

POEMs

Patient-Oriented Evidence That Matters

Aspirin No Different Than Rivaroxaban for Prevention of VTE After TKA or THA

Clinical Question

Is aspirin as effective as rivaroxaban (Xarelto) for prevention of venous thromboembolism (VTE) after total hip arthroplasty (THA) or total knee arthroplasty (TKA)?

Bottom Line

Extended prophylaxis with low-dose aspirin is similar in efficacy to rivaroxaban for the prevention of symptomatic VTE following TKA or THA. Aspirin is cheap, widely available, and effective, making it a good alternative to the more costly direct oral anticoagulants. (Level of Evidence = 1b)

Synopsis

In this study, investigators tested the efficacy of aspirin (81 mg) compared with rivaroxaban (10 mg) for extended VTE prophylaxis following TKA or THA. All patients in the study initially received in-hospital prophylaxis with rivaroxaban, 10 mg daily for five days, following surgery. Patients randomized to the rivaroxaban group (n = 1,718) continued this treatment, whereas those randomized to the other group (n = 1,709) started aspirin, 81 mg daily. Additionally, patients taking preoperative aspirin (81 mg) were allowed to continue its use in the postoperative phase. Study treatment was continued for nine additional days in patients who underwent TKA and 30 additional days in patients who underwent THA. The two pills, rivaroxaban or aspirin, were administered in identical gelatin capsules. Patients in the two groups had similar baseline characteristics and were followed for 90 days. In

the intention-to-treat analysis, low-dose aspirin was noninferior to rivaroxaban for the primary efficacy outcome of symptomatic proximal deep venous thrombosis or pulmonary embolism (0.64% vs. 0.70%; $P < .001$ for noninferiority). For the primary safety outcome of major bleeding or clinically relevant nonmajor bleeding, there was no significant difference detected between the two groups (1.29% in aspirin group vs. 0.99% in rivaroxaban group; $P = .43$).

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Inpatient (any location) with outpatient follow-up

Reference: Anderson DR, Dunbar M, Murnaghan J, et al. Aspirin or rivaroxaban for VTE prophylaxis after hip or knee arthroplasty. *N Engl J Med.* 2018;378(8):699-707.

Nita Shrikant Kulkarni, MD

Assistant Professor in Hospital Medicine
Northwestern University
Chicago, Ill.

Medications Ineffective to Prevent Cognitive Decline or Dementia

Clinical Question

Are there any medications that can prevent or delay cognitive decline, cognitive impairment, or dementia?

Bottom Line

None of the medications in this systematic review prevented or delayed cognitive decline, cognitive impairment, or dementia. (Level of Evidence = 1a-)

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Synopsis

These researchers searched four databases, including the Cochrane Library, to identify randomized and nonrandomized controlled trials in English that enrolled adults without dementia. They also searched reference lists of previous studies and included a previous report that evaluated interventions to prevent cognitive decline. Two reviewers evaluated the quality of the studies, and one reviewer extracted the data from the studies, which were checked by another reviewer. This wide-ranging review identified three studies of acetylcholinesterase inhibitors, although most of the impact was from a single study of donepezil (Aricept) in 512 patients with preexisting cognitive deficit. After three years, active treatment did not affect the progression to Alzheimer disease, nor did it affect any cognitive test result as compared with placebo. Other treatments were also ineffective, including antihypertensives, diabetes medication, lipid-lowering medication, nonsteroidal anti-inflammatory drugs, and testosterone. Estrogen alone or with progestin increased the risk of dementia in one low-quality trial. High-dose raloxifene (Evista), but not the usual dosage of 60 mg daily, decreased the likelihood of developing mild cognitive impairment, but not dementia, in a single study (low-quality evidence).

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Various (meta-analysis)

Reference: Fink HA, Jutkowitz E, McCarten R, et al. *Pharmacologic interventions to prevent cognitive decline, mild cognitive impairment, and clinical Alzheimer-type dementia: a systematic review.* *Ann Intern Med.* 2018;168(1):39-51.

Allen F. Shaughnessy, PharmD, MMedEd

Professor of Family Medicine
Tufts University
Boston, Mass.

Systolic Blood Pressure of At Least 140 mm Hg Best Place to Begin Treatment

Clinical Question

At what systolic blood pressure should we begin treatment for the most benefit?

