Protective Effects of Steroids in Cardiac Surgery: A Meta-Analysis of Randomized Double-Blind Trials

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Objective: Cardiac surgery and cardiopulmonary bypass (CPB) induce an acute inflammatory response contributing to postoperative morbidity. The use of steroids as anti-inflammatory agents in surgery using CPB has been tested in many trials and has been shown to have good anti-inflammatory effects but no clear clinical advantages for the lack of an adequately powered sample size. The aim of this study was to evaluate the effects of steroid treatment on mortality and morbidity after cardiac surgery.

Design: A systematic meta-analysis of randomized double-blind trials (RDBs).

Setting: A university hospital.

Participants: Adult patients who underwent cardiac surgery.

Methods: Measurements and Main Results: A trial search was performed through PubMed and Cochrane databases from 1966 to January 2009. Among 104 clinical trials reviewed, 31 RDB trials (1,974 patients) were considered suitable to be analyzed. A quality assessment of the trials was performed using the Jadad score. The types of steroid used in these trials were methylprednisolone (51.4%), dexamethasone (34.3%), hydrocortisone (5.7%), prednisolone (2.9%), or a combination of methylprednisolone and dexamethasone (5.7%). Steroid prophylaxis provided a protective effect preventing postoperative atrial fibrillation (odds ratio = 0.56; confidence interval [CI] 0.44-0.72, p < 0.0001), reducing postoperative blood loss (mean difference = -204.2 mL; CI from -287.4 to -121 mL; p < 0.0001), and reducing intensive care unit (mean difference = -6.6 hours; CI from -10.5 to -2.7 hours, p = 0.0007) and overall hospital stay (mean difference = -0.8 days; CI from -1.4 to -0.2 days, p = 0.01). Steroid prophylaxis had no effect on postoperative mortality, mechanical ventilation duration, re-exploration for bleeding, and postoperative infection.

Conclusions: A systematic review of RDB trials reveals that steroid prophylaxis may reduce morbidity after cardiac surgery and does not increase the risk of postoperative infections.

KEY WORDS: cardiopulmonary bypass, inflammatory response, complications, atrial fibrillation, infections

CARDIAC SURGERY and cardiopulmonary bypass (CPB) induce a systemic acute inflammatory response characterized by leukocytes, platelets and complement activation, and elevated levels of inflammatory mediators1 that may contribute to postoperative morbidity. The use of steroids as anti-inflammatory agents in surgery using CPB has been tested in many trials and has been shown to have good anti-inflammatory effects but no clear clinical advantages for the lack of an adequately powered sample size. The aim of this study was to evaluate the effects of steroid treatment on mortality and morbidity after cardiac surgery.

A systematic review of the literature was performed to determine the effects of steroid prophylaxis on hospital mortality and the incidence of postoperative infections, atrial fibrillation, length of mechanical ventilation, intensive care unit (ICU) stay, overall hospital stay, postoperative blood loss, and re-exploration for bleeding after cardiac surgery.

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and 1,974 patients fulfilled the criteria and were included in this meta-analysis.

Quality assessment of the trials was obtained using the Jadad score. Because all studies included were randomized and double blind, none of them had a Jadad score lower than 2. Four studies were assessed as relatively poor (score 2), and the remaining were considered good or excellent (score 3-5). Outcome measures were abstracted from each trial by 2 independent researchers (GC and CR). The divergences about quality assessment and abstracted data were resolved by a third author (DP).

**Study Design**

Summary characteristics of included studies are depicted in Table 1. Twenty-one trials included patients undergoing isolated coronary artery bypass graft (CABG) surgery, 4 trials CABG surgery or valve surgery, 3 trials only valve surgery, and 3 mixed cardiac operations with the use of CPB. The overall percentage of patients undergoing isolated CABG surgery was 80%. The primary endpoints of the included trials were classified into 3 groups: clinical, biologic (laboratory analyses; ie, the assay of inflammatory markers), and physiologic (instrumental measurements; ie, hemodynamic or respiratory parameters). The most common (58.1%) primary endpoint among the trials was biologic followed by clinical endpoints (29%) and physiologic endpoints (12.9%). Almost half of the patients enrolled in the meta-analysis (44.4%) belonged to 4 RDB trials. Sixteen of 31 trials included diabetic patients; in those studies, the incidence of diabetic patients ranged between 15% and 30%; none of the studies was conducted only on diabetics.

