > 0.05$) (Figure 6).

4. Discussion

This meta-analysis represents the first evaluation of propafenone's efficacy and safety in preventing and terminating POAF among cardiac surgical patients, demonstrating that propafenone effectively prevents and terminates POAF.

POAF is a prevalent complication after CS, which independently predicts a range of adverse outcomes, primarily resulting in a 2–4 fold increased risk of stroke in patients, as well as secondary complications in other cardiovascular and cerebrovascular systems. Furthermore, POAF is associated with a rise in all-cause mortality at both 30 days and 6 months following CS in patients [27–34]. Twenty-five studies, involving 1,105 patients, explored propafenone's role in preventing AF. The proportion of patients maintaining sinus rhythm was 55.4% at 6 months and 56.8% at 12 months [35]. The findings of the present study align with this research, indicating that administering propafenone as a preventive measure can reduce the incidence of POAF in patients undergoing CS. In comparing PG and group saline, the prevalence of POAF was 24.3% vs. 42.2% [15]. Another study showed that in comparison of PG (450 mg/d, *po*), PG (475 mg/d, *po*), and group saline, the prevalence of POAF was 17.2%, 8.25%, 19.6% ($P = 0.02$) [16], respectively.

TABLE 1: Characteristics of included trials.

Trials	Sample size	Effects	Male/female		Protocols (postoperative)		Outcomes
			PG	CG	PG	CG	
Mörike et al. (1) [15]	82	Prevent	33/4	37/8	1 mg/kg iv, 1 hour 4 mg/kg, iv, 24 hour 450 mg, po, 6 days (n=37)	Saline (n=45)	①②③
Mörike et al. (2) [15]	150	Prevent	60/15	63/12	1 mg/kg, iv, 1 hour (n=75)	Saline (n=75)	④⑧
Kowey et al. [16]	293	Prevent	① 86/13; ② 76/21	80/17	① 450 mg/d, po (n=99) ② 675 mg/d, po (n=97)	Saline (n=97)	①⑧⑩
Merrick et al. [17]	207	Prevent	83/22	87/15	300 mg, bid, po, 7 days (n=105)	Atenolol, 50 mg, po, qd (n=102)	①②④⑦
Nemati and Astaneh [18]	122	Treatment	NM	NM	600 mg, po, 2 hours 150 mg, po, q8h, 24 hours 150 mg, po, 10 days after AF (n=67)	Amiodarone, 150 mg, iv, 1 hour; 600 mg, iv, 24 hours; 150 mg, iv, 10 days after AF (n=55)	⑤⑦⑨
Soucier et al. [19]	42	Treatment	16/4	① 8/2; ② 9/3	600 mg, po (n=20)	① ibutilide, 1-2 mg, iv (n=10); ② control (n=12)	④⑤⑧⑩
Geelen et al. [20]	62	Treatment	8/21	12/21	2 mg/kg 10 min (n=29)	Procainamide, 20 mg/kg, iv (n=33)	⑤⑥⑧
Larbuisson et al. [21]	40	Treatment	17/1	20/2	1-2 mg/kg, iv, 10 min 420 mg, iv, 24 hours (n=18)	Amiodarone, 2.5-5 mg/kg, iv, 10 min; 900 mg, 24 hours (n=22)	④⑤⑧
Di Biasi et al. [12]	84	Treatment	32/6	36/10	2 mg/kg, iv, 15 min 10 mg/kg, iv, 24 hours (n=38)	Amiodarone, 5 mg/kg, iv, 15 min; 15 mg/kg, iv, 24 hours (n=46)	⑤⑥⑧
Connolly et al. [22]	14	Treatment	14/0	10/0	2 mg/kg, iv (n=14)	Saline (n=10)	⑤⑥

AF: atrial fibrillation, PG: propafenone group, CG: control group, iv: intravenous injection, NM: not mentioned, and po: peros. Reported outcomes: ①: atrial fibrillation and atrial flutter; ②: supraventricular tachyarrhythmias (SVT); ③: atrial tachycardia; ④: adverse events; ⑤: the success rate of atrial fibrillation treatment; ⑥: percentage decrease in heart rate; ⑦: mortality; ⑧: postoperative adverse effects; ⑨: electrical cardioversion; ⑩: length of stay: ICU stay days and hospital stay.

(a)

