Review Article

Colchicine for prevention of postoperative atrial fibrillation following cardiac surgery: a meta-analysis of randomized controlled trials

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Abstract: The most common complication following cardiac surgery, postoperative atrial fibrillation (POAF) increases hospital costs and morbidity. Therefore, POAF prevention is of great importance for clinical management. It has been postulated that inflammation is implicated in the development of POAF [4]. Therefore, use of an agent with anti-inflammatory properties may be effective in preventing POAF [5]. Colchicine, an ancient and natural anti-inflammatory drug, in patients with gout, has unique antiarrhythmic properties, arousing interest regarding its use in POAF prevention [6].

Recently, several studies regarding effects of colchicine in POAF prevention have been published [7-10]. However, the role of colchicine in POAF prevention following cardiac surgery, especially CABG, remains unknown. This study, therefore, undertook a meta-analysis of published studies, evaluating the effects of colchicine in POAF prevention following cardiac surgery, to ascertain the significance of colchicine-related adverse events.

Materials and methods

Search strategy

Published randomized controlled trials (RCTs), reporting the effects of colchicine in POAF prevention, were searched up to the end of February 2017 in Cochrane library, EMBASE, and PubMed databases. The following keywords were used in the search: “Coronary Artery Bypass”, “Coronary Artery Bypass Surgery”, “Aortocoronary Bypass”, “Coronary Artery Bypass Grafting”, “CABG”, “coronary artery bypass gra-
Eligibility criteria and exclusion criteria

Studies were selected for meta-analysis if they fulfilled the following entry criteria [11]: (1) Participants: patients after heart surgery; (2) Intervention: colchicine (no matter what regimen applied); (3) Control: control (placebo or no colchicine); (4) Outcome: incidence of POAF; and (5) Study design: randomized design. No language restrictions were applied.

Data extraction and outcome measures

All data were independently abstracted, in duplicate, by two investigators (Z.L and Z.Y.J). Discrepancies were resolved by consensus. When necessary, original authors were contacted for supplementary information. The following data were extracted from each study: first author’s last name, number of patients, country, design, colchicine dose, type of surgery, definition of AF to meet endpoint, method of AF detection, follow up, cohort mean age, mean ejection fraction, gender, diabetes, hypertension, chronic obstructive pulmonary disease (COPD), current smoker, previous history of AF, prior congestive heart failure (CHF), previous cardiac surgery, CABG surgery, valvular surgery, and aortic surgery. Extracted data were entered into a standardized Excel file.

Risk of bias assessment

Risk of bias was evaluated on the basis of Cochrane Risk of Bias Methods [12], by two authors (Y.C.H. and L.M.Y.), and assigned a value of ‘high’, ‘low’, or ‘unclear’ based on the following: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting.

Grading quality of evidence

The GRADE system was used to assess quality of evidence. Evidence from cohort studies began with a grade of “Low”. The quality of evi-
Table 1. Characteristics of included studies

<table>
<thead>
<tr>
<th>First author</th>
<th>N</th>
<th>Country</th>
<th>Design</th>
<th>Colchicine dose</th>
<th>Type of Surgery</th>
<th>Definition of AF to Meet Endpoint</th>
<th>Method of AF detection</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tabbalat, 2016</td>
<td>360</td>
<td>Jordan</td>
<td>MC, OL</td>
<td>2 mg 12-24 hours before surgery, 1 mg day of surgery, and 0.5 mg bid from 1 day postoperative until discharge and 0.25 mg bid if &lt;70 kg or intolerant to highest dose</td>
<td>Cardiac surgery</td>
<td>AF lasting more than 5 min</td>
<td>ECG monitor</td>
<td>2 months</td>
</tr>
<tr>
<td>Imazio, 2014</td>
<td>360</td>
<td>Italy</td>
<td>MC, DB</td>
<td>Colchicine: 0.5 mg bid for 1 month if ≥70 kg and 0.25 mg twice daily if &lt;70 kg or intolerant to highest dose</td>
<td>Cardiac surgery</td>
<td>AF lasting more than 30 s</td>
<td>cECG monitor</td>
<td>3 months</td>
</tr>
<tr>
<td>Sarzaeem, 2014</td>
<td>216</td>
<td>Iran</td>
<td>DB</td>
<td>1 mg night before and on day of surgery, 0.5 mg bid for 5 days postoperative</td>
<td>CABG only</td>
<td>AF lasting at least 10 min</td>
<td>ECG</td>
<td>6 months</td>
</tr>
<tr>
<td>Imazio, 2011</td>
<td>336</td>
<td>Italy</td>
<td>MC, DB</td>
<td>1.0 mg bid on first day, then maintenance dose of 0.5 mg bid for 1 month if ≥70 kg and 0.25 mg bid if &lt;70 kg or intolerant to highest dose</td>
<td>Cardiac surgery</td>
<td>AF lasting more than 5 min</td>
<td>cECG monitor</td>
<td>12 months</td>
</tr>
</tbody>
</table>

MC = multicenter; OL = open-label; AF = atrial fibrillation; ECG = electrocardiography; bid. = Bis in die; DB = double-blind; cECG = continuous electrocardiography; CABG = coronary artery bypass grafting.