Of the 31 RDBs, 3 had multiple intervention arms evaluating different steroids or different dosages of the same steroid. Thus, according to Cochrane guidelines, in order to achieve independent comparisons between each intervention group and placebo, patients belonging to the placebo group were divided into subgroups of equal size that were compared with each intervention group of those trials. In this way, the total number of patients belonging to the placebo group remained the same. Thus, from the original 31 trials considered, 35 comparisons between intervention and placebo groups were included, and, therefore, of 1,974 total patients, 1,020 underwent steroid prophylaxis and 954 were given placebo. Table 2 describes the type of steroid used in the selected trials and the number of patients who underwent each treatment. In the majority of

<p>| Table 1. The Characteristics of the Included Trials |</p>
<table>
<thead>
<tr>
<th>RDB Trials</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>31</td>
</tr>
<tr>
<td>Decades (%)</td>
<td></td>
</tr>
<tr>
<td>1979-1988</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>1989-1998</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>1999-2009</td>
<td>26 (83.9)</td>
</tr>
<tr>
<td>Jadad score (%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>3</td>
<td>12 (38.7)</td>
</tr>
<tr>
<td>4</td>
<td>10 (32.3)</td>
</tr>
<tr>
<td>5</td>
<td>5 (16.1)</td>
</tr>
<tr>
<td>Primary endpoint (%)</td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td>9 (29)</td>
</tr>
<tr>
<td>Biologic</td>
<td>18 (58.1)</td>
</tr>
<tr>
<td>Physiologic</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>Sample sizes (%)</td>
<td></td>
</tr>
<tr>
<td>≤30 patients</td>
<td>12 (38.7)</td>
</tr>
<tr>
<td>31-100 patients</td>
<td>15 (48.4)</td>
</tr>
<tr>
<td>&gt;100 patients</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>Intervention arms per trial (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>28 (90.3)</td>
</tr>
<tr>
<td>&gt;1</td>
<td>3 (9.7)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>Diabetic patients included</td>
<td>16 (51.6)</td>
</tr>
<tr>
<td>Only insulin-dependent diabetic patients excluded</td>
<td>9 (29)</td>
</tr>
<tr>
<td>All types of diabetic patients excluded</td>
<td>6 (19.4)</td>
</tr>
</tbody>
</table>

<p>| Table 2. The Type of Steroid Prophylaxis in Patients Belonging to the Treatment Group |</p>
<table>
<thead>
<tr>
<th>Comparisons (%)</th>
<th>No. of Patients in Treatment Group (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>35</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>18 (51.4)</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>12 (34.3)</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Methylprednisolone/dexamethasone association</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td></td>
</tr>
<tr>
<td>Pre- and intraoperative</td>
<td>26 (74.3)</td>
</tr>
<tr>
<td>Pre-, intra-, and postoperative</td>
<td>9 (25.7)</td>
</tr>
</tbody>
</table>
trials (74.3%), steroids were administered preoperatively or intraoperatively; few trials extended treatment in the postoperative course.

Definitions

The following endpoints were defined as follows: postoperative mortality was considered as all-cause mortality occurring up to 30 days postoperatively or before hospital discharge. New onset of atrial fibrillation was considered if it occurred before hospital discharge. The length of intubation was measured in minutes, ICU stay was measured in hours, and overall stay was measured in days. Postoperative infections include any type of infection that occurred after surgery. Postoperative chest tube drainage was measured in milliliters.

Statistical Analysis

Categoric variables were presented as absolute numbers (percentages), whereas continuous variables were presented as mean ± standard deviation. In case the continuous data abstracted from the trials had been presented differently from mean ± standard deviation, they were transformed into mean ± standard deviation according to the directions of the Cochrane Handbook before being analyzed.

Effect sizes measured were odds ratio (OR) for categoric variables and mean difference (MD) for continuous variables. The I² test was used to evaluate statistical heterogeneity. An I² <25% was considered low heterogeneity. However, because of a noticeable clinical heterogeneity caused by the use of different types and doses of steroids in each trial, the random-effect model was used to perform all meta-analyses. Continuity correction was calculated according to the “reciprocal of the opposite treatment arm size” method in case of 0 cells, whereas trials without any event in both treatment and control groups (“zero-sum” trials) were excluded from calculations. Analyses were performed using Meta-analysis with Interactive Explanation Software (Version 1.61 for Windows; Leon Bax, Department of Medical Informatics, Graduate School of Medical Sciences, Kitasato University, Japan).

