

Low-dose aspirin reduced DVT and pulmonary embolism but increased postoperative bleeding requiring transfusion in hip-surgery patients

Pulmonary Embolism Prevention (PEP) Trial Collaborative Group. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. *Lancet*. 2000 Apr 15;355:1295-302.

QUESTION

Does low-dose aspirin reduce the risk for pulmonary embolism (PE) and deep venous thrombosis (DVT) in patients having either surgery for hip fracture or elective arthroplasty?

DESIGN

Randomized (allocation concealed*), blinded (patients, clinicians, and outcome assessors),* controlled trial with follow-up for 35 days.

SETTING

148 hospitals in Australia, New Zealand, Sweden, and the United Kingdom.

PATIENTS

13 356 patients with hip fracture (mean age 79 y, 79% women) and 4088 patients having elective hip or knee arthroplasty (mean age 67 y, 53% women). Exclusion criteria were clear indication for aspirin (e.g., recent myocardial infarction) or contraindication to aspirin (e.g., active peptic ulcer). Follow-up at day 35 was > 99%.

INTERVENTION

6679 patients with hip fracture and 2047 patients having elective arthroplasty were allocated to a 5-week calendar supply of

enteric-coated aspirin, 160 mg/d, which was to be started immediately after randomization, with the first dose chewed or broken. 6677 patients with hip fracture and 2041 patients having elective arthroplasty were allocated to a matching placebo.

MAIN OUTCOME MEASURES

Mortality and in-hospital morbidity (primarily DVT, PE, and bleeding).

MAIN RESULTS

Analysis was by intention to treat. Among patients with hip fracture, those who received aspirin had a lower risk for symptomatic DVT and PE than did those who received placebo (Table) and a higher risk for any postoperative bleeding episode requiring transfusion (197 vs 157 episodes, $P = 0.04$); the groups did not differ for overall deaths. Among patients having elective arthroplasty, the groups did not differ for any of the above outcomes.

Low-dose aspirin vs placebo in patients having hip surgery†

Outcomes at 35 d	Aspirin	Placebo	RRR (95% CI)	NNT (CI)
Symptomatic deep venous thrombosis	1%	1.5%	29% (3 to 48)	232 (140 to 2239)
Pulmonary embolism	0.7%	1.2%	43% (18 to 60)	195 (140 to 466)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

CONCLUSIONS

Low-dose aspirin reduced the risk for deep venous thrombosis and pulmonary embolism in patients having surgery for hip fracture, but increased the risk for postoperative bleeding episodes requiring transfusion. No risk reduction was found for patients having elective arthroplasty.

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*See Glossary.

COMMENTARY

The Pulmonary Embolism Prevention (PEP) trial supports the results of a previous meta-analysis (1) and leaves no doubt that aspirin prevents venous thromboembolism after surgery for hip fracture. Of the 2 predefined outcome measures, the first, mortality to day 35 (including vascular death) was not reduced by aspirin, whereas objectively confirmed, symptomatic DVT or PE was reduced by about 36%. The benefit from aspirin continued for 5 weeks and was not offset by the small increase in bleeding. Aspirin did not reduce vascular death, myocardial infarction, or stroke but did reduce the risk for fatal PE by 58%. However, although PE is often found at autopsy, it is usually not the cause of death. Because fatal PE was not a predefined primary end point and the criteria for attributing death to PE were not clearly stated, this large difference may be an overestimate caused by misclassification of vascular deaths.

What are the clinical implications of the PEP trial? When mandatory venography is used to assess the outcome, aspirin is considerably less effective than either warfarin or low-molecular-weight heparin in

preventing DVT (2). Therefore, until aspirin is compared with other forms of prophylaxis in large trials using clinical end points, it cannot be recommended over low-molecular-weight heparin or warfarin. Given aspirin's ease of use, low cost, and proven safety, however, using it alone after hospital discharge following major orthopedic surgery in the many centers that currently discontinue anticoagulant prophylaxis at the time of hospital discharge is reasonable.

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References

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