POEMs

Patient-Oriented Evidence That Matters

Supplemental Vitamin D Does Not Reduce the Risk of Fracture in Older Adults

Clinical Question

Does supplemental vitamin D reduce the risk of fracture in older adults?

Bottom Line

Vitamin D level is a very good marker of ill health but not a very good treatment target. A large study showed that supplemental vitamin D does not reduce the risk of fracture, even in people with low baseline vitamin D levels or a previous fracture. (Level of Evidence = 1b)

Synopsis

The study randomized 25,871 patients, including men 50 years and older and women 55 years and older, in a two-by-two factorial design to receive 2,000 IU of vitamin D or placebo per day, and 1,000 mg of omega-3 fatty acid or placebo per day. Patients were not selected based on their fracture risk or vitamin D levels; participants with a history of cancer, cardiovascular disease, or hypercalcemia were excluded. The primary goal of the VITAL trial was to evaluate the effect of these supplements on cancer and cardiovascular outcomes. Fractures were assessed based on patient self-reported data in an annual survey and confirmed by medical record review. The mean age of participants was 57 years, 51% were women, and 20% were Black. Approximately 25% of patients had a baseline vitamin D level less than 24 ng per mL (59.90 nmol per L), and 1.5% had levels less than 12 ng per mL (29.95 nmol per L). In each group, 42% were taking supplemental vitamin D, and those patients agreed to limit the amount they were taking to no more than 800 mg per day during the study. There was a total of 1,991 fractures in 1,551 patients, with no difference in total, nonvertebral, or osteoporotic fractures (i.e., hip, wrist, humerus, and spine). The authors did a series of prespecified subgroup analyses and found no benefit in patients in the placebo group who were not taking supplemental vitamin D or calcium or in patients with a previous fragility fracture. The mean 25-hydroxyvitamin D level was 30.7 ng per mL (76.63 nmol per L) at baseline, and there was no difference in fracture rates in different quartiles of vitamin D levels, including in patients with vitamin D levels less than 24 ng per mL (hazard ratio = 1.04; 95% CI, 0.80 to 1.36) and less than 12 ng per mL (hazard ratio = 1.03; 95% CI, 0.36 to 2.95). There were no differences among groups regarding renal stones, episodes of hypercalcemia, or other adverse events.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *LeBoff MS, Chou SH, Ratliff KA, et al. Supplemental vitamin D and incident fractures in midlife and older adults.* N Engl J Med. *2022;387(4):299-309.*

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Medication Abortion a Reasonable Option for Pregnancy of Unknown Location

Clinical Question

Is same-day initiation of medication abortion safe and effective for early pregnancy of unknown location?

Bottom Line

The retrospective cohort study suggests that the same-day start of medication abortion is a reasonable option for more rapid pregnancy termination and exclusion of ectopic pregnancy for

patients who had their last menstrual period within 42 days and initial ultrasonography results showing no gestational sac. Patients with major risk factors for or symptoms suggesting ectopic pregnancy were not eligible for same-day medication abortion. A larger randomized controlled trial is necessary to verify the relative effectiveness and safety of same-day initiation of medication abortion vs. delaying it until the diagnosis of intrauterine pregnancy. (Level of Evidence = 2b)

Synopsis

The study is a retrospective cohort of 452 patients with a positive pregnancy test result seeking medication abortion within 42 days of their last menstrual period. Initial ultrasonography showed no gestational sac (intrauterine or ectopic). Those with major risk factors for ectopic pregnancy (e.g., intrauterine device in situ, prior tubal surgery, prior ectopic pregnancy) were not eligible for same-day treatment and were excluded from the study. Of the study cohort, 55 (12%) had initial hCG testing and received same-day start of medication abortion at the discretion of the treating clinician using mifepristone, 200 mg orally, followed by misoprostol, 800 mcg orally within 48 hours, and serial quantitative human chorionic gonadotropin (hCG) testing. The remaining patients had hCG testing and were not treated until intrauterine or ectopic pregnancy was determined (i.e., delay-for-diagnosis group).

Initial hCG results were received after medication administration. If the hCG level was less than 2,000 mIU per mL (2,000 IU per L), medication abortion could proceed as planned. An hCG level from 2,000 to 2,999 mIU per mL (2,000 to 2,999 IU per L) required repeat ultrasonography on the same day as results were received. If the hCG level was 3,000 mIU per mL (3,000 IU per L) or greater, the patient was referred to the emergency department for further evaluation to exclude ectopic pregnancy. The rate of ectopic pregnancy was 31 out of 452 patients (6.9%; 95% CI, 4.7 to 9.6), 25 of whom presented with symptoms of ectopic pregnancy at initial evaluation, all of which were in the delay-for-diagnosis group. Among the rest of the delay-for-diagnosis group, 161 patients (40.9%) proceeded with the medication abortion regimen and 62 (15.7%) were switched to uterine aspiration.

The primary outcome of median time to diagnosis of pregnancy location was five days in the same-day-treatment group and nine days in the delay-for-diagnosis group ($P = .005$). In the delay-for-diagnosis group, there were nine (2.4%) patients with adverse events (e.g., ruptured ectopic pregnancy, hemorrhage of more than 500 mL, blood transfusion, hospital admission), compared with zero in the same-day treatment group. The analysis of medication abortion effectiveness included only the 170 patients who received it and had known pregnancy outcomes. Successful abortion, defined as at least a 50% decrease in serum hCG level 48 to 72 hours after taking mifepristone or an 80% decrease one week after taking misoprostol, was lower in the same-day treatment group (85% vs. 97%; $P = .013$) and the rate of ongoing pregnancy was higher (10% vs. 3%; $P = .041$). Nonadherence to follow-up did not differ between groups.