Table 2. Baseline clinical characteristics of selected studies

<table>
<thead>
<tr>
<th></th>
<th>Colchicine (n = 636)</th>
<th>Placebo (n = 636)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs</td>
<td>64.4±12.1 (n = 457)</td>
<td>65.7±10.6 (n = 455)</td>
<td>0.10</td>
</tr>
<tr>
<td>LVEF</td>
<td>53.3±10.6 (n = 636)</td>
<td>53.3±10.2 (n = 636)</td>
<td>0.88</td>
</tr>
<tr>
<td>Female</td>
<td>167/636 (26.26%)</td>
<td>187/636 (29.40%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>207/636 (32.55%)</td>
<td>209/636 (32.86%)</td>
<td>0.90</td>
</tr>
<tr>
<td>Hypertension</td>
<td>412/636 (64.78%)</td>
<td>409/636 (64.31%)</td>
<td>0.86</td>
</tr>
<tr>
<td>COPD</td>
<td>28/636 (4.40%)</td>
<td>32/636 (5.03%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Current smoker</td>
<td>120/467 (25.70%)</td>
<td>125/469 (26.65%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Previous history of AF</td>
<td>26/528 (4.92%)</td>
<td>26/528 (4.92%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Prior CHF</td>
<td>27/348 (7.76%)</td>
<td>37/348 (10.63%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>18/349 (5.16%)</td>
<td>20/347 (5.76%)</td>
<td>0.72</td>
</tr>
<tr>
<td>CABG surgery</td>
<td>392/636 (61.64%)</td>
<td>363/636 (57.08%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Valvular surgery</td>
<td>128/528 (24.24%)</td>
<td>147/528 (27.84%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Aortic surgery</td>
<td>17/528 (3.22%)</td>
<td>20/528 (3.79%)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

LVEF, left ventricular ejection fraction; COPD, chronic obstructive pulmonary disease; AF, atrial fibrillation; CHF, congestive heart failure; CABG, Coronary artery bypass grafting.

Inspection was upgraded for large magnitude of effect, plausible residual confounding that would not reduce the effect size, and a dose response gradient. It was downgraded for inconsistency, indirectness, imprecision, and publication bias. Finally, quality of evidence was categorized as high, moderate, low, and very low [13].

Statistical analysis

All statistical analyses were conducted with Review Manager Version 5.3, Stata Version 12 and GRADE system. A two-tailed P-value <0.05 was considered statistically significant. Results are expressed as odds ratios (OR) or mean difference (MD) 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). Heterogeneity across studies was tested by using I² statistic. I² statistic of 25% to 50%, 50% to 75%, and 75% to 100% were, respectively, considered to have low heterogeneity, moderate heterogeneity, and high degree of heterogeneity. An I² value greater than 50% indicates significant heterogeneity. A fixed-effects model was used (I²<50%) and random-effects model was used in the case of significant heterogeneity (I²>50%) [14]. Potential publication bias was assessed using Begg's funnel plot test [15].

Results

Study identification and selection

The initial search yielded 31 relevant publications, of which 24 were excluded for various reasons (11 duplications, or 13 reviews) based on titles and abstracts. The remaining seven were then retrieved for full text review. Three of them were also excluded because they were irrelevant to the current analysis. Thus, four studies were included in the final analysis [7-10]. A flow chart of studies included in the meta-analysis is shown in Figure 1.
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Study characteristics

Characteristics of included studies are shown in Table 1 and baseline clinical characteristics of selected studies are presented in Table 2. Of the 4 included trials, two were done in Italy [9, 10], one in Jordan [7], and one in Iran [8]. These studies were published between 2011 and 2016. Sample sizes of these studies ranged from 216 to 360 (total 1272). One study in this meta-analysis enrolled patients undergoing CABG only [8]. The remaining three studies included patients undergoing CABG and/or other cardiac surgery [7, 9, 10]. Different regimens of colchicine were administered orally. Timing of initiation for colchicine was 1/2-3 days pre-operation or 3 day post-operation and continued for 5 days or 1 month, or until discharge [7-10] (Table 1). Three studies administered colchicine during the perioperative period [7-9], while one study administered colchicine after surgery [10]. There were no statistically significant differences in baseline clinical characteristics of selected studies (Table 2).