Table 3. Meta-analyses

<table>
<thead>
<tr>
<th>Trials</th>
<th>Mortality</th>
<th>Atrial fibrillation</th>
<th>Blood loss (mL)</th>
<th>Re-exploration</th>
<th>Postoperative infections</th>
<th>Sternal wound Infections</th>
<th>Ventilation (min)</th>
<th>ICU stay (h)</th>
<th>Overall stay (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Pt Enrolled</td>
<td>Odd Ratio</td>
<td>Mean Difference</td>
<td>95% CI</td>
<td>p Value</td>
<td>I² (%)</td>
<td>P</td>
<td>I² CI</td>
</tr>
<tr>
<td>All</td>
<td>9</td>
<td>1,081</td>
<td>0.71</td>
<td>—</td>
<td>0.29-1.73</td>
<td>0.46</td>
<td>0</td>
<td>0-65</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>5</td>
<td>259</td>
<td>0.51</td>
<td>—</td>
<td>0.14-1.82</td>
<td>0.3</td>
<td>0</td>
<td>0-79</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>3</td>
<td>581</td>
<td>0.97</td>
<td>—</td>
<td>0.25-3.83</td>
<td>0.97</td>
<td>0</td>
<td>0-90</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>15</td>
<td>1,344</td>
<td>0.56</td>
<td>—</td>
<td>0.44-0.72</td>
<td>&lt;0.0001</td>
<td>0</td>
<td>0-53</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>7</td>
<td>342</td>
<td>0.73</td>
<td>—</td>
<td>0.44-1.23</td>
<td>0.24</td>
<td>0</td>
<td>0-71</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>6</td>
<td>675</td>
<td>0.56</td>
<td>—</td>
<td>0.39-0.79</td>
<td>0.001</td>
<td>0</td>
<td>0-75</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>7</td>
<td>399</td>
<td>—</td>
<td>-204.2</td>
<td>-287.4 to -121</td>
<td>&lt;0.0001</td>
<td>0</td>
<td>0-71</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>4</td>
<td>226</td>
<td>—</td>
<td>-205.6</td>
<td>-310.8 to -100.4</td>
<td>0.0001</td>
<td>0</td>
<td>0-85</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>2</td>
<td>48</td>
<td>—</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>4</td>
<td>695</td>
<td>1.26</td>
<td>—</td>
<td>0.4-3.99</td>
<td>0.69</td>
<td>4</td>
<td>0-85</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>1</td>
<td>35</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>1</td>
<td>294</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>6</td>
<td>710</td>
<td>1.31</td>
<td>—</td>
<td>0.57-3.03</td>
<td>0.51</td>
<td>0</td>
<td>0-74</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>3</td>
<td>116</td>
<td>1.03</td>
<td>—</td>
<td>0.20-5.23</td>
<td>0.96</td>
<td>0</td>
<td>0-90</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>2</td>
<td>510</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>4</td>
<td>641</td>
<td>0.92</td>
<td>—</td>
<td>0.49-1.75</td>
<td>0.8</td>
<td>4</td>
<td>0-85</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>1</td>
<td>20</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>1</td>
<td>294</td>
<td>NC</td>
<td>—</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td>NC</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>23</td>
<td>1,358</td>
<td>—</td>
<td>-14.3</td>
<td>-55.3 to 26.7</td>
<td>0.49</td>
<td>90</td>
<td>86-93</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>13</td>
<td>485</td>
<td>24.8</td>
<td>—</td>
<td>-77.6 to 127.3</td>
<td>0.63</td>
<td>68</td>
<td>42-82</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>8</td>
<td>712</td>
<td>-23.7</td>
<td>—</td>
<td>-48.9 to 1.4</td>
<td>0.06</td>
<td>73</td>
<td>44-67</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>17</td>
<td>882</td>
<td>—</td>
<td>-6.7</td>
<td>-10.5 to -2.8</td>
<td>0.0007</td>
<td>89</td>
<td>85-93</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>7</td>
<td>281</td>
<td>-5.5</td>
<td>—</td>
<td>-10.6 to -0.46</td>
<td>0.03</td>
<td>46</td>
<td>0-77</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>8</td>
<td>440</td>
<td>-7.2</td>
<td>—</td>
<td>-11.5 to -2.9</td>
<td>0.001</td>
<td>85</td>
<td>73-92</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>16</td>
<td>901</td>
<td>—</td>
<td>-0.8</td>
<td>-1.4 to -0.2</td>
<td>0.01</td>
<td>46</td>
<td>3-70</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>11</td>
<td>464</td>
<td>-0.6</td>
<td>—</td>
<td>-1.5 to 0.3</td>
<td>0.17</td>
<td>53</td>
<td>7-76</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>3</td>
<td>315</td>
<td>-0.7</td>
<td>—</td>
<td>-1.78 to 3.21</td>
<td>0.18</td>
<td>48</td>
<td>0-85</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: NC, not calculated because the number of trials available in that subgroup was <3.
RESULTS

Postoperative Mortality

Twenty-three RDB trials reported data on postoperative death. The overall postoperative mortality was low; only 19 patients (1%) died (8 [0.8%] in the treatment and 11 [1.1%] in the control group, respectively). In fact, 15 of 24 comparisons did not present any postoperative death event (“zero-sum” studies); therefore, the remaining 9 RDB trials (1,081 patients) were used to perform the meta-analysis (Table 3). As shown in Figure 2A, the administration of steroid prophylaxis during cardiac surgery did not influence postoperative mortality (OR = 0.71; confidence interval [CI], 0.29-1.73; p = 0.46). This result is also confirmed by analyzing the methylprednisolone and dexamethasone subgroups.

