POEMs

Patient-Oriented Evidence That Matters

Screening Smokers for Lung Cancer with Low-Dose CT Decreases Lung Cancer Mortality

Clinical Question

Does low-dose computed tomography (CT) screening for lung cancer prevent mortality in smokers?

Bottom Line

High-quality trials show that low-dose CT screening decreased lung cancer mortality in smokers. (Level of Evidence = 1a)

Synopsis

A systematic review of nine randomized trials that screened smokers for lung cancer using low-dose CT was summarized in another POEM by Essential Evidence. The authors of the current study used references from a systematic review (published in 2019) and conducted a supplemental search of PubMed. They only included randomized trials at low risk of bias (based on the Cochrane Risk of Bias tool) and identified the same nine randomized trials. One was deemed to be at high risk of bias, leaving eight studies with 90,475 participants. The eight studies enrolled people with 20 to 30 or more pack-years of smoking and who ranged from 45 to 75 years of age. The median follow-up ranged from 5.2 years to 10 years, and the lung cancer mortality rate varied from 1.6% to 4.6%. After pooling the results, people screened with low-dose CT were less likely to die from lung cancer (relative risk = 0.81; 95% CI, 0.74 to 0.89; number needed to treat = 250). Although all-cause mortality was slightly lower in the screened group, this was not statistically significant (relative risk = 0.96; 95% CI, 0.92 to 1.01). The mortality data were fairly homogeneous across studies. Other than identifying an overdiagnosis rate of approximately 20%, the authors do not report on the harms of screening.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Unknown/not stated

Setting: Various (meta-analysis)

Reference: *Ebell MH, Bentivegna M, Hulme C. Cancer-specific mortality, all-cause mortality, and overdiagnosis in lung cancer screening trials: a meta-analysis.* Ann Fam Med. *2020;18(6): 545-552.*

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SGLT2 Inhibitors Improve All-Cause and Cardiovascular Mortality in Patients Regardless of Diabetes or Heart Failure Status

Clinical Question

What effect do sodium-glucose cotransporter-2 (SGLT2) inhibitors have on mortality and cardiovascular and renal outcomes in patients with and without diabetes mellitus, heart failure, or kidney disease?

Bottom Line

SGLT2 inhibitors—medications ending in -flozin, such as canagliflozin (Invokana), dapagliflozin (Farxiga), empagliflozin (Jardiance), and ertugliflozin (Steglatro)—reduce all-cause and cardiovascular mortality in patients regardless of the presence of type 2 diabetes, heart failure, or chronic kidney disease. Similar mortality reduction occurs in patients with diabetes regardless of comorbid heart failure, and in patients with heart failure regardless of the presence of diabetes. SGLT2 inhibitors also reduce the progression of renal disease in all patients. (Level of Evidence = 1a–)

Synopsis

Two researchers independently searched three databases, including Cochrane CENTRAL, with the bibliographies of identified studies and abstracts of major cardiology meetings, to identify randomized studies in any language that evaluated the impact of treatment with an SGLT2 inhibitor in patients with or without heart failure or type 2 diabetes. Two researchers independently abstracted the data. The researchers followed PRISMA guidelines and assessed the quality of evidence. They included eight studies of 59,747 patients, comprising three studies that included patients without diabetes. Treatment with an SGLT2 inhibitor reduced the risk of mortality due to all causes (hazard ratio

[HR] = 0.84; 95% CI, 0.78 to 0.91), cardiovascular mortality (HR = 0.84; 95% CI, 0.76 to 0.93), and hospitalization for heart failure (HR = 0.69; 95% CI, 0.64 to 0.74) compared with placebo, and reduced a composite of end-stage kidney disease, a doubling of the serum creatinine level, and kidney-related mortality (HR = 0.62; 95% CI, 0.56 to 0.70). There were similar mortality and renal benefits for patients with or without diabetes and patients with or without heart failure. Heterogeneity among study results was moderate for mortality outcomes and low for heart failure hospitalization and kidney outcomes.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Salah HM, Al'Aref SJ, Khan MS, et al. Effect of sodium-glucose cotransporter 2 inhibitors on cardiovascular and kidney outcomes–systematic review and meta-analysis of randomized placebo-controlled trials.* Am Heart J. *2020;232:10-22.*

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Early Introduction of Dietary Gluten Delays the Diagnosis of Celiac Disease in Breastfed Infants

Clinical Question

Does introducing gluten to exclusively breastfed infants at four months of age, compared with six months of age, reduce the prevalence of celiac disease in the first three years of life?