(b)
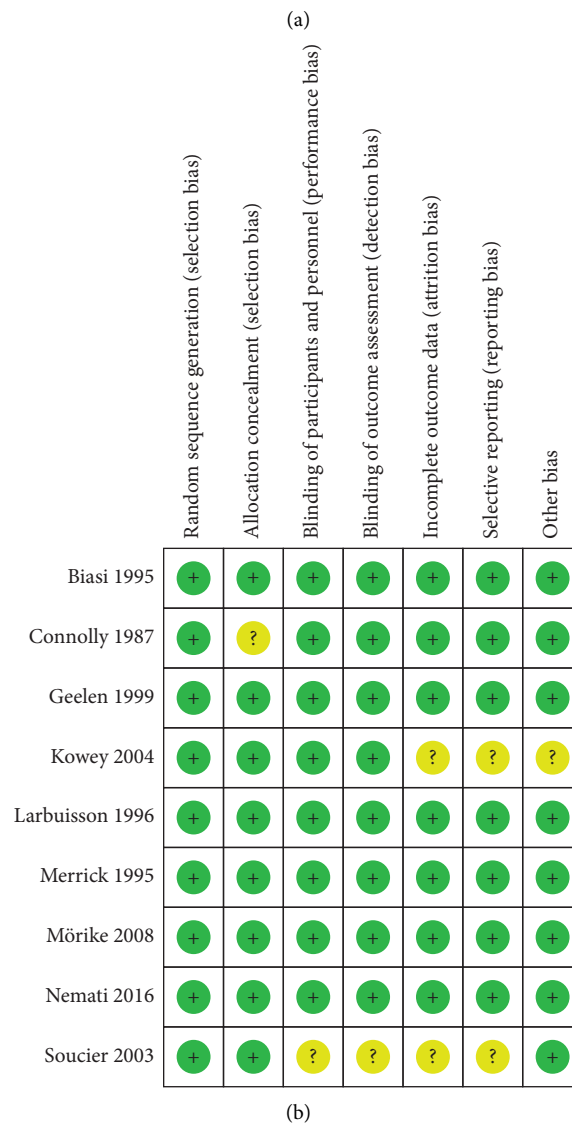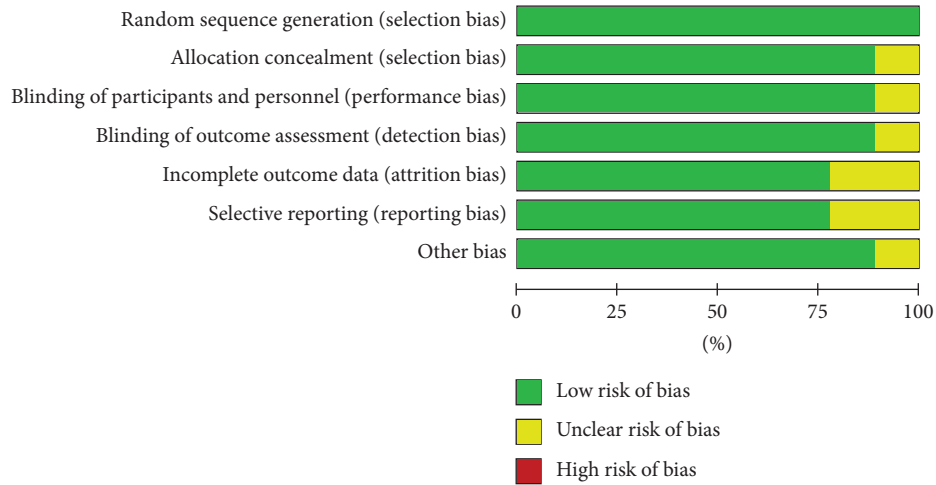
FIGURE 2: (a) Risk of bias graph for each included study. (b) Risk of bias summary for each included study.

TABLE 2: Modified Jadad score of included trials.