Atrial Fibrillation

Fourteen of 31 RDB trials (1,344 patients) reported the incidence of postoperative atrial fibrillation.
One of these$^{88}$ had 2 treatment groups; therefore, 15 comparisons finally were analyzed (Table 3 and Fig 2B). There were no “zero-sum” studies for this outcome. The overall incidence of atrial fibrillation was 31% (418 patients), 25.1% in treatment (172 patients) and 37.3% (246 patients) in the placebo group. Meta-analysis showed that steroid prophylaxis reduced the onset of postoperative atrial fibrillation (OR = 0.56; CI, 0.44-0.72; $p < 0.0001$). In 5 of 14 trials,$^{90,92,102,103,107}$ a significant reduction of atrial fibrillation was observed, whereas none showed an increase of postoperative atrial fibrillation when steroids were administered. Subgroup analysis showed that this protective effect was related to dexamethasone administration (OR = 0.56; CI, 0.39-0.79; $p = 0.001$).

**Postoperative Blood Loss and Re-exploration**

Seven trials (399 patients) reported the amount of postoperative blood loss,$^{79,84,91,100,103,106,109}$ which was decreased by the administration of steroids (MD = −204.2 mL; CI, −287.4 mL to −121 mL; $p < 0.0001$). Figure 3A shows that 6 of 7 trials reported reduced chest tube drainage in the treatment group; in 3 cases, this reduction was statistically significant.$^{79,84,100}$ The protective effect on blood loss also was confirmed in the methyl-

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**Figure 3.** A Forest plot for (A) postoperative blood loss and (B) ICU stay after cardiac surgery in RDB trials comparing steroid prophylaxis with placebo. In the Forest plot, each trial is presented with MD (expressed in milliliters for blood loss and in hours for ICU stay), CI, and weight on a linear scale. The vertical line represents the overall meta-analyzed effect size. MD < 0 milliliters represents a protective effect of steroids.
predisolone subgroup (MD = −205.6; CI, −310.8 to −100.4; p = 0.0001). Nevertheless, meta-analysis about re-exploration on 4 trials and 695 patients did not show any difference between treatment and placebo.

### Postoperative Infections

Eleven RDB trials enrolling 1,002 patients reported the incidence of postoperative infections. The overall incidence of postoperative infections was 2.5%; 2.7% in the treatment group, and 2.2% in the placebo group, respectively. Five of the RDB trials resulted in “zero-sum” trials. In the remaining 6 RDB trials (710 patients), steroid prophylaxis did not increase the incidence of postoperative infections (OR = 1.31; CI, 0.57-3.03; p = 0.51). Nine trials reported data on wound infection. In the remaining 6 RDB trials (710 patients), steroid prophylaxis did not affect the incidence of wound infection after cardiac surgery (OR = 0.92; CI, 0.49-1.75; p = 0.8).

### Mechanical Ventilation

Twenty-one trials reported the time on mechanical ventilation after the operation. No difference between treatment and placebo groups was observed (Table 3). A trend for a reduced time on mechanical ventilation in steroid-treated patients was observed in the dexamethasone subgroup (8 trials, 712 patients) (MD = −23 minutes; CI, −48 to 1.4 min; p = 0.06).

### ICU and Overall Hospital Length of Stay

Seventeen trials (882 patients) reported the ICU length of stay. Meta-analysis of these trials revealed that steroid prophylaxis significantly reduced ICU stay (MD = −6.7 hours; CI, −10.5 hours to −2.8 hours; p = 0.0007). Figure 3B shows that all trials except 2103,108 evidenced a lower ICU length of stay in the treatment groups; in 6 cases, this difference was statistically significant. Steroid-induced immune suppression has been considered potentially able to increase the risk of postoperative infections. This is one of the factors preventing physicians from administering steroids in cardiac surgery. The relationship between the postoperative inflammatory state and the predisposition to develop postoperative infections still requires specific physiopathologic investigations. However, in large observational studies, a direct correlation between the preoperative inflammatory state and postoperative infection has been documented and a possible explanation for the higher rate of postoperative infective complications in patients with high preoperative inflammatory status is based on the observation that bacterial growth is increased in the presence of elevated concentrations of proinflammatory mediators.

