
To the Editor:

We read with great interest the meta-analysis by Ho and Tan¹ on the impact of prophylactic corticosteroid use on atrial fibrillation in adult patients undergoing cardiac surgery. In their meta-analysis, Ho and Tan demonstrate that perioperative corticosteroid use significantly reduces the relative risk (RRR) of postoperative atrial fibrillation by 25%. They conducted subgroup analysis, stratifying studies to low-dose (<1000 mg hydrocortisone equivalents), medium-dose (1000 to 10 000 mg), and high-dose (>10 000 mg) groups, and then used meta-regression to assess whether the antifibrillatory (among other) benefits varied by corticosteroid dosing intensity. They conclude that the ability of corticosteroids to prevent atrial fibrillation “... was not significantly different between different doses” and that low-dose corticosteroids should be used.

We are concerned that Ho and Tan may be oversimplifying the dose-response relationship seen between corticosteroids and the reduction in atrial fibrillation risk. Although their subgroup analysis revealed that the RRRs achieved with different doses (RRRLow = 23%, RRRMedium = 35%, RRRHigh = 10%) were not statistically different, a failure to prove statistical significance does not rule out the possibility that a true difference exists. In fact, we believe that a thoughtful qualitative review of the above-mentioned results suggests that a U-shaped relationship exists, with medium doses showing the most benefit and low and high doses showing blunted antifibrillatory effects. Consequently, the use of meta-regression analysis to support the conclusions of subgroup analysis is inappropriate because this methodology assumes a linear relationship between corticosteroid dose and clinical outcome.²

Furthermore, it is likely that the cut points used by Ho and Tan¹ to define the different dosing categories may have contributed to their lack of significant findings. In a previous meta-analysis conducted by our research group evaluating the impact of corticosteroids on postoperative atrial fibrillation in cardiothoracic surgery patients,³ we also divided patients into 3 dosing strata but used different cut points. In our analysis, we found a similar U-shaped relationship (reduction in oddsLow = 20%, reduction in oddsMedium = 64%, reduction in oddsHigh = 14%), with the studies in the medium-dose group showing the most benefit (P≤0.03 for interaction for low and high versus medium dose). In our article, we hypothesized that lower corticosteroid doses did not provide enough antiinflammatory potency to be beneficial, whereas the higher doses possibly worsened outcomes by promoting sodium and water reabsorption in addition to increased risk of infection and glucose abnormalities.³

Given the present data, it should not be summarily assumed that no dose-response relationship exists. Additional research is needed to determine whether a U-shaped relationship exists and, if so, to elucidate the pharmacological rationale for the effect.

Disclosures

None.

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References

Letter by Baker et al Regarding Article, "Benefits and Risks of Corticosteroid Prophylaxis in Adult Cardiac Surgery: A Dose-Response Meta-Analysis"
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