Study	Modified Jadad score				
	Randomization	Allocation	Blindness	Withdrawals	Total
Merrick et al. [17]	2	2	2	1	7
Mörike et al. [15]	2	1	2	1	6
Nemati and Astaneh [18]	2	2	2	1	7
Di Biasi et al. [12]	2	1	2	1	6
Geelen et al. [20]	2	2	2	0	6
Kowey et al. [16]	2	1	2	0	5
Larbuisson et al. [21]	2	2	2	1	7
Soucier et al. [19]	2	1	0	1	4
Connolly et al. [22]	2	1	2	1	6
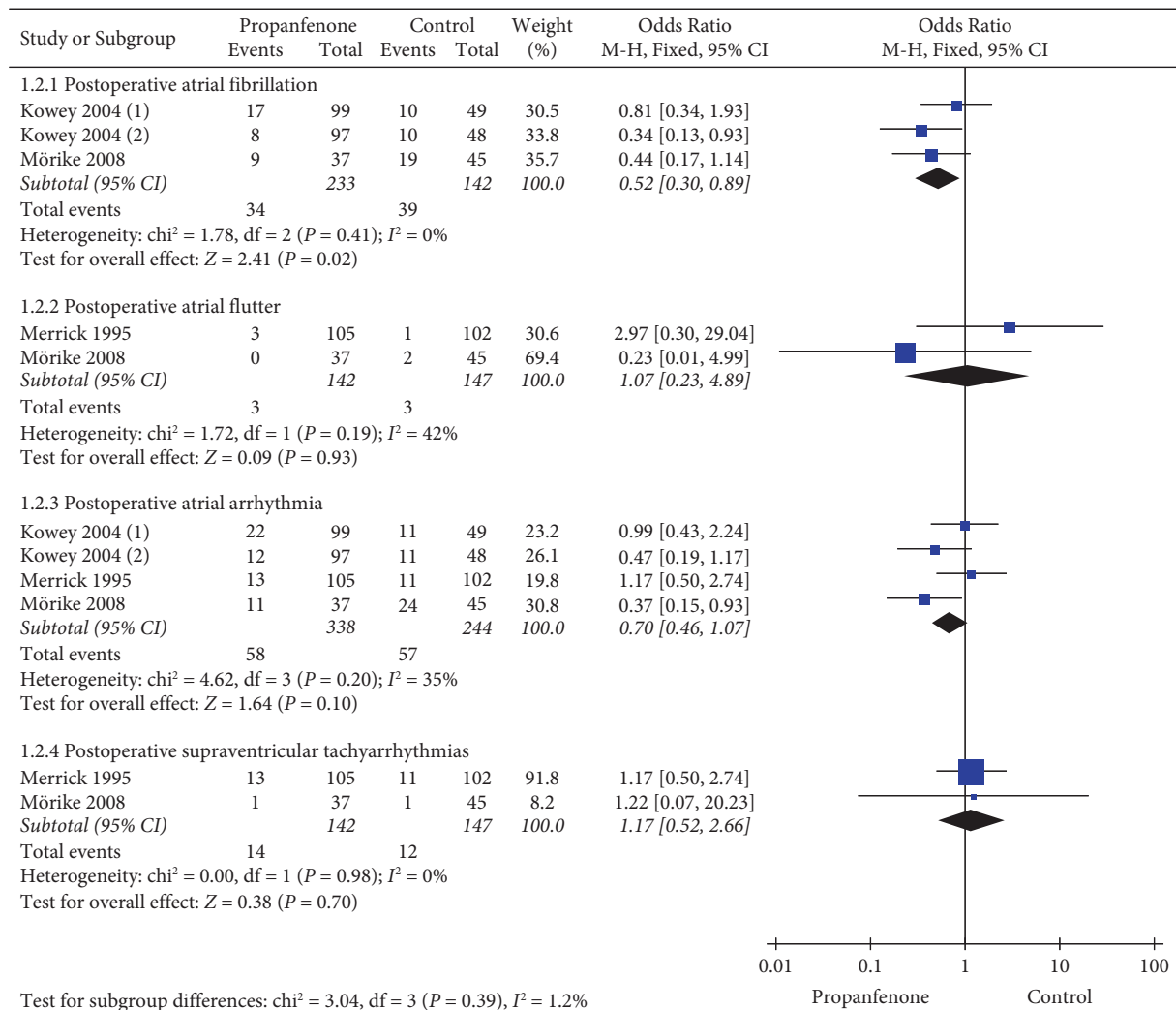
FIGURE 3: Forest plot comparing propafenone and control for postoperative arrhythmia.

Meanwhile, compared with the CG (atenolol), the PG had similar effectiveness in preventing POAF after CS [17]. However, the prophylactic propafenone administration did not significantly influence postoperative atrial arrhythmia, postoperative atrial flutter, and postoperative supraventricular tachyarrhythmia.

Several research studies have shown that the medications used to restore normal heart rhythm in cases of recent-onset AF consists of class I and class III drugs [36–39]. Several RCTs have confirmed the effectiveness and safety of propafenone for pharmacological converting recent-onset AF. In the meantime, the effective percentage varying between 58%

| Study or Subgroup | Propafenone | | Control | | Weight | Odds Ratio | Odds Ratio |
	Events	Total	Events	Total	(%)	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
3.1.1 Incidence of conversion from atrial fibrillation to sinus rhythm (20 min)							
Larbuisson 1996	5	18	3	22	42.4	2.44 [0.49, 12.01]	
Geelen 1999	17	29	6	33	50.5	6.38 [2.01, 20.19]	
Connolly 1987	6	14	0	10	7.1	16.06 [0.79, 327.50]	
Subtotal (95% CI)		61		65	100.0	5.39 [2.25, 12.91]	
Total events	28		9				
Heterogeneity: chi² = 1.54, df = 2 (P = 0.46); I² = 0%							
Test for overall effect: Z = 3.79 (P = 0.0002)							
3.1.2 Incidence of conversion from atrial fibrillation to sinus rhythm (1 h)							
Geelen 1999	22	29	20	33	42.3	2.04 [0.68, 6.14]	
Biasi 1995	17	38	9	46	42.2	3.33 [1.26, 8.77]	
Larbuisson 1996	7	18	3	22	15.5	4.03 [0.86, 18.86]	
Subtotal (95% CI)		85		101	100.0	2.89 [1.50, 5.57]	
Total events	46		32				
Heterogeneity: chi² = 0.64, df = 2 (P = 0.73); I² = 0%							
Test for overall effect: Z = 3.17 (P = 0.002)							
3.1.3 Incidence of conversion from atrial fibrillation to sinus rhythm (24 h)							
Soucier 2003 (1)	4	10	10	10	16.2	0.03 [0.00, 0.72]	
Soucier 2003 (2)	3	10	6	12	10.0	0.43 [0.07, 2.50]	
Biasi 1995	26	38	38	46	28.4	0.46 [0.16, 1.27]	
Larbuisson 1996	12	18	17	22	13.3	0.59 [0.15, 2.38]	
Nemati 2016	38	55	44	67	32.1	1.17 [0.55, 2.50]	
Subtotal (95% CI)		131		157	100.0	0.63 [0.38, 1.04]	
Total events	83		115				
Heterogeneity: chi² = 6.61, df = 4 (P = 0.16); I² = 40%							
Test for overall effect: Z = 1.80 (P = 0.07)							
3.1.4 Recurrence of atrial fibrillation							
Soucier 2003 (1)	4	9	9	10	17.9	0.09 [0.01, 1.03]	
Soucier 2003 (2)	3	8	7	12	13.2	0.43 [0.07, 2.68]	
Nemati 2016	17	55	23	67	54.1	0.86 [0.40, 1.83]	
Biasi 1995	5	38	5	46	14.8	1.24 [0.33, 4.66]	
Subtotal (95% CI)		110		135	100.0	0.72 [0.40, 1.29]	
Total events	29		44				
Heterogeneity: chi² = 3.96, df = 3 (P = 0.27); I² = 24%							
Test for overall effect: Z = 1.10 (P = 0.27)							

