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# Posterior pericardiotomy for the prevention of atrial fibrillation after coronary artery bypass grafting: A meta-analysis of randomized controlled trials



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#### ABSTRACT

*Background:* Posterior pericardiotomy (PP) has been shown to be effective in patients after cardiac surgery complicated by a reduced the incidence of atrial fibrillation (AF). However, the role of PP in patients following coronary artery bypass graft (CABG) remains ambiguous. We aimed to systematically evaluate the efficacy of PP in preventing postoperative AF in adult patients after CABG.

Methods: Studies were identified by searching multiple electronic databases (PubMed, Embase, and the Cochrane Library) through February, 2016, and by reviewing reference lists of obtained articles. The outcome measure was the incidence of postoperative AF. The meta-analysis was performed with the fixed-effect model or random-effect model according to heterogeneity.

Results: Ten randomized trials incorporating 1648 patients were included in this meta-analysis (822 in the PP group and 826 in the control group). The cumulative incidence of AF was 10.6% in the PP group and 24.9% in the control group. Meta-analysis with all studies using a random-effects model suggested that PP had significant effect on the prevention of postoperative AF ( $I^2$  55%; P < 0.00001; OR, 0.36; 95% CI, 0.23–0.56; RR, 0.45; 95% CI, 0.31–0.64). Sensitivity analyses by methodological quality and surgical technique yields similar results.

Conclusions: This meta-analysis indicates that PP shows beneficial efficacy in preventing postoperative AF in adult patients after CABG. This finding encourages the use of PP to prevent postoperative AF after CABG, but, more high quality randomized controlled trials are still warranted to confirm the safety.

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#### 1. Introduction

Postoperative atrial fibrillation (AF) is one of the most common complications encountered after cardiac surgery [1,2]. Its incidence varies from 20% to 40% after coronary artery bypass graft (CABG) [3,4]. Although most cases are self-limiting, postoperative AF may cause serious complications, increased cost and prolonged hospital stay [5]. The prevention of postoperative AF is thus clearly an important priority on hospital resources.

In past decades, concern has mounted regarding the premature incidence associated with postoperative AF, with growing interest in altering risk factors and antiarrhythmic drugs [6]. However, the effect of individual components or interactions between drugs is still limited, surgical procedure may explain some of this beneficial effect. Recent clinical studies have shown that posterior pericardiotomy (PP) is effective in preventing AF, and PP has been reported as a useful technique to reduce postoperative AF after CABG [7–10]. However, studies regarding

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PP have reported mixed and inconclusive results on its efficacy in preventing postoperative AF [11,12].

Furthermore, a meta-analysis also showed that PP seems to significantly reduce the incidence of postoperative AF after CABG [13]. But the data from studies included by previous meta-analysis were limited to February 2009. Nowadays, many more clinical studies were published from then on, which allow more detailed analysis of the effect of PP on postoperative AF after CABG [14–17]. However, these studies have a modest sample size and convey inconclusive results. To obtain a more comprehensive estimate of the effect of PP on preventing postoperative AF, we carried out a meta-analysis of randomized trials to systematically evaluate the efficacy of PP in preventing postoperative AF in adult patients after CABG.

#### 2. Materials and methods

#### 2.1. Search strategy

The search strategy was conducted according to the *Cochrane Handbook for Systematic Reviews* [18]. We performed a systematic search of PubMed, Embase, and the Cochrane Library (including Cochrane Central Register of Controlled Trials) through February, 2016. The following key

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words were used in our search strategies: "posterior pericardiotomy," "pericardial fenestration," "pericardial window," and "CABG," "coronary artery bypass graft," "cardiac surgery," "cardiothoracic surgery," "heart surgery," "cardiopulmonary bypass," "CPB," "CAB." We restricted the search to human studies. To maximize the sensitivity, no language restriction was used. In addition, we reviewed the references lists of obtained articles to identify additional relevant studies.

#### 2.2. Eligibility criteria and exclusion criteria

Studies were selected for the meta-analysis if they fulfilled the following entry criteria: (1) the study of adult patients ( $\geq$ 18 years of age) had a prospective, randomized design; (2) randomly assigned to receive PP or conventional treatment (no PP); (3) the enrolled patients undergoing CABG; and (4) study outcomes had to report on postoperative AF. Studies were excluded if the study was non-randomized designs, animal studies, existing preoperative AF, pediatric patients or age < 18 years old.