Another interesting result of this study is the effect of steroids on the onset of atrial fibrillation. An increasing body of evidence recently has highlighted the role of inflammation in the pathogen-
esis of postoperative atrial fibrillation.118,119 The present meta-analysis confirmed that steroid prophylaxis reduced the incidence of postoperative atrial fibrillation by 30%.

The present authors also observed that steroid prophylaxis reduces postoperative blood loss. Even though chest tube drainage removal timing and protocols may vary from trial to trial, the authors found that in 6 of 7 trials chest tube drainage was lower in the treatment group; it was statistically significant in 3 of these.79,84,100 Approximately 20% of patients bleed significantly after cardiac surgery; the causes of this complication may vary from the presence of surgical bleeders to preoperative treatment with antiplatelet drugs to CPB-induced coagulopathy.120 A significant interaction exists between inflammation and coagulation; this cross-talk leads to the activation of all major pathways involved in the pathogenesis of the hemostatic derangement observed during severe inflammation.121 Because the activation of the inflammatory and coagulation systems presents similar pathways,122 a better preservation of the coagulation system with reduced perioperative thrombin generation may be the cause of reduced postoperative bleeding in steroid-treated patients.

Chaney et al.93,88 demonstrated the detrimental effects of methylprednisolone on pulmonary function and postulated the increase of pulmonary shunt and the A-a oxygen gradient as possible causes of prolonged mechanical ventilation in patients who were given methylprednisolone perioperatively. In the meta-analysis, the length of mechanical ventilation seemed not to be affected by steroid prophylaxis when trials using different steroids were pooled together. Nevertheless, when considering only trials using dexamethasone, a trend toward a shorter length of mechanical ventilation could be identified.

ICU and overall hospital lengths of stay were significantly reduced by steroid prophylaxis. The reduced length of stay in steroid-treated patients probably reflects the consequences of reduced postoperative bleeding; the incidence of atrial fibrillation; and, possibly, a general healthier state associated with a reduced postoperative inflammatory response.

The present systematic review has several limitations. The most important one is the significant variety of types and dosages of steroids used across the studies included. Although the analysis of postoperative mortality did not show any obvious difference between the treatment and control groups, the overall incidence of this event throughout the included trials is very low. A larger randomized trial should clarify this point, as neurologic and gastrointestinal complications that were not considered in the present review because of the excessive heterogeneity of their definitions. Moreover, the trials included in the analysis are from a 30-year span, and the difference in medications, techniques, and demographics may have had a significant effect on the outcomes measured.

The lack of data regarding the outcome in diabetics should limit the use of steroids in this subset of patients. The very low risk profile of the patients enrolled in the RDB trials included (80% isolated CABG surgery) suggests that the conclusions of this meta-analysis cannot be automatically extended to high-risk patients although patients with complex procedures and long CPB times may benefit more from the use of steroids.

Recently, Whitlock et al.123 published a meta-analysis reporting similar results on the effects of steroids in patients undergoing cardiac surgery. However, there are differences between the 2 studies. The most important is the exclusion in the present meta-analysis of open-label trials. Even if this choice reduced the number of trials included, the quality of the analysis was higher (mean Jadad score, 3.5 ± 0.9 vs 2.7 ± 1.4). Another difference was the observed mortality (1% vs 3.2%), which may reflect a different case mix of patients enrolled (80% vs 70% of isolated CABG surgery). Even with the higher mortality and sample size of the Whitlock series, they found no difference in hospital mortality. Moreover, to reduce the heterogeneity caused by the use of different types of steroids, the authors repeated the analysis for the 2 most represented molecules (dexamethasone and methylprednisolone), finding that the use of dexamethasone only is associated with the protective effect on atrial fibrillation. Considering that dexamethasone is long lasting and does not present any mineralocorticoid effect (potentially creating fluid and electrolytes imbalance) compared with methylprednisolone, future studies should identify the best steroid compound for cardiac surgery. The authors deliberately decided not to include outcomes like postoperative myocardial infarction, neurologic complications, and gastrointestinal complications because of the lack of precise definitions throughout the trials.

In conclusion, the present meta-analysis of RDB trials shows that steroid prophylaxis is generally safe and effective at reducing the incidence of some postoperative complications after cardiac surgery. A forthcoming large randomized clinical trial (http://www.clinicaltrials.gov/ct2/show/NCT00427388) will probably be able to evaluate the unanswered questions left by the present study.

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