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This series is coordinated by Sumi Sexton, MD, Associate Deputy Editor.

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Some Benefit to Treating Mild Hypertension to Prevent Stroke, CV Deaths, and Overall Mortality

Clinical Question

What are the benefits of treating mild hypertension?

Bottom Line

Treating mild hypertension over five years decreases the risk of stroke, cardiovascular (CV) death, and overall mortality in a small proportion of patients. The numbers needed to treat (NNT)—the numbers of patients who need to be treated to prevent one additional outcome from occurring—are below. Pay attention to the confidence intervals (CIs), which tell us the best/worst case possibilities. Also, note that some of these intervals are very large, meaning that we cannot place much confidence in the reported NNT. (Level of Evidence = 1a)

Synopsis

The authors used the literature search results of a previous Cochrane meta-analysis and updated it by searching several databases. They included studies that lasted at least one year and evaluated treatment of grade 1 hypertension (range = 140/90 mm Hg to 159/99 mm Hg) in patients with no previous cardiac disease. They were able to use individual patient data (instead of comparing only the results across studies) for a total of

15,266 patients. The risk of bias in the studies was low. The research included single-drug treatment and stepped-care approaches. Over an average five years of treatment, there was no significant decrease in overall CV events, coronary events, or, predictably, heart failure. The likelihood of a stroke, death due to a CV event, or all-cause mortality was lower with treatment (see below). Overall, 5.6% of patients withdrew from treatment because of adverse effects (number needed to treat to harm = 36; 95% CI, 23 to 75). Other NNTs for the five years (95% CI) included: stroke = 173 (108 to 810); CV death = 95 (55 to 1,188); overall mortality = 99 (66 to 273); heart failure = not significant; and coronary events = not significant.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Various (meta-analysis)

Reference: Sundström J, Arima H, Jackson R, et al.; Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of blood pressure reduction in mild hypertension: a systematic review and meta-analysis. *Ann Intern Med.* 2015;162(3):184-191.

ALLEN F. SHAUGHNESSY, PharmD, MMedEd
Professor of Family Medicine
Tufts University
Boston, Mass.

Adding Sitagliptin Does Not Reduce or Increase the Risk of Cardiovascular Outcomes

Clinical Question

Does adding sitagliptin (Januvia) to existing therapy for type 2 diabetes mellitus improve outcomes?

Bottom Line

The glass half full is that sitagliptin does not increase the risk of cardiovascular events in patients with type 2 diabetes. The glass half empty is that it does not reduce the risk, either. And that is the important message: In patients with a mean glycated hemoglobin level of 7.2%, adding sitagliptin at a cost of

approximately \$350 per month does not affect cardiovascular outcomes at all. (Level of Evidence = 1b)

Synopsis

To date, the only drug shown to reduce the risk of cardiovascular events or death in patients with type 2 diabetes is metformin. Sitagliptin is one of a class of dipeptidyl-peptidase-4 inhibitors that reduces glucose levels by decreasing glucagon levels and increasing insulin secretion. A previous meta-analysis found a 25% relative increase in the likelihood of hospitalization for heart failure with the use of these agents. In this study, the researchers recruited adults older than 50 years with type 2 diabetes; current treatment with metformin, pioglitazone (Actos), a sulfonylurea, or insulin; and a glycated hemoglobin level between 6.5% and 8.0%. Patients with two or more recent episodes of severe hypoglycemia were excluded, as were patients with impaired renal function. The patients were randomized to receive 100 mg of sitagliptin daily (50 mg if the glomerular filtration rate was 30 to 50 mL per minute per 1.73 m²) or placebo. The primary outcome was a composite of cardiovascular death, nonfatal myocardial infarction or stroke, or hospitalization for unstable angina.

This was designed as a noninferiority (or “no worse than”) trial, with the stated goal of determining whether sitagliptin was no worse than placebo at causing cardiovascular events. However, the researchers also looked at whether sitagliptin was superior to placebo for preventing cardiovascular events. They recruited 14,735 patients and followed up for a median of three years. The groups were balanced at the beginning of the study, and the mean duration of type 2 diabetes was 12 years, with a mean glycated hemoglobin level of 7.2%. The drug did lower glycated hemoglobin levels a bit, by 0.4% after four months, but that decreased as time went on. There was no difference in the likelihood of the primary composite outcome, of a composite that did not include unstable angina, or of individual cardiovascular outcomes or mortality for both per protocol and intention-to-treat analyses. Death from any cause occurred in

7.5% in the sitagliptin group and in 7.3% in the placebo group, and hospitalization for heart failure occurred in 3.1% in each group.