Study design: Cohort (retrospective)

Funding source: Foundation

Setting: Outpatient (any)

Reference: *Goldberg AB, Fulcher IR, Fortin J, et al. Mifepristone and misoprostol for undesired pregnancy of unknown location.* Obstet Gynecol. *2022:139(5):771-780.*

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Editor's Note: We strive to provide the best available evidence to counsel patients presenting with an undesired pregnancy, but recognize this is a controversial topic.—Sumi Sexton, MD, Editor-in Chief

Long-term Risks Are Similar for CTA and Invasive Coronary Angiography as Initial Diagnostic Strategy for Stable Chest Pain

Clinical Question

For stable chest pain, what are the risks of using computed tomography angiography (CTA) as an initial diagnostic strategy for identifying obstructive coronary artery disease (CAD)?

Bottom Line

For patients with stable chest pain and an intermediate risk of obstructive CAD, an initial diagnostic strategy using CTA has a similar risk of long-term major adverse cardiovascular events compared with a strategy using invasive coronary angiography. Starting with CTA leads to a decreased need for invasive procedures and fewer procedure-related complications. (Level of Evidence = 1b)

Synopsis

In this study from Europe, the investigators enrolled patients 30 years and older who were referred for invasive coronary angiography for stable chest pain and had an intermediate pretest probability (10% to 60%) of obstructive CAD. Using concealed allocation, study patients were randomized to undergo CTA (n = 1,833) or invasive coronary angiography (n = 1,834) as an initial diagnostic strategy to identify obstructive CAD. Patients found to have obstructive CAD with this initial testing were treated according to guidelines; the others were referred to their physicians

for further management. The two study groups were similar at baseline: median age was 61 years, 56% were female, and one-third had functional stress testing performed before enrollment in the trial. Overall, 25% of patients in each group were identified as having obstructive CAD. The primary outcome was a composite of major adverse cardiovascular events, including cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke. After a median follow-up of 3.5 years, the primary outcome was similar in the two groups (2.1% in the CTA group vs. 3.0% in the invasive coronary angiography group). Only 22% of patients in the CTA group had invasive coronary angiography performed during the initial management period, compared with 97% in the invasive coronary angiography group, resulting in fewer major procedure–related complications with CTA as an initial strategy (0.5% in the CTA group vs. 1.9% in the invasive coronary angiography group; hazard ratio = 0.26; 95% CI, 0.13 to 0.55). During the follow-up period, the CTA group had more functional testing (18.6% vs. 12.9%) but required fewer revascularization procedures (14.2% vs. 18.0%). There was no significant difference in the incidence of angina (less than 10% in both groups) during the last four weeks of follow-up.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Maurovich-Horvat P, Bosserdt M, Kofoed KF, et al.; DISCHARGE Trial Group. CT or invasive coronary angiography in stable chest pain.* N Engl J Med. *2022;386(17):1591-1602.*

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Another Study Fails to Find Platelet-Rich Plasma Injections Effective for Adults With Degenerative Joint Disease of the Knee

Clinical Question

Are platelet-rich plasma injections, single or multiple, more effective than saline injections in adults with early symptomatic degenerative joint disease of the knee?

Bottom Line

The study is higher quality than others and finds leukocyte-poor platelet-rich plasma injections, singly or serially, to be no better than saline injections in improving outcomes in adults with mild, radiographically confirmed degenerative joint disease of the knee. (Level of Evidence = 1b)

Synopsis

The authors point out that platelet-rich plasma injections are controversial because the studies, with largely negative results, have been at high risk of bias. However, the biases in those studies are generally in favor of platelet-rich plasma. The authors thought it was necessary to improve on the previous work. They recruited adults with at least four months of knee pain (with or without swelling) who had mild degeneration on radiography (if plain radiography found no signs of degeneration, magnetic resonance imaging was used to confirm the diagnosis). The participants were randomized to receive three weekly saline injections (n = 28), a single platelet-rich plasma injection followed by two weekly saline injections (n = 47), or three weekly platelet-rich plasma injections (n = 27). The researchers collected blood at each visit to be used as the platelet-rich plasma source or as a procedural disguise and blindfolded each patient to prevent unmasking of the intervention. The authors do not describe if the injections were guided by ultrasound or if a local anesthetic was used. The clinician performing the injections was unmasked but had no other involvement in the study procedures. The researchers evaluated the participants at six weeks, 12 weeks, six months, and 12 months after enrollment. Using intention-to-treat analysis applied to several standardized measures of pain, function, and quality of life, at no point in the study were platelet-rich plasma injections, singly or serially, superior to saline injections. Other than a higher risk of transient localized swelling in the participants who received platelet-rich plasma injections, the authors reported no differences in redness or bruising and that no participant experienced infections. The authors used leukocyte-poor platelet-rich plasma injections, but recent studies have found no meaningful differences between leukocyte-poor and leukocyte-rich injections in people with knee osteoarthritis.

Study design: Randomized controlled trial (double-blinded)

Funding source: Foundation

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: *Lewis E, Merghani K, Robertson I, et al. The effectiveness of leucocyte-poor platelet-rich plasma injections on symptomatic early osteoarthritis of the knee: the PEAK randomized controlled trial.* Bone Joint J. *2022;104-B(6):663-671.*

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Editor's Note: Dr. Ebell is deputy editor for evidence-based medicine for *AFP* and cofounder and editor-in-chief of Essential Evidence Plus, published by Wiley-Blackwell. ■