Bottom Line

The introduction of dietary allergens, including gluten, to exclusively breastfed infants at four months of age, compared with six months of age, delays the prevalence of celiac disease at three years of age. (Level of Evidence = 2b)

Synopsis

The Enquiring About Tolerance study was an open-label trial that randomized exclusively breastfed infants in Wales and England to receive dietary allergens at four months of age (early introduction; n = 652) or at six months of age (control; n = 651). The dietary allergens included cow's milk, hen's eggs, peanuts, sesame, cod fish, and wheat. In this component of the study, the researchers gave two wheat-based biscuits (4 g of wheat; 3.2 g of gluten) every week to the infants randomized to early gluten introduction. During the three years of follow-up, the parents were asked to complete dietary questionnaires at various intervals. All study participants were tested for antitransglutaminase type 2 antibodies and those with abnormal values were referred to gastroenterologists for final diagnosis. During the follow-up period, 72 infants were lost to follow-up (7% of the early introduction group and 4% of the control group) and an additional 15% in each group had either no blood drawn or an insufficient quantity of blood drawn. By three years of age, nine children, six of whom had symptoms attributable to celiac disease, had elevated antitransglutaminase type 2 antibodies and were referred to gastroenterologists. Three of the children had biopsies, two of which confirmed celiac disease. Six of the symptomatic children improved after being fed gluten-free diets. The authors concluded that none of the children in the early introduction group had celiac disease compared with seven children (1.4%) in the control group (number needed to treat = 72; 95% CI, 39 to 167).

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Uncertain

Setting: Population-based

Reference: *Logan K, Perkin MR, Marrs T, et al. Early gluten introduction and celiac disease in the EAT study: a prespecified analysis of the EAT randomized clinical trial.* JAMA Pediatr. *2020;174(11):1041-1047.*

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Colchicine Reduces MI and Revascularization in Patients with Established Coronary Artery Disease

Clinical Question

Does colchicine reduce the risk of cardiovascular events in patients with chronic coronary artery disease?

Bottom Line

Colchicine, 0.5 mg daily, significantly reduces the risk of myocardial infarction (MI) and ischemia-driven revascularization. For the compositive outcome of cardiovascular death, MI, or ischemic

stroke, the number needed to treat (NNT) was 67 over 29 months. The cost is $8 per month in Canada and $65 per month in the United States. There was increased noncardiovascular mortality, but no clear pattern with regard to cause of death. (Level of Evidence = 1b)

Synopsis

Colchicine has been shown to reduce a broad composite of cardiovascular outcomes in patients with recent MI, and a small open-label trial of patients with chronic coronary artery disease showed a similar outcome. The authors identified 6,528 patients, 35 to 82 years of age, with documented coronary artery disease on computed tomography angiogram, by invasive angiography, or with a coronary artery calcium score of at least 400 Agatston units. Patients with at least moderate renal disease, severe valvular heart disease, or heart failure were excluded, as were those who were intolerant of colchicine. The study began with an open-label run-in period that excluded 15% of patients, largely because of drug adverse effects. The remaining 5,522 were randomized to receive colchicine, 0.5 mg once daily, or placebo. Analysis was by intention to treat, and groups were similar at baseline. The patients' mean age was 66 years, 15% were women, 12% were smokers, and 18% had diabetes. Most had a previous revascularization, largely stenting. All patients were from the Netherlands (66%) or Australia (34%). Patients were followed up for a median of 29 months, and 10.5% in each group stopped taking the medication or placebo. There were no differences between groups in withdrawals or perceived adverse effects. The authors examined four different composite outcomes. They found a reduction in the primary composite of cardiovascular death, MI, ischemic stroke, or coronary revascularization due to ischemia with colchicine (6.8% vs. 9.6%; $P < .001$; NNT = 36 for 29 months). The composite that dropped revascularization showed a somewhat smaller difference between groups, but a statistically and clinically significant result (4.2% vs. 5.7%; $P = .007$; NNT = 67 for 29 months). Regarding individual endpoints, MI and ischemia-driven coronary revascularization were significantly reduced with colchicine, with no significant difference in ischemic stroke, cardiovascular mortality, or all-cause mortality. There were trends toward fewer cardiovascular deaths, but more noncardiovascular deaths (1.9% vs. 1.3%; hazard ratio = 1.51; 95% CI, 0.99 to 2.31). Myalgias were slightly more common in the colchicine group (21.2% vs. 18.5%; $P < .05$; number needed to harm = 37 over 29 months).

Study design: Randomized controlled trial (double-blinded)

Funding source: Government

Allocation: Concealed

Setting: Outpatient (any)

Reference: *Nidorf SM, Fiolet ATL, Mosterd A, et al.; LoDoCo2 Trial Investigators. Colchicine in patients with chronic coronary disease.* N Engl J Med. *2020; 383(19):1838-1847.*

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