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Setting: Outpatient (any)

Reference: Green JB, Bethel MA, Armstrong PW, et al.; TECOS Study Group. Effect of sitagliptin on cardiovascular outcomes in type 2 diabetes [published correction appears in *N Engl J Med*. 2015; 373(6):586]. *N Engl J Med*. 2015;373(3):232-242.

MARK H. EBELL, MD, MS
Professor
University of Georgia
Athens, Ga.

An Oral Appliance Does Not Improve Sleep in Patients with Less Severe Sleep Apnea

Clinical Question

Can an oral appliance decrease snoring, improve quality of life, and decrease daytime sleepiness with mild to moderate obstructive sleep apnea?

Bottom Line

An oral appliance does not improve daytime sleepiness or other measures of a good night's sleep. It does, however, decrease apnea scores, snoring, and restless legs. Although not studied, these improvements may be valuable for bed partners who sleep each night enduring patients' lower limb restlessness and breathing irregularities ranging from loud snoring to silence until breathing resumes. (Level of Evidence = 1b)

Synopsis

The Swedish researchers evaluated the effectiveness of an oral appliance in 96 patients with snoring, daytime sleepiness, and mild to moderate obstructive sleep apnea (apnea-hypopnea index < 30). The appliance, worn at night, holds the patient's jaw forward to maintain a patent airway. The patients were assigned, using concealed allocation, to receive a custom-fitted oral appliance or a placebo appliance that did not affect the jaw placement. The patients were not told of their treatment assignment, although an Internet

search could bring up a picture of the appliance for curious patients. Nonetheless, there was no difference in daytime sleepiness (using the Epworth score) between the two groups after four months of treatment. Similarly, the appliance did not improve measures of sleepiness, sleep resistance, quality of life, or functional outcomes of sleep (all measures of the results of sleep). However, snoring, symptoms of restless legs, and the measure of obstructive sleep apnea were improved. These results, although not part of the study, may be valuable for bed partners.

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (specialty)

Reference: Marklund M, Carlberg B, Forsgren L, Olsson T, Stenlund H, Franklin KA. Oral appliance therapy in patients with daytime sleepiness and snoring or mild to moderate sleep apnea: a randomized clinical trial. *JAMA Intern Med.* 2015;175(8):1278-1285.

ALLEN F. SHAUGHNESSY, PharmD, MMedEd
Professor of Family Medicine
Tufts University
Boston, Mass.

CCTA and Radionuclide Stress Testing Similar for Evaluation of Chest Pain

Clinical Question

Is coronary computed tomography angiography (CCTA) better than stress testing for detecting coronary artery disease?

Bottom Line

For the evaluation of chest pain in intermediate-risk patients, CCTA is comparable with myocardial perfusion imaging in its ability to select patients for invasive management. Both modalities are also similar when it comes to downstream resource use and adverse cardiovascular events. CCTA is associated with less radiation exposure. (Level of Evidence = 1b)

Synopsis

The effectiveness of a noninvasive coronary imaging modality lies in its ability to identify patients who will need invasive management. In this study, intermediate-risk patients admitted to telemetry for the evaluation of chest pain who clinically required noninvasive imaging were randomized, using concealed allocation, to receive CCTA or radionuclide stress myocardial perfusion imaging. At baseline, the mean age in both groups was 57 years, two-thirds of the patients were women, and more than 90% were ethnic minorities. Analysis was by intention to treat. The primary outcome was the rate of cardiac catheterization that did not lead to revascularization within one year of the imaging test. There was no significant difference between the two groups for this outcome. However, in a subgroup analysis of patients with significantly abnormal results on their imaging test, there was a nonsignificant trend toward fewer catheterizations without revascularization in the CCTA group (25% vs. 52%; $P = .083$). For secondary outcomes, there were no differences detected between the two groups in length of stay, major adverse cardiovascular events, or downstream resource use, including rehospitalizations and further imaging. The CCTA group had less radiation exposure and reported a better patient experience.

Study design: Randomized controlled trial (nonblinded)

Funding source: Foundation

Allocation: Concealed

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

Reference: Levsky JM, Spevack DM, Travin MI, et al. Coronary computed tomography angiography versus radionuclide myocardial perfusion imaging in patients with chest pain admitted to telemetry: a randomized trial. *Ann Intern Med.* 2015;163(3):174-183.

NITA SHRIKANT KULKARNI, MD
Assistant Professor in Hospital Medicine
Northwestern University
Chicago, Ill. ■