Bottom Line

Beginning antihypertensive treatment when the systolic blood pressure is greater than 140 mm Hg delays death and prevents major cardiovascular

events in some persons without preexisting heart disease; in patients with existing heart disease, it prevents further events, but does not extend life. These results may appear to conflict with those from the Systolic Blood Pressure Intervention Trial (SPRINT), which found benefit with lowering systolic blood pressure to below 120 mm Hg. However, the SPRINT investigators measured blood pressure using automated devices, which give readings 10 to 20 mm Hg lower than typical office measurements. The goal of less than 120 mm Hg in the SPRINT study is likely to be very similar to the goal of less than 140 mm Hg in this study. (Level of Evidence = 1a)

Synopsis

The authors followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to search three databases, including Cochrane Central, as well as reference lists of identified studies to identify all randomized trials with at least 1,000 patient-years of follow-up that compared drug treatment with placebo or compared blood pressure targets against one another. Two researchers independently extracted the data and assessed the quality of the research (more than two-thirds of the studies had a low risk of bias). They identified 74 studies enrolling 306,273 patients (60.1% men, average age = 63.6 years).

In patients without preexisting heart disease (i.e., primary prevention), lowering systolic blood pressure that was initially greater than 140 mm Hg decreased the risk of death (relative risk [RR] = 0.93; 95% confidence interval [CI], -0.88 to 1.0 if systolic blood pressure is greater than 160 mm Hg; RR = 0.87; 95% CI, 0.75 to 1.0 if systolic blood pressure is 140 to 159 mm Hg) and major cardiovascular events (RR = 0.78; 95% CI, 0.7 to 0.87 if systolic blood pressure is greater than 160 mm Hg; RR = 0.88; 95% CI, 0.8 to 0.96 if systolic blood pressure is 140 to 159 mm Hg). Treating systolic blood pressure that was initially less than 140 mm Hg did not affect morbidity or mortality. In patients with previous coronary heart disease and a mean systolic blood pressure of 138 mm Hg, treatment reduced the risk of further major cardiovascular events (RR = 0.9; 95% CI, 0.84 to 0.97), but did not extend life. There was a high degree of heterogeneity among these trial results, reducing our confidence in the results. There was some evidence of publication bias in the studies that evaluated the effect on

major cardiovascular events, meaning that the studies failing to show a difference in outcomes were not published.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Foundation

Setting: Various (meta-analysis)

Reference: Brunström M, Carlberg B. Association of blood pressure lowering with mortality and cardiovascular disease across blood pressure levels: a systematic review and meta-analysis. *JAMA Intern Med.* 2018;178(1):28-36.

Allen F. Shaughnessy, PharmD, MMedEd

Professor of Family Medicine
Tufts University
Boston, Mass.

Pulmonary Embolism Rule-Out Criteria Reduces the Need for CT Pulmonary Angiography in Low-Risk Patients

Clinical Question

Can the pulmonary embolism rule-out criteria (PERC) clinical decision rule reduce the need for computed tomographic (CT) pulmonary angiography in low-risk patients with suspected pulmonary embolism (PE)?

Bottom Line

Use of the PERC clinical decision rule significantly reduces the need for CT pulmonary angiography in adults with an initial low-risk clinical estimate of suspected PE. (Level of Evidence = 1b)

Synopsis

The PERC decision rule is an eight-item set of clinical criteria, including arterial oxygen saturation of 94% or less, pulse rate of at least 100 beats per minute, patient age at least 50 years, unilateral leg swelling, hemoptysis, recent trauma or surgery, prior PE or deep venous thrombosis, and exogenous estrogen use. These investigators identified all consenting adults who presented to an emergency department with new-onset presence or worsening of shortness of breath or chest pain and a low clinical probability of PE (estimated

by the treating physician as less than 15% probability). The patients (N = 962) were cluster-randomized (concealed allocation assignment) based on emergency department location to a control group or to an intervention group with a diagnostic workup that included an initial calculation of the PERC score. Patients who scored zero had no additional workup for PE. Patients with a PERC score above zero had a standard diagnostic workup that included D-dimer testing, followed by CT pulmonary angiography if the D-dimer result was positive (based on age-adjusted thresholds). The control group received only the standard workup without a preceding PERC calculation. The intervention strategy continued for six months, followed by a two-month washout period, and then the two groups crossed over to the other diagnostic strategy protocol. Individuals who assessed outcomes remained masked to group assignments. Follow-up occurred for 97% of patients at three months.

Using both intention-to-treat and per-protocol analyses, there was no significant difference in the proportion of patients in the PERC group who were given an initial diagnosis of PE compared with patients in the control group (1.5% vs. 2.7%). Only one PE (0.1%) was diagnosed during follow-up in the PERC group; none were diagnosed in the control group. CT pulmonary angiography occurred in significantly fewer patients in the PERC group than in the control group (13% vs. 23%; difference = -10%; 95% confidence interval, -13% to -6%).

Study design: Decision rule (validation)

Funding source: Government

Setting: Emergency department

Reference: Freund Y, Cachanado M, Aubry A, et al. Effect of the pulmonary embolism rule-out criteria on subsequent thromboembolic events among low-risk emergency department patients: the PROPER randomized clinical trial. *JAMA.* 2018;319(6):559-566.

David Slawson, MD

Professor of Family Medicine
University of North Carolina at Chapel Hill
Chapel Hill, N.C. ■