POEMs

Aspirin Is as Safe and Effective as LMWH for Extended Thromboprophylaxis After Total Hip Arthroplasty

Clinical Question

Is aspirin as effective as dalteparin (Fragmin) for extended venous thromboembolism prophylaxis in patients who have undergone total hip arthroplasty?

Bottom Line

Aspirin is as effective as dalteparin for extended thromboprophylaxis in patients who had total hip arthroplasty and had initially received 10 days of dalteparin prophylaxis postoperatively. Because of its relative safety, low cost, and easy administration, aspirin is an attractive alternative to low-molecular-weight heparin (LMWH) when used for this purpose. (Level of Evidence = 1b)

Synopsis

Previous studies have confirmed the benefit of extended thromboprophylaxis with LMWH in patients who have undergone elective total hip arthroplasty. The cost of LMWH and the inconvenience of administering daily subcutaneous injections are high, however. In this study, investigators enrolled patients undergoing elective total hip arthroplasty to receive extended thromboprophylaxis with LMWH, specifically dalteparin, or with aspirin. All patients received an initial eight to 10 days of postoperative dalteparin prophylaxis. This was followed by randomization to dalteparin at a dosage of 5,000 units daily or aspirin at a dosage of 81 mg daily for the next 28 days. To preserve masking, placebo aspirin tablets and placebo dalteparin injections were also administered. Patients with metastatic cancer or those with conditions that precluded the use of an anticoagulant or aspirin were excluded. An amendment to the initial study protocol allowed patients using long-term aspirin therapy at a dosage of less than 100 mg daily to be enrolled. These patients were assigned to dalteparin or 81 mg of aspirin in addition to their usual dose of aspirin.

Because of slow recruitment, study enrollment was halted prematurely after 786 patients of a targeted group of 1,100 had entered. Baseline characteristics in the two groups were similar, with a mean age of 58 years and mean hospital stay of five days. More than 90% of the patients in the study reported adherence to all doses of the study medications. After a 90-day follow-up period, aspirin was found to be as effective as dalteparin for the prevention of symptomatic venous thromboembolism (1.3% with venous thromboembolism events in the dalteparin group vs. 0.3% in the aspirin group; $P < .001$ for noninferiority). There were no differences in clinically significant bleeding events between the two groups, although the trend favored aspirin (1.3% with dalteparin vs. 0.5% with aspirin). In the subset of patients using long-term aspirin therapy (n = 39), one patient assigned to the aspirin group had a clinically significant, nonmajor bleeding event, but there were no venous thromboembolism events in either group.

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Concealed

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

Reference: *Anderson DR, Dunbar MJ, Bohm ER, et al. Aspirin versus low-molecular-weight heparin for extended venous thromboembolism prophylaxis after total hip arthroplasty: a randomized trial.* Ann Intern Med. *2013;158(11):800-806.*

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Vitamin D Does Not Affect Isolated Systolic Hypertension

Clinical Question

Does treatment with vitamin D lower blood pressure in older patients with isolated systolic hypertension and low vitamin D levels?

Bottom Line

Vitamin D supplementation in patients with isolated systolic hypertension and low levels of vitamin D does not decrease systolic blood pressure after one year of treatment. (Level of Evidence = 1b)

Synopsis

Because low vitamin D levels are associated with hypertension, Scottish researchers investigated the role of ▶

vitamin D supplementation in 159 patients, at least 70 years of age, with isolated systolic hypertension greater than 140 mm Hg and vitamin D levels (25-hydroxyvitamin D) of less than 30 ng per mL (75 nmol per L). Using concealed allocation, patients were randomized to receive oral placebo or cholecalciferol at a dosage of 100,000 IU every three months for one year. As expected, vitamin D levels increased an average of 8 ng per mL (20 nmol per L) in the treated patients. Systolic blood pressure, though, did not significantly change or differ between the groups (0.8 mm Hg). Similarly, other measures—24-hour blood pressure, arterial stiffness, endothelial function—did not change.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Witham MD, Price RJ, Struthers AD, et al. Cholecalciferol treatment to reduce blood pressure in older patients with isolated systolic hypertension: the VitDISH randomized controlled trial [published ahead of print August 12, 2013].* JAMA Intern Med. *http://archinte.jamanetwork.com/article.aspx?articleid=1726994. Accessed October 4, 2013.*

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Finasteride Prevents Low-Grade Prostate Cancers, but Does Not Reduce Mortality

Clinical Question

Does the use of finasteride (Propecia) affect overall mortality or grade-specific survival rates following a diagnosis of prostate cancer?

Bottom Line

Although finasteride prevents low-grade prostate tumors, it does not affect overall survival or survival after prostate cancer diagnosis. Although high-grade cancers were more common among men taking finasteride, up to 18 years of follow-up failed to show increased mortality in this group. The only potential advantage to using finasteride is that the lower rate of low-grade cancers may reduce the likelihood that men would be treated for a cancer that is highly unlikely to harm them. (Level of Evidence = 1b)

Synopsis

The original Prostate Cancer Prevention Trial (PCPT) randomized 18,880 men from 221 sites (median age = 63 years) to receive 5 mg of finasteride per day or placebo. The men were followed at regular intervals via office visits and telephone calls, and underwent annual prostate-specific antigen tests and digital rectal examinations. Biopsy was recommended for patients with prostate-specific antigen levels higher than 4.0 ng per mL (4.0 mcg per L) and for those with an abnormal rectal examination result. Histologic confirmation classified cancer as low grade (Gleason score = 2 to 6) or high grade (Gleason score = 7 to 10). Previously published PCPT results showed that finasteride decreased the relative risk of prostate cancer by 24.8%, but increased the risk of high-grade prostate tumors by 26.9% compared with placebo.

This study, which collected additional incidence data through 2009, is a post-hoc analysis of overall survival and survival rates after diagnosis of prostate cancer. Cause of death, established through review of clinical summaries and death certificates, was determined by participating PCPT centers and through a search of the Social Security Death Index in May 2012. Men who received finasteride were less likely to be given a diagnosis of prostate cancer than men who received placebo (10.5% vs. 14.9%; relative risk = 0.70; 95% confidence interval [CI], 0.65 to 0.76). High-grade tumors were slightly more common in the finasteride group (3.5% vs. 3.0%; relative risk = 1.17; 95% CI, 1.00 to 1.37). However, there were no differences in all-cause mortality rates between patients who took finasteride vs. placebo (hazard ratio = 1.02; 95% CI, 0.97 to 1.08). Fifteen-year survival rates were 78.0% in the finasteride group and 78.2% in the placebo group. Study enrollment was lower than expected because of unforeseen closure of some of the original study centers. One center did not release Social Security numbers of their participants, resulting in missing data. For many men, cause of death was not readily available, thus prostate cancer–specific mortality could not be calculated. But because all-cause mortality was the same between groups, this is not an important limitation.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Uncertain

Setting: Outpatient (any)

Reference: *Thompson IM Jr, Goodman PJ, Tangen CM, et al. Long-term survival of participants in the prostate cancer prevention trial.* N Engl J Med. *2013;369(7):603-610.*

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