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CORRESPONDENCE

Comparison of milrinone with dobutamine in patients undergoing cardiac surgery: a systematic review and meta-analysis

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To the Editor,

Patients undergoing cardiac surgery are at high risk of perioperative morbidity and mortality. One of the most common complications is a low cardiac output state, often treated with intravenous inotropes. The impact of dobutamine compared with milrinone, the most used inotropes in Canada, on clinical outcomes after cardiac surgery is unclear. We conducted a systematic review and meta-analysis of randomized trials in adults undergoing cardiac surgery to examine their comparative effect on mortality, intensive care unit (ICU) length of stay, quality of life, new arrhythmia, dialysis, major adverse cardiovascular events, and hemodynamics.

Following protocol registration (PROSPERO [CRD42022316325]; registered 11 April 2022), we developed a search strategy in collaboration with an information specialist using a combination of medical subject headings and text words related to milrinone, dobutamine, and cardiac surgical procedures. We applied the search strategy to MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) for articles published from database inception until 10 February 2022. Title and abstract screening, full text review, and data extraction were performed in duplicate. Meta-analysis using random effects models was used to pool effect estimates. Risk of bias assessment was performed.

We identified 1,548 titles and abstracts, and after removal of duplicates 934 articles were reviewed. We performed a full-text review on 34 citations, and five randomized controlled trials with a total of 240 patients meeting the final inclusion criteria.[1–5] Our primary outcome, mortality, was only reported in one study,[1] where the mortality rate was 5% in each group. Intensive care unit length of stay was also only reported in one study,[1] and no significant difference was found between groups. Onset of a new arrythmia was reported in two studies,[1,5] and our meta-analysis found no differences between groups; the pooled relative risk for milrinone was 0.56 (95% confidence interval [CI], 0.15 to 2.09; $P = 0.08$; $I^2 = 68\%$; Figure). No study reported quality of life, dialysis, or major adverse cardiovascular events.

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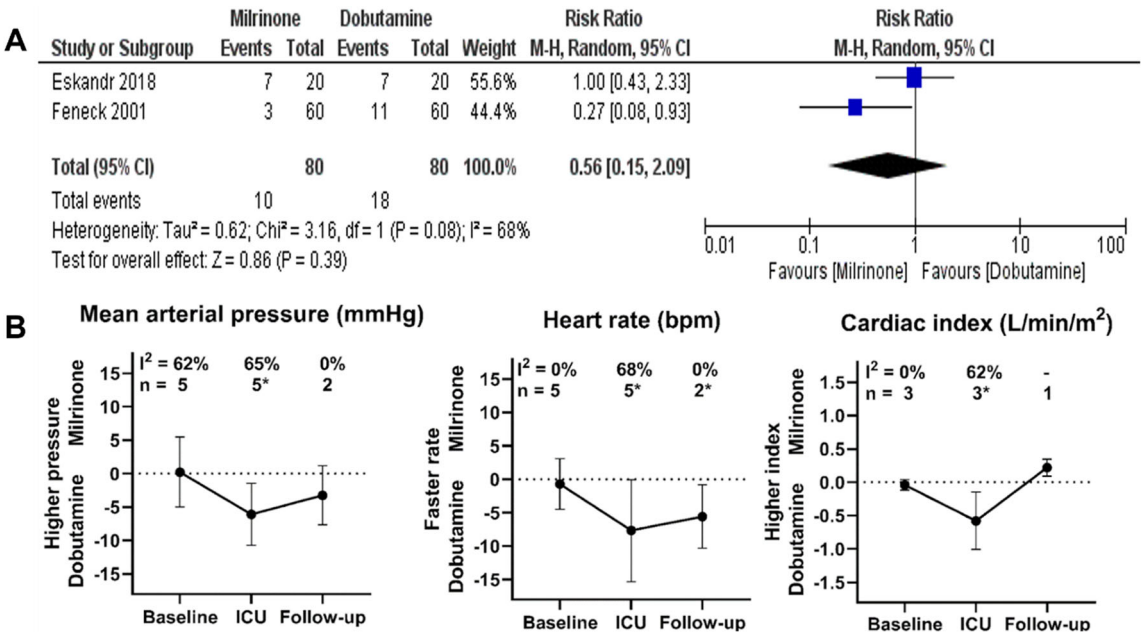

Figure Meta-analysis of incidence of new arrythmias (A) and hemodynamic changes (B) in cardiac surgery patients receiving milrinone *vs* dobutamine. Hemodynamic changes are represented by mean difference plots, where each point shows the mean difference between milrinone and dobutamine for all available studies combined, with the error bars representing the 95% CI of the combined effect resulting from random-effects meta-analysis. Heterogeneity (I^2), the number of studies included at each time point, and statistical significance of the mean difference at a given time point (*$P > 0.05$) are shown above each line. The time point "ICU" denotes the first time point measured in the ICU following onset of drug administration. bpm = beats per minute; CI = confidence interval; ICU = intensive care unit

All five studies reported varying hemodynamic parameters. For mean arterial pressure, no significant difference between milrinone and dobutamine was observed at either baseline or 12-hr follow-up. At the first measurement after onset of infusion, dobutamine exerted a significantly greater increase in mean arterial pressure than milrinone did (mean difference, 6.1 mm Hg; 95% CI, 1.5 to 10.8; $P = 0.01$; $I^2 = 65\%$; Figure). Heart rate was not significantly different between the milrinone and dobutamine groups at baseline. Nevertheless, dobutamine administration resulted in a significantly higher heart rate than milrinone did at the first ICU (mean difference, 7.7 beats per minute [bpm]; 95% CI, 0.1 to 15.3; $P = 0.05$; $I^2 = 68\%$) and follow-up time points (mean difference, 5.6 bpm; 95% CI, 0.8 to 10.3; $P = 0.02$; $I^2 = 0\%$, Figure). The cardiac index was not significantly different at baseline, but at the first ICU measurement, dobutamine administration resulted in significantly greater cardiac index than milrinone did (mean difference, 0.6 $L \cdot min^{-1} \cdot m^{-2}$; 95% CI, 0.2 to 1.0; $P = 0.008$; $I^2 = 62\%$).

Only one study was deemed to be at low risk of bias,[1] whereas the other four were deemed to be at high risk of bias.[2–5]

We had planned subgroup analyses by type of cardiac surgery, use of cardiopulmonary bypass, timing of initiation of medication, dose of medication, and overall study risk of bias; however, this was precluded by inadequate data.

In patients undergoing cardiac surgery, there is limited reporting on clinical and patient-centred outcomes when comparing the administration of dobutamine and milrinone. Dobutamine showed a favourable hemodynamic profile shortly after administration; however, the clinical implications of this are unknown. Prospective randomized trials focused on clinical and patient-centred outcomes are needed to better inform decision-making in patients requiring inotropes after cardiac surgery.

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