Test for subgroup differences: chi² = 27.53, df = 3 (P < 0.00001), I² = 89.1%

0.002   0.1   1   10   500
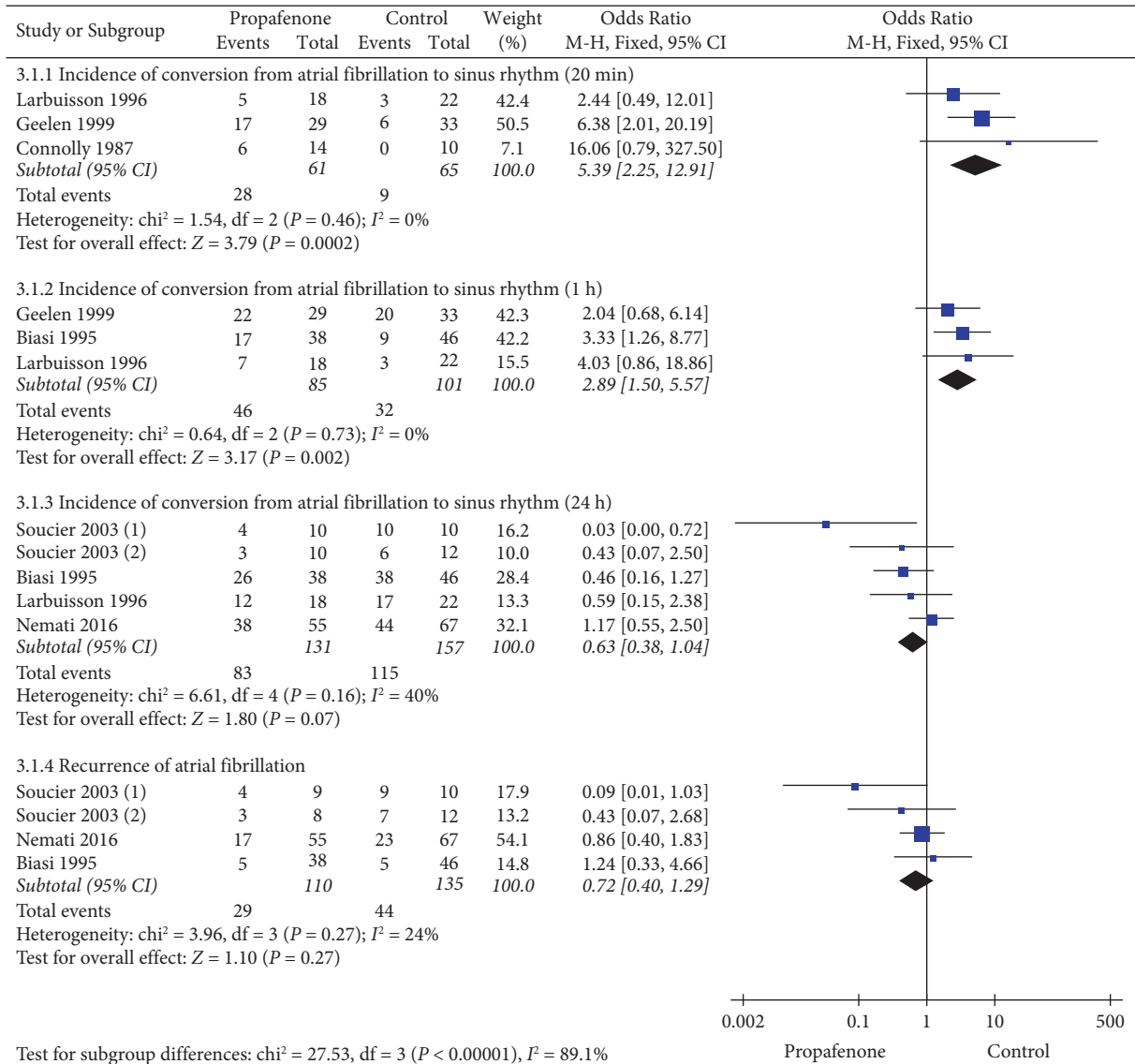Propafenone   Control