#### 2.3. Data abstraction

All data were independently abstracted in duplicate by two investigators (Z.Z, and J.Y.). Discrepancies were resolved by consensus. When necessary, the original authors were contacted for supplementary information. The following data were extracted from each study: first author's last name, publication year, type of surgery, number of participants, participants' age, intraoperative data, and study quality.

#### 2.4. Assessment of study quality and risk-of-bias

The validated Jadad 5 point scale was used to assess the quality of studies [19]. The quality was evaluated in the following three major components: randomization (0-2 points), blinding (0-2 points) and dropouts and withdrawals (0-1 points). One point was given when one quality criterion was met. A higher score represents better methodological quality. The full score was 5 points. Studies were graded as the high-quality if they met >3 awarded points [20]. The risk of bias has been assessed independently by two investigators (X.H., and Y.C.) according to the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0) [18]. Discrepancies were resolved by consensus. When necessary, the original authors were contacted. Trials that met following eligibility criteria have been assessed: (1) selection bias (random sequence generation and allocation concealment); (2) performance bias (blinding of participants and personnel); (3) detection bias (blinding of outcome assessment); (4) attrition bias (incomplete outcome data); (5) reporting bias (selective reporting); and (6) other bias.

#### 2.5. Statistical analysis

The statistical significant level for a two-tailed test for each primary hypothesis was 0.05. All of the statistical analyses were conducted with the Review Manager version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK) and Stata version 11 (Stata Corporation, College Station, TX, USA). The results were expressed as Mantel-Haenszel odds ratios (OR) and risk ratio (RR), with 95% confidence intervals (CI) (using a fixed-effect approach unless there was significant heterogeneity, in which case a random-effects statistical model was used) [21]. We tested heterogeneity between trials results using  $I^2$  and  $\chi^2$ test;  $l^2$  less than 50% was considered to have nonimportant heterogeneity [22]. If there was evidence of heterogeneity, we conducted sensitivity analyses based on the quality of the trial (high quality (>3) versus lower quality ( $\leq$ 3) and CABG technique. We performed the Egger's regression test to visualize a possible asymmetry [23,24]. On the other hand, when the limited number (below 10) of studies was included in each analysis, publication bias was not assessed [18].

#### 3. Results

#### 3.1. Literature search

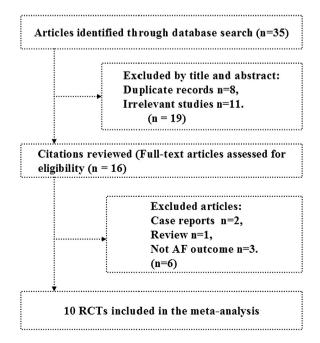
Fig. 1 displays the flow chart of literature research and selection. We initially identified 35 relevant citations. After excluding duplicates and studies that did not fulfill the inclusion criteria, 16 studies remained, and we further evaluated the full articles of potentially 16 publications. After full-text reviews, we excluded 6 studies for the following reasons: no AF outcomes (n = 3), case reports (n = 2) and review (n = 1). Finally, 10 studies met the inclusion criteria and were included in the meta-analysis [7–12,14–17].

#### 3.2. Trial characteristics

The characteristics of the studies and of their participants are presented in Table 1 and Supplemental Tables A and B. A total of 822 participants were randomly assigned to PP group and 826 to control group [7–12,14–17]. Among 10 studies, 4 were conducted primarily in the Turkey [8-10,12], 3 from Asian countries (including China, Iran and Thailand) [14–16], 2 studies were from European countries (United Kingdom) [7,11] and 1 from an African country (Egypt) [17]. The number of participants ranged from 20 in the study by Kongmalai et al. [15] to 458 in the study by Zhao et al. [14]. All studies in this meta-analysis enrolled patients undergoing CABG only. The definition and monitoring of postoperative AF varied across studies, in most of the studies, the electrocardiographic (ECG) was monitored during the in-hospital stay. Continuous ECG monitoring was performed during the first 2 to 3 postoperative days and then daily or as required (Supplemental Table B). The quality of the included studies was assessed by the Jadad score, overall quality scores ranged for 3 to 4, and the median score was 4.

#### 3.3. PP and postoperative AF

Overall, 1648 participants were included in this analysis (822 in the PP group and 826 in the control group). The cumulative incidence of AF was 10.6% in the PP group and 24.9% in the control group. Meta-analysis with all studies using a random-effects model suggested that PP had significant effect on the prevention of postoperative AF ( $I^2$  55%;



**Fig. 1.** Process of literature search and study selection. AF: atrial fibrillation; RCTs: randomized controlled trials.

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