Methodological bias of included studies

Details concerning risks of biases of the included studies, according to the Cochrane assessment tool, are listed in Figure 2. Both of the included comparisons were RCTs, three in a double-blind design [8-10] and one in an open-label design [7]. Overall quality was good, although only one trial [10] was at low risk of bias for all quality criteria. Sarzaee et al. described methods of randomized and double blind but had no sufficient information to determine blinding of outcome assessment and selective reporting [8], leading to unclear risk of bias for the two items. Imazio et al. described methods of randomized and double blind but had no sufficient information to determine blinding of outcome assessment [9], leading to unclear risk of bias for these items. Tabbalat et al. [7] described methods of randomized but performed an open-label study, leading to high risk of bias for items such as allocation concealment, blinding of participants and personnel, and blinding of outcome assessment. They also had no sufficient information to determine selective reporting, leading to unclear risk of bias for the two items.

Effect of colchicine on incidence of POAF

Overall, four studies, including 1272 patients, were included in this analysis (636 in the colchicine group and 636 in the control group). Meta-analysis of the two studies, using a fixed effects model, suggested that colchicine significantly reduced incidence of POAF in patients undergoing cardiac surgery (OR = 0.6, 95% CI =
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0.45 - 0.79; P<0.001; Figure 3A), especially Coronary Artery Bypass Grafting (OR = 0.5, 95% CI = 0.31 - 0.80; P<0.01; Figure 3C), compared with controls. There were no heterogeneities among the studies ($I^2 = 0\%$ and 0%, heterogeneity $p = 0.48$ and 0.33; Figure 3A and 3C). Although one of the experimental studies was an open-label study [7], when we removed the study, heterogeneity was not reduced but increased ($I^2 = 15\%$, Figure 3B). Thus, the open-label study did not have any effect on the accuracy of results indicating that colchicine significantly reduced incidence of POAF in patients undergoing cardiac surgery.

Effect of colchicine on length of hospitalization (LOH)

Four trials [7-10] reported the effect of colchicine on POAF but only 2 trials [8, 10] provided available data in LOH (expressed as mean ± standard deviation), with a total of 288 patients. Pooled analysis, using a fixed effects model, showed that colchicine significantly reduced LOH after surgery (MD = -1.35, 95% CI = -1.76 - -0.94; P<0.001; Figure 4), with no statistical heterogeneity between the trials ($I^2 = 34\%$, heterogeneity $P = 0.22$).

Gastrointestinal side effects and treatment discontinuation

Pooled analysis revealed that colchicine use was associated with increased incidence of gastrointestinal side effects (anorexia, diarrhea, nausea, vomiting, and abdominal pain), compared to placebo (OR = 3.44, 95% CI = 2.27 - 5.22; P<0.001, $I^2 = 42\%$) (Figure 5). However, the rate of treatment discontinuation was not significantly different between colchicine group and placebo (OR = 2.44; 95% CI = 0.76 - 7.8; $P = 0.13$, $I^2 = 77\%$) (Figure 6A). Due to significant heterogeneity of the studies ($I^2 = 77\%$), sensitivity analyses were performed to ascertain the reliability and stability of results. In sensitivity analyses, 1 study [7], whose research design was open-label, was removed and results were dramatically changed (OR =

Figure 3. Forest plots from meta-analyses for the effects of colchicine on incidence of POAF undergoing cardiac surgery (A), the effects of colchicine on incidence of POAF undergoing cardiac surgery after removing 1 study in open-label study (B) and CABG (C). The effect size of each study is proportional to the statistical weight. A diamond indicates the overall summary estimate for the analysis; the width of the diamond represents the 95% CI. POAF, postoperative atrial fibrillation; CI, confidence interval.
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<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Mean SD</td>
<td></td>
<td>IV Fixed, 95% CI</td>
</tr>
<tr>
<td>Mahmoodreza Sarzeem 2014</td>
<td>6.6 1.5 108</td>
<td>8.1 2 168</td>
<td>75.5% -1.50[1.87, 1.03]</td>
<td></td>
</tr>
<tr>
<td>Massimo Imazio 2011</td>
<td>9.4 3.7 180</td>
<td>10.3 4.3 180</td>
<td>24.5% -0.90[1.73, 0.07]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 288
Heterogeneity: Chi² = 1.52, df = 1 (P = 0.22), I² = 34%
Test for overall effect: Z = 6.47 (P = 0.000001)