FIGURE 4: Forest plot comparing propafenone and control for incidence of conversion from atrial fibrillation to sinus rhythm.

and 83%, mainly impacted by the length of AF and the period of observation after medication, is given [40–46]. The findings of the present study align with the aforementioned studies, indicating that the administration of propafenone treatment can notably enhance the occurrence of conversion to sinus rhythm from AF within 20 min and 1 hour after administration. In comparison of PG and group procainamide [20]/amiodarone [12, 21]/saline [22], the occurrence of conversion to sinus rhythm from AF are 58.6% *vs.* 18.2% [20], 27.8% *vs.* 13.6% [21], and 42.9% *vs.* 0% [22] (*P* = 0.0002) in 20 min after administration, and 75.9% *vs.* 60.6% [20], 38.9% *vs.* 13.6% [21], and 44.7% *vs.* 19.6% [12] (*P* = 0.002) in 1 hour after administration. Interestingly, the administration of propafenone did not have a statistically significant effect on the rate of conversion to sinus rhythm from AF 24 hours after administration. The incidence rates were 69.1% *vs.* 65.7% [18] and 70%, 100% (ibutilide) *vs.* 50% (saline) [19], 66.7% *vs.* 77.3% [21], and 68.4% *vs.* 82.6% [12],

when comparing PG and group amiodarone [12, 18, 21]/ ibutilide [19]/saline [19]. Moreover, a meta-analysis demonstrated that propafenone achieved no statistically significant influence on the recurrence of AF with control. Given the potential for AF to convert spontaneously, the efficacy estimates of the placebo in this analysis are unsurprising. Danias et al. demonstrated that 68% of patients naturally transitioned to sinus rhythm at 72 hours after experiencing AF. It was found that the most accurate indicator of spontaneous conversion was within a 24-hour timeframe [47–52].

Nevertheless, the precise reasons and mechanisms behind the emergence of POAF are still uncertain, involving elements such as oxidative stress, stimulation of the sympathetic nervous system, and sudden inflammation. Furthermore, people who have a medical background of heart conditions might display anomalies in their structure, disorders in their ion channels, and changes in the atrium of

| Study or Subgroup | Propafenone | | Control | | Weight | Odds Ratio | Odds Ratio |
	Events	Total	Events	Total	(%)	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
4.1.1 Postoperative adverse events							
Biasi 1995	6	38	5	46	8.2	1.54 [0.43, 5.50]	
Geelen 1999	9	22	13	33	13.2	1.07 [0.35, 3.20]	
Kowey 2004 (1)	5	49	22	99	28.1	0.40 [0.14, 1.12]	
Kowey 2004 (2)	5	48	11	97	14.0	0.91 [0.30, 2.78]	
Larbuisson 1996	3	18	3	22	4.8	1.27 [0.22, 7.20]	
Mörike 2008	25	75	16	75	22.9	1.84 [0.89, 3.83]	
Soucier 2003 (1)	2	10	3	10	5.2	0.58 [0.07, 4.56]	
Soucier 2003 (2)	1	10	2	12	3.5	0.56 [0.04, 7.21]	
Subtotal (95% CI)		270		394	100.0	1.04 [0.70, 1.55]	
Total events	56		75				
Heterogeneity: chi^2 = 6.64, df = 7 (P = 0.47); I^2 = 0%							
Test for overall effect: Z = 0.19 (P = 0.85)							
4.1.2 Postoperative hypotension							
Biasi 1995	2	38	5	46	35.3	0.46 [0.08, 2.49]	
Geelen 1999	2	29	9	33	64.7	0.20 [0.04, 1.01]	
Subtotal (95% CI)		67		79	100.0	0.29 [0.09, 0.92]	
Total events	4		14				
Heterogeneity: chi^2 = 0.49, df = 1 (P = 0.49); I^2 = 0%							
Test for overall effect: Z = 2.09 (P = 0.04)							
4.1.3 Postoperative bradycardia							
Biasi 1995	2	38	4	46	35.8	0.58 [0.10, 3.37]	
Mörike 2008	7	75	2	75	18.9	3.76 [0.75, 18.72]	
Soucier 2003 (1)	1	10	3	10	28.2	0.26 [0.02, 3.06]	
Soucier 2003 (2)	1	10	2	12	17.1	0.56 [0.04, 7.21]	
Subtotal (95% CI)		133		143	100.0	1.09 [0.45, 2.62]	
Total events	11		11				
Heterogeneity: chi^2 = 4.33, df = 3 (P = 0.23); I^2 = 31%							
Test for overall effect: Z = 0.19 (P = 0.85)							
4.1.4 Discontinuation due to adverse events							
Kowey 2004 (1)	22	99	11	49	31.1	0.99 [0.43, 2.24]	
Kowey 2004 (2)	11	97	11	48	35.4	0.43 [0.17, 1.08]	
Larbuisson 1996	1	18	2	22	4.6	0.59 [0.05, 7.07]	
Mörike 2008	25	75	16	75	28.9	1.84 [0.89, 3.83]	
Subtotal (95% CI)		289		194	100.0	1.02 [0.65, 1.61]	
Total events	59		40				
Heterogeneity: chi^2 = 6.09, df = 3 (P = 0.11); I^2 = 51%							
Test for overall effect: Z = 0.08 (P = 0.93)							

