Does the use of preoperative aspirin increase the risk of bleeding in patients undergoing coronary artery bypass grafting surgery: systematic review and meta-analysis

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CRD summary
This review concluded that aspirin is associated with an increased risk of post-operative bleeding and a greater need for blood product transfusion in patients undergoing first-time elective coronary artery bypass grafting surgery. These conclusions seem reliable, although there is a possibility of language and publication bias.

Authors' objectives
To evaluate the effects of pre-operative aspirin on bleeding and the need for blood transfusions in patients undergoing elective coronary artery bypass grafting (CABG) surgery.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched from inception to March 2006; the search terms were reported. The search was limited to articles published in English. The reference lists of included studies were also screened.

Study selection
Randomised controlled trials (RCTs) and non-randomised studies were included in the review.

Studies of adults undergoing on-pump elective first-time CABG surgery were eligible for inclusion. Studies of patients undergoing non-elective or repeat surgery, or procedures other than CABG, were excluded. The average age of the patients ranged from 53.2 to 70 years.

Eligible interventions were pre-operative aspirin intake of at least 75 mg/day within 7 days of surgery. The included studies assessed aspirin doses ranging from at least 75 mg/day or greater to at least 600 mg/day or greater. Aspirin was given 4 to 10 days pre-operatively. Details of the control interventions were not reported.

The primary outcome was the total amount of post-operative chest tube drainage. The secondary outcomes were packed red blood cell transfusion units, platelet transfusion units, fresh frozen plasma transfusion units, and the numbers of patients re-examined for bleeding during their stay.

Two reviewers independently selected studies for inclusion. Any disagreements were resolved by consensus.

Assessment of study quality
Study quality was assessed using criteria from the U.S. Preventive Services Task Force. The studies were rated as high or low quality, but further details were not provided.

Study quality was assessed as part of the data extraction, by two reviewers independently and with any discrepancies resolved by consensus.

Data extraction
If studies included multiple treatment arms, comparisons were only made between aspirin and control where possible. Mean differences were calculated for amount of chest tube drainage and units of different blood transfusions, and relative risks (RRs) calculated for dichotomous outcomes, along with corresponding 95% confidence intervals (CIs).

Two reviewers independently extracted the data, with any disagreements resolved by consensus.

Methods of synthesis
Pooled weighted mean differences (WMDs) and RRs were estimated using random-effects models.

Clinical heterogeneity was assessed by considering the study populations, interventions, control groups and outcomes. Statistical heterogeneity was assessed with a $\chi^2$ test (considered significant if $p<0.05$). Subgroup analyses were used to assess the effects of year of study conduct, study design (randomised versus non-randomised) and excluding studies with outlying results.

**Results of the review**

Ten studies (1,748 participants: 913 in the aspirin groups and 835 in the control groups).

All studies were considered to be of a low quality.

Total postoperative blood loss (8 studies): aspirin significantly reduced blood loss compared with control (WMD 210 mL, 95% CI: 87, 333, $p<0.001$). Similar results were seen for the subgroup of randomised studies only (WMD 315 mL, 95% CI: 218, 413, $p<0.001$; based on 4 studies). There was moderate heterogeneity overall ($I^2=68.4\%$) and for the non-randomised studies ($I^2=58.3\%$), but not for the randomised studies ($I^2=0\%$). Subgroup analyses showed a greater blood loss with aspirin in earlier studies (before 1990).

Blood transfusion: aspirin use was associated with significantly increased packed red blood cell transfusion (WMD 0.65 units/patient, 95% CI: 0.19, 1.10, $p=0.005$; based on 5 studies; $I^2=63.6\%$) and significantly increased fresh frozen plasma transfusion (WMD 0.61 units/patient, 95% CI: 0.07, 1.16, $p=0.03$; based on 5 studies; $I^2=90.3\%$). Aspirin use was also associated with an increase in platelet transfusion, although this difference was not statistically significant ($p=0.06$). Subgroup analyses showed similar conclusions for aspirin when the analysis was restricted to the randomised studies.

Re-exploration for bleeding (9 studies): aspirin was associated with a higher rate of re-exploration for bleeding compared with control (RR 2.32, 95% CI: 1.31, 4.08, $p=0.004$; $I^2=0\%$). Similar results were seen in the subgroup of randomised studies.

**Authors' conclusions**

Aspirin is associated with an increased risk of post-operative bleeding and may be associated with a greater need for transfusion of blood products. High-quality prospective studies are needed to explore the relationship between pre-operative aspirin use and important clinical outcomes.

**CRD commentary**

This review addressed a focused question that was supported by clear inclusion and exclusion criteria. The search covered a number of relevant databases, but limiting it to only those studies published in English means that the review may be subject to language and publication bias. Appropriate steps were taken to minimise bias and error in the selection of studies. A quality assessment was conducted in which the studies were classified as being of a high or low quality, but further details on how this distinction was made were not reported. The methods of meta-analysis were appropriate, with randomised studies pooled separately from non-randomised studies, and the overall results were reported. The authors' conclusions seem reliable, but the possibility of language and publication bias should be considered.

**Implications of the review for practice and research**

Practice: The authors support the current ACC/AHA guidelines, which state that the value of aspirin in treating acute coronary syndromes often outweighs the increased risk of peri-operative bleeding, but in certain patients (chronic stable angina, low-risk plaque morphology) the cessation of aspirin and platelet inhibitors before elective surgery appears prudent.

Research: Further high-quality prospective research is needed to assess the effect of aspirin on important post-operative outcomes.
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