Figure 4. Forest plots from meta-analyses for the effects of colchicine on length of hospitalization. The effect size of each study is proportional to the statistical weight. A diamond indicates the overall summary estimate for the analysis; the width of the diamond represents the 95% CI. CI, confidence interval.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td></td>
</tr>
<tr>
<td>Massimo Imazio 2011</td>
<td>16 169</td>
<td>7 167</td>
<td>2.39[0.96, 5.97]</td>
</tr>
<tr>
<td>Massimo Imazio 2014</td>
<td>26 100</td>
<td>12 160</td>
<td>2.36[1.15, 4.85]</td>
</tr>
<tr>
<td>Ramzi A. Tabbaa 2016</td>
<td>55 179</td>
<td>14 181</td>
<td>5.28[2.81, 9.94]</td>
</tr>
</tbody>
</table>

Total (95% CI): 528
Heterogeneity: Chi² = 3.45, df = 2 (P = 0.18), I² = 42%
Test for overall effect: Z = 5.82 (P = 0.000001)

Figure 5. Forest plots from meta-analyses for the effects of colchicine on gastrointestinal side effects. The effect size of each study is proportional to the statistical weight. A diamond indicates the overall summary estimate for the analysis; the width of the diamond represents the 95% CI. CI, confidence interval.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td></td>
</tr>
<tr>
<td>Massimo Imazio 2011</td>
<td>20 169</td>
<td>11 167</td>
<td>1.90[0.88, 4.11]</td>
</tr>
<tr>
<td>Massimo Imazio 2014</td>
<td>39 180</td>
<td>32 180</td>
<td>1.28[0.76, 2.15]</td>
</tr>
<tr>
<td>Ramzi A. Tabbaa 2016</td>
<td>23 179</td>
<td>0 181</td>
<td>54.51[3.28, 994.73]</td>
</tr>
</tbody>
</table>

Total (95% CI): 528
Heterogeneity: Tau² = 0.70, Chi² = 6.72, df = 2 (P = 0.01), I² = 77%
Test for overall effect: Z = 1.50 (P = 0.13)

Figure 6. Forest plots from meta-analyses for the effects of colchicine on treatment discontinuation (A) and the effects of colchicine on treatment discontinuation after removing 1 study in open-label study (B). The effect size of each study is proportional to the statistical weight. A diamond indicates the overall summary estimate for the analysis; the width of the diamond represents the 95% CI. CI, confidence interval.

1.45; 95% CI = 0.95 - 2.24; P = 0.09, I² = 0%  
(Figure 6B).

Publication bias

Begg’s funnel plot of the included studies did not suggest any significant publication bias regarding the effects of ranolazine on incidence of AF (Begg’s test p = 0.145, Figure 7).

Quality of evidence

Following the GRADE system, evidence quality was assessed by reviewing whether the studies had limitations or flaws. The results of the four studies were not completely consistent, downgrading the quality of evidence for this outcome. Two studies reported that colchicine had no significant protective effects on POAF [7, 9].
but the other two reported that colchicine did have a preventive effect on POAF [8, 10]. It was a moderate type of evidence that colchicine had a preventive effect on POAF (Table 3).

Discussion

This study, by pooling results of available randomized controlled trials, found that colchicine could significantly reduce incidence of POAF following cardiac surgery, especially CABG, and shorten LOH, compared with controls. Although colchicine therapy has been associated with increased incidence of gastrointestinal side effects, it was not increased to the point of treatment discontinuation. Therefore, colchicine may prove beneficial for POAF prevention following cardiac surgery.

It has been postulated that inflammatory processes triggered by cardiac surgery have been implicated in the development of POAF [4]. Therefore, use of an agent with anti-inflammatory properties may be effective in preventing POAF [5]. Colchicine is an ancient and natural anti-inflammatory drug [6]. Recently, several studies, regarding effects of colchicine in POAF prevention, have been published [7-10]. Some studies have shown that colchicine can prevent POAF. In 2011, Imazio et al. found that a significant reduction in incidence of POAF was noted in patients treated with 1 mg colchicine, twice daily (12.0% vs. 22.0%, p<0.05), in 336 patients [10]. In 2014, Sarzaeem et al. reported their findings regarding 216 patients treated with colchicine vs. placebo; POAF was significantly reduced in the colchicine group (14.8% vs. 30.6%, p<0.01) [8]. One other study has shown that colchicine cannot effectively prevent POAF. In 2014, Imazio et al. evaluated the efficacy of colchicine in preventing AF, after cardiac surgery, in 360 patients [9]. Their results, however, indicated that colchicine has no significant protective effect on POAF, inconsistent with previous results. In 2016, Tabbalat et al. further assessed the effects of colchicine therapy for POAF prevention in 360 patients. POAF occurred in 14.5% of patients on colchicine (p = 0.14), compared with 20.5% of patients with no colchicine [7]. Colchicine failed to significantly reduce incidence of POAF. Therefore, the role of colchicine in POAF prevention, following cardiac surgery, especially CABG, remains unknown.