Test for subgroup differences: chi^2 = 4.39, df = 3 (P = 0.22), I^2 = 31.7%
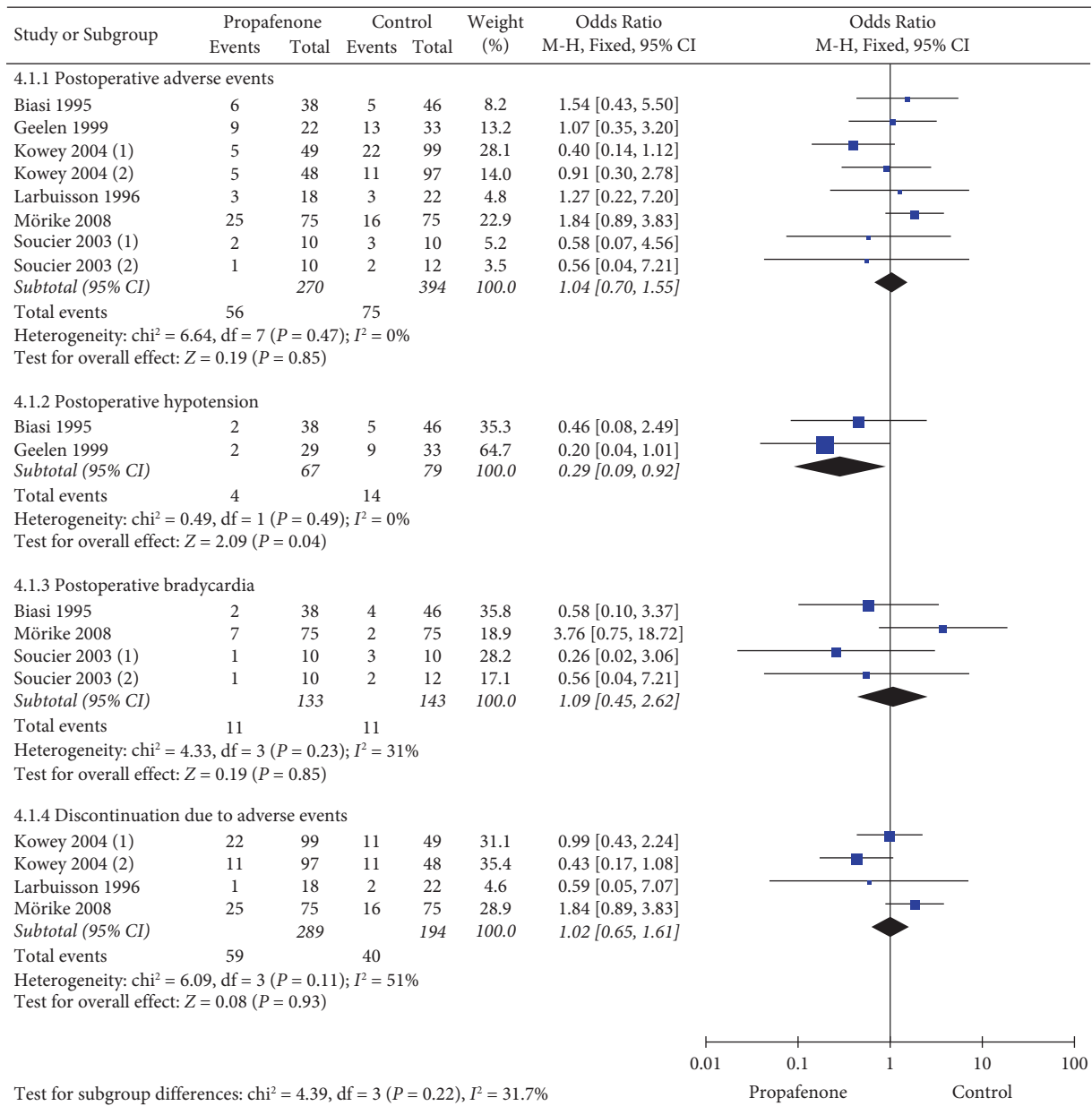
(Scale: 0.01 0.1 1 10 100; Propafenone — Control)

Figure 5: Forest plot comparing propafenone and control for postoperative adverse events.

their heart [53, 54]. The study results indicate that after the reperfusion of cardiac tissues in patients who undergo CABG, oxidative stress can cause an increase in the activity of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase in the corresponding atrial appendage tissue. This heightened oxidase activity has been identified as a crucial independent predictor for the onset of POAF [55].

