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Colchicine for Prevention of Post-Operative Atrial Fibrillation

A Meta-Analysis

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ABSTRACT

OBJECTIVES This study sought to investigate the efficacy and safety of colchicine for prevention of post-operative atrial fibrillation.

BACKGROUND Proinflammatory processes induced during cardiac surgery may contribute toward post-operative atrial fibrillation (AF). Colchicine is a potent anti-inflammatory agent, which may have a role in post-operative AF prevention.

METHODS We searched PubMed, EMBASE, Web of Science, CINAHL, ClinicalTrials.gov, and the Cochrane Library databases for randomized controlled trials (RCT) comparing colchicine versus placebo for prevention of post-operative AF. The main outcome measure of interest was the development of AF within 12 months after cardiac surgery. The overall risk ratio (RR) for the development of post-operative AF was computed using a random-effects model.

RESULTS Data analyzed from 3 randomized studies with a total of 912 patients, where 457 patients received colchicine and 455 patients received placebo, showed that perioperative colchicine therapy was associated with a reduced incidence of post-operative AF (RR: 0.65; 95% confidence interval [CI]: 0.46 to 0.91; $p < 0.01$). Although colchicine therapy was associated with increased incidence of gastrointestinal intolerance (RR: 2.20; 95% CI: 1.31 to 3.70; $p = 0.003$), it was not associated with early treatment discontinuation (RR: 1.37; 95% CI: 0.95 to 1.96; $p = 0.09$).

CONCLUSIONS In conclusion, current evidence suggests that colchicine therapy is efficacious for the prevention of post-operative AF, and may be considered as adjunctive prophylaxis. Further studies may be required to determine the optimal treatment protocol to reduce the incidence of gastrointestinal intolerance. (J Am Coll Cardiol EP 2016;2:78–85)

Atrial fibrillation (AF) is the most common arrhythmia and is a significant source of morbidity and mortality (1). It has a high occurrence rate following cardiac surgery (2). Post-operative AF may lead to longer hospital stays, increased health care costs, poorer neurocognitive outcomes, and increased incidence of stroke (3–6). Given the increased morbidity, prevention of post-operative AF is becoming an important management goal supported by many guidelines (7–9). It has been postulated that increased inflammation may precede AF (10). Inflammatory processes triggered by cardiac surgery have been implicated in the development of post-operative AF (11). Therefore, the use of an agent with anti-inflammatory properties may be effective in the goal of preventing post-operative AF. Corticosteroid therapy has been shown to be successful due to its potent anti-inflammatory effect, but its use remains controversial owing to potential adverse effects, including perioperative hyperglycemia, wound healing impairment, and infection (12). Colchicine, which may be a relatively safer alternative, has been evaluated for the use of prevention of post-operative AF (13–15). There has yet to be a

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systematic overview that would provide a more precise estimate of the efficacy and safety of the colchicine in post-operative AF. In our study, we aim to summarize the available data on colchicine's efficacy to prevent AF post-operatively, as well as to ascertain the significance of colchicine related adverse events.

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METHODS

SEARCH STRATEGY. A systematic literature review was planned and performed using methods specified in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic review (16). Both controlled vocabulary terms (e.g., MeSH) and key words were used to search for articles addressing the post-operative use of colchicine in patients undergoing cardiac surgery. The following databases were searched: PubMed/MEDLINE (1946 to 2014), Embase (1947 to 2014), Cochrane Library (1898 to 2014), Web of Science (1898 to 2014), EBSCO/CINAHL (Plus with Full Text) (1981 to 2014), and ClinicalTrials.gov (1997 to 2014). Literature searches were completed on June 18, 2014. The complete PubMed/MEDLINE search strategy, upon which the other database searches were also built, is available in the Online Appendix. Citations to and reference lists within the selected articles were also searched for studies that would meet inclusion criteria. All retrieved references were reviewed to identify prospective randomized trials that compared the clinical outcome of colchicine therapy for prevention of post-operative AF. No language or study type restriction was used for initial extraction of the data. No restrictions on the subheadings were applied. All references of relevant trials were also reviewed. We did not limit the language of the manuscript to be included in our meta-analysis. All non-English manuscripts were translated prior to consideration for inclusion.

STUDY SELECTION. Our pre-specified selection criteria were as follows: 1) randomized controlled trials; 2) head-to-head comparisons of perioperative administration of colchicine versus placebo; and 3) study participants who underwent any cardiac surgery. Exclusion criteria were: 1) studies with inadequate reporting of outcome data to meet our primary endpoint; 2) studies without peer-reviewed publication of the manuscripts; and 3) studies on procedures other than cardiac surgery. Our primary endpoint was the development of post-operative AF. Other outcomes of interest included the incidence of adverse events and early treatment discontinuation.

DATA EXTRACTION. Two independent reviewers performed the study selection (J.Z.L., S.-W.L.). In case of disagreements, a third reviewer (C.L.H.) cast the deciding vote. Titles and abstracts of retrieved references were screened for inclusion and full texts of potential articles were further analyzed to see if they met inclusion criteria (Figure 1). Case reports, letters, editorials, and systematic reviews or meta-analyses were excluded. Both individuals who collected the data used the following study-specific characteristics: study name, sample size of treatment group and control group per intention-to-treat analysis, event number and rate in both the treatment group and control group, statistical effect estimates used in the individual studies, dose and time period of colchicine, specific cardiac surgery performed, inclusion and exclusion criteria of individual studies, AF as specified in individual studies, rate of adverse

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

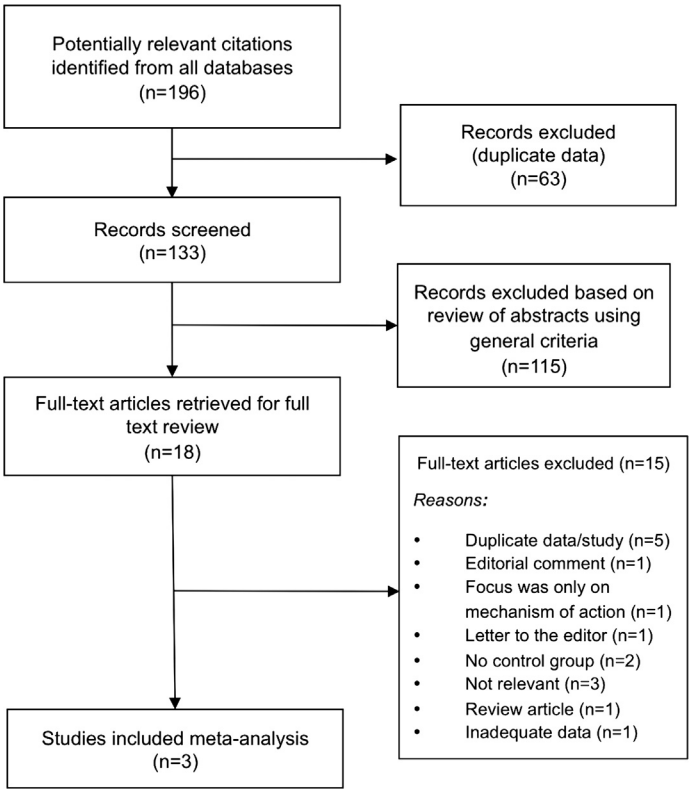
CABG = coronary artery bypass grafting

CI = confidence interval

RCT = randomized controlled trial

RR = risk ratio

FIGURE 1 Study Selection Diagram



Flow diagram of identification of published records retrieved from published data searches and from other sources. Reasons for exclusion of potentially eligible studies are listed.