This study, therefore, performed meta-analysis of published studies to assess the efficacy of colchicine in POAF prevention for patients after heart surgery. The results of this meta-analysis suggest that colchicine administration is effective and safe for POAF prevention, following cardiac surgery, especially CABG. Interestingly, Wang’s [16] findings were not consistent with our findings, as they found that colchicine therapy was not associated with a significant protective effect on POAF. It is believed that the reasons for this are multifaceted and are mainly attributable to the selection of studies: First, the studies they included were missing Sarzaeem’s [8] findings in 2014. Second, the two included articles [17, 18] were not direct studies about the effects of colchicine on prevention of AF, thus, there was no inaccurate record of occurrence of AF. Third, the heterogeneity of their research was high (I^2 = 47.3%), whereas this present study does not show heterogeneity (I^2 = 0%). It is worth mentioning that...
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**Table 3. Summary of findings table using GRADE methodology for colchicine on prevention of POAF**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumed risk</td>
<td>Corresponding risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>Incidence of postoperative atrial fibrillation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effects of colchicine in preventing postoperative atrial fibrillation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>204 per 1000</td>
<td>118 per 1000 (89 to 154)</td>
<td>OR 0.52 (0.38 to 0.71)</td>
<td>1248 (4 studies)</td>
<td>⊕ ⊕ ⊕</td>
</tr>
<tr>
<td></td>
<td>207 per 1000</td>
<td>120 per 1000 (90 to 156)</td>
<td></td>
<td></td>
<td>⊝</td>
</tr>
</tbody>
</table>

*The basis for the assumed risk (e.g., the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval; OR: Odds ratio; GRADE Working Group grades of evidence. High quality: Further research is very unlikely to change our confidence in the estimate of effect. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate. †The results are inconsistent.
the findings of this current study were also confirmed by Lee [5], Kreidieh [19], and Trivedi [20]. However, this present research is slightly different from the three studies mentioned above. Not only does this study find colchicine playing a preventive role in POAF, following cardiac surgery, but also in POAF following CABG. Similarly, due to an increase in the number of selected studies, none of the above studies showed heterogeneity. Although Trivedi’s findings also showed no statistically significant heterogeneity [20], only one of the included three studies regarded cardiac surgery [10] and the remaining two concerned radiofrequency ablation [21, 22]. This was not enough to show that colchicine has a preventive effect on POAF following cardiac surgery.

Although POAF may be transient, it can increase hospital stays, thus, increasing health-care costs [23]. This study’s results found that patients receiving colchicine had shorter overall hospital stays. Therefore, colchicine can not only prevent POAF but also reduce patient health-care costs.

A statistically higher incidence of gastrointestinal side effects (anorexia, diarrhea, nausea, vomiting, and abdominal pain) in the colchicine group has attracted a high degree of attention. Fortunately, rates of treatment discontinuation have shown no significant statistical differences in the colchicine group. These findings are similar to another meta-analysis performed on colchicine for POAF [5]. Colchicine is currently in Class IIb recommendations for reduction of POAF [24, 25]. One strategy to reduce in gastrointestinal side effects may be to optimize dosage and timing of colchicine therapy, avoiding pre-operative administration. Another strategy is to choose the right patients, especially those at higher risk of POAF, such as those with heart failure, advanced age, and COPD [26] instead of routine administration to all patients undergoing cardiac surgery. Further studies may be required in determining the optimal treatment protocol to reduce incidence of gastrointestinal intolerance, so that patients may benefit from adjunctive prophylaxis with colchicine.

Several potential limitations of this meta-analysis merit consideration. First, overestimation of the treatment effect is more likely in smaller studies compared with larger samples. Second, these studies lacked homogeneity regarding the dose of colchicine. This may lead to potential underestimation and/or overestimation of the true incidence of POAF. Third, it was possible that missing and unpublished data may have led to bias in effect size.

In conclusion, despite various limitations, this present study is clinically valuable because it reveals that colchicine leads to lower incidence of POAF, following cardiac surgery, especially CABG. Additional large-scale, multicenter, randomized controlled parallel trials are necessary to confirm these positive results.

Acknowledgements

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Disclosure of conflict of interest

None.

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