In the present investigation, it was found that four tests were conducted verbally, four utilized intravenous injection, and one study employed a mixture of intravenous and oral administration. Clinical study findings suggest that intravenous injection has a faster onset effect, but ultimately, both can effectively suppress AF. The research conducted by Botto et al. [46] revealed that the intravenous treatment had much higher effectiveness than the oral loading treatment

within the first hour of observation (48% *vs.* 15%, P = 0.05). However, this superiority was not maintained over more extended observation periods of 4 and 8 hours. On the other hand, the oral treatment showed greater conversion rates, with a statistically significant distinction seen after 8 hours (71% *vs.* 50% at 4 h, P = NS; 78% *vs.* 53% at 8 h, P < 0.03).

Undeniably, propafenone also has some common clinical side effects, such as dizziness, palpitations, gastrointestinal discomfort, and so on [56]. Interestingly, the six studies included in our analysis found no noteworthy difference in postoperative adverse effects between the PG and the CG [12, 15, 16, 19–21]. These results align with those of a prior meta-analysis, which similarly indicated no noteworthy distinctions in side effects between the PG and other noncardiac treatment groups. However, our meta-analysis

Table 3: Influence of statistical model on estimated treatment effects of primary outcomes.

Outcomes	Effects	Heterogeneity		OR (95% CI)		Overall effect P	
		I^2	P	FEM	REM	FEM	REM
Postoperative arrhythmia (%)							
Atrial fibrillation	Prevent	0	0.41	0.52 (0.30, 0.89)	0.52 (0.30, 0.89)	0.02	0.02
Atrial flutter	Prevent	42	0.19	1.07 (0.23, 4.89)	1.03 (0.09, 12.20)	0.93	0.98
Atrial arrhythmia	Prevent	35	0.20	0.70 (0.46, 1.07)	0.69 (0.40, 1.18)	0.10	0.18
Supraventricular tachyarrhythmias	Prevent	0	0.98	1.17 (0.52, 2.66)	1.17 (0.52, 2.66)	0.70	0.70
Incidence of conversion from AF to sinus rhythm (%)							
20 min after administration	Treatment	0	0.46	5.39 (2.25, 12.91)	5.12 (2.10, 12.49)	0.0002	0.0003
1 hour after administration	Treatment	0	0.73	2.89 (1.50, 5.57)	2.89 (1.50, 5.59)	0.002	0.002
24 hours after administration	Treatment	40	0.16	0.63 (0.38, 1.04)	0.57 (0.27, 1.22)	0.07	0.15
Atrial fibrillation recurrence (%)	Treatment	24	0.27	0.72 (0.40, 1.29)	0.69 (0.32, 1.50)	0.27	0.35
Postoperative adverse events (%)							
Total adverse events	Prevent/treatment	0	0.47	1.04 (0.70, 1.55)	1.07 (0.71, 1.62)	0.85	0.75
Hypotension	Treatment	0	0.49	0.29 (0.09, 0.92)	0.29 (0.09, 0.95)	0.04	0.04
Bradycardia	Treatment	31	0.23	1.09 (0.45, 2.62)	0.93 (0.28, 3.13)	0.85	0.91
Discontinued due to adverse events (%)	Prevent/treatment	51	0.11	1.02 (0.65, 1.61)	0.93 (0.46, 1.90)	0.93	0.84

CI: confidence interval, FEM: fixed effects model, OR: odds ratio, and REM: random effects models.

TABLE 4: Sensitivity analyses of the influence of the individual study on the overall effects.

Outcomes	Excluded trials	Heterogeneity		OR		95% CI		Overall effect P	
		I^2 (%)	P	FEM	REM	FEM	REM	FEM	REM
Atrial fibrillation recurrence	Soucier et al. [19]	0	0.63	0.94	0.94	(0.49, 1.82)	(0.49, 1.82)	0.85	0.85
Postoperative bradycardia	Mörike et al. [15]	0	0.86	0.46	0.47	(0.13, 1.61)	(0.13, 1.63)	0.23	0.23

CI: confidence interval, FEM: fixed effects model, OR: odds ratio, and REM: random effects models.

TABLE 5: Sensitivity analyses of high heterogeneity outcomes.

Heterogeneity outcomes	Excluded trials	Heterogeneity		OR		95% CI		Overall effect P	
		I^2 (%)	P	FEM	REM	FEM	REM	FEM	REM
Discontinued due to adverse events	Mörike et al. [15]	0	0.42	0.68	0.68	(0.38, 1.23)	(0.37, 1.23)	0.20	0.20
Incidence of conversion from AF to sinus rhythm (24 h)	Soucier et al. [19] (1)	0	0.44	0.75	0.75	(0.44, 1.27)	(0.44, 1.27)	0.28	0.28

CI = confidence interval, FEM = fixed effects model, OR = odds ratio, and REM = random effects models.
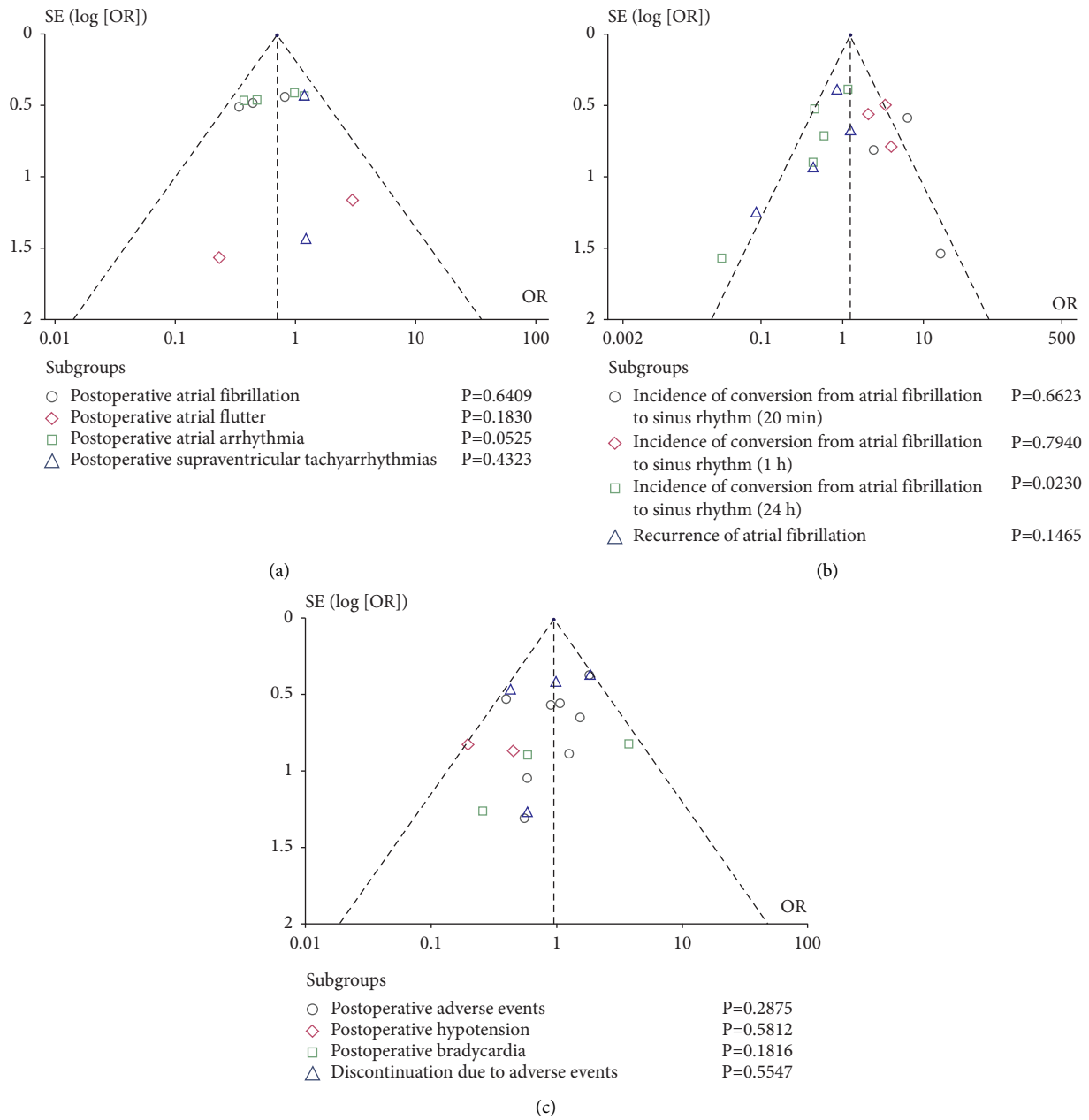
FIGURE 6: Funnel plot comparing propafenone and control for (a) postoperative arrhythmia, (b) frequency of transition from atrial fibrillation to normal sinus rhythm, and (c) postoperative adverse events.

revealed a notable decrease in the occurrence of postoperative hypotension with propafenone. It is crucial to highlight that the limited number of included studies may warrant caution in interpreting these results, despite low heterogeneity.

4.1. Limitations. Several limitations are present in our study. Firstly, the inclusion of only nine studies results in a relatively small sample size. Secondly, the study only included publications in the English language, which may introduce publication bias. Thirdly, all studies included in our analysis did not conduct extended-term monitoring of patients after

discharge. Future studies should include extended-term monitoring to provide more comprehensive insights. Finally, determining the optimal protocols and dosages of propafenone for perioperative use awaits exploration in future research. Additional properly conducted clinical trials are required to validate our discoveries and address these limitations.

5. Conclusions

The present study suggests that the postoperative administration of propafenone to adult CS patients is both safe and effective for preventing and treating POAF.

Data Availability

The original contributions presented in the study are included in the article/supplementary material; further inquiries can be directed to the corresponding author.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Jin-He Deng performed the formal analysis, investigated the data, and wrote the manuscript; Yun-Tai Yao performed project administration and supervised the work; Jing Li was involved in data curation and was responsible for software; Fan-Rong He was responsible for methodology.

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Supplementary Materials

The content of Supplementary Table 1 is the database search strategies. (*Supplementary Materials*)

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