POEMs

Patient-Oriented Evidence That Matters

SGLT2 Inhibitors or GLP-1 Receptor Agonists Reduce Cardiovascular Outcomes in Patients with Type 2 Diabetes

Clinical Question

Do sodium-glucose cotransporter 2 (SGLT2) inhibitors or glucagon-like peptide-1 (GLP-1) receptor agonists reduce patient-oriented outcomes in patients with type 2 diabetes mellitus?

Bottom Line

SGLT2 inhibitors, the diabetes medications ending in -flozin (such as dapagliflozin [Farxiga]), and GLP-1 receptor agonists, the -tide medications (such as dulaglutide [Trulicity]), decrease cardiovascular and renal outcomes to a greater extent than placebo or other treatments. They should be considered in addition to metformin and other glucose-lowering treatments for most patients with type 2 diabetes. (Level of Evidence = 1a)

Synopsis

The researchers searched three databases, including Cochrane CENTRAL, to identify randomized trials that compared SGLT2 inhibitors or GLP-1 receptor agonists with other treatment approaches. Two researchers independently screened studies for inclusion, extracted the data, and assessed the studies for risk of bias. Because there are a handful of drugs in each class that have not been directly compared with one another, the researchers completed a network meta-analysis, which combines direct and indirect evidence across studies to allow cross-comparison. They identified 764 trials including 421,346 patients, which allowed a view of the results according to patient baseline cardiovascular risk. The quality of the studies was generally high, with no heterogeneity for most outcomes. Both drug classes lowered all-cause mortality, cardiovascular mortality, nonfatal myocardial infarction, and kidney failure. SGLT2 inhibitors were more effective at reducing hospital admission, and GLP-1 receptor agonists were more likely to reduce nonfatal stroke. The absolute benefit of treatment varied based on underlying cardiac risk; for example, two to five fewer deaths per 1,000 patients over five years in patients at low risk and 24 to 48 fewer deaths per 1,000 patients at high risk. A calculator is available (https://magicevidence.org/match-it/200820dist/#!/) that estimates benefit at various risk levels.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Self-funded or unfunded

Setting: Various (meta-analysis)

Reference: *Palmer SC, Tendal B, Mustafa RA, et al. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials.* BMJ. *2021;372:m4573.*

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More than One-Half of Adults Hospitalized for COVID-19 Still Report Significant Symptoms at Four Months Postdischarge

Clinical Question

Are adult survivors of COVID-19 still experiencing significant symptoms four months or more after hospital discharge?

Bottom Line

This study found that more than one-half of the adults (51%) who had been hospitalized for COVID-19 reported a significant amount of persistent symptoms four months after discharge. (Level of Evidence = 1b)

Synopsis

The investigators identified a cohort of adult patients, 18 years or older, who had been admitted to a hospital in France for COVID-19 from March 1, 2020, to May 29, 2020. Inclusion criteria were survival at four months after hospital discharge and a diagnosis of SARS-CoV-2 infection by polymerase chain reaction or clinical features associated with typical findings on computed tomography (CT) of the lung. Of the 834 eligible patients, 478 (57%) consented to respond by telephone to a questionnaire about their general condition and respiratory, cognitive, and neurologic symptoms. All patients who had been admitted to the intensive care unit (ICU) and those with continued symptoms were invited for an in-person evaluation. All patients seen in person received high-resolution CT of the lungs and psychometric testing, including an interview with a neuropsychologist. All those admitted to the ICU underwent transthoracic echocardiography. More than one-half (51%) of the patients reported at least one symptom that did not exist before their COVID-19 infection, including fatigue (31.1%), memory difficulties (17.5%), dyspnea (16.3%), and persistent paresthesia (12.1%). Psychometric testing and evaluation confirmed cognitive impairment in 38.4% of patients. Persistent abnormalities on CT and echocardiography were also commonly noted, especially among patients who required admission to the ICU.

Study design: Cohort (prospective)

Funding source: Government

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

Reference: *Writing Committee for the COMEBAC Study Group, Morin L, Savale L, Pham T, et al. Four-month clinical status of a cohort of patients after hospitalization for COVID-19.* JAMA. *2021;325(15):1525-1534.*

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Inhaled Budesonide Reduces the Risk of Emergency Department Evaluation or Hospitalization in Early COVID-19

Clinical Question

Does inhaled budesonide (Pulmicort) safely reduce the likelihood of requiring emergency department consultation or hospitalization in patients with new-onset, symptomatic COVID-19?

Bottom Line

Inhaled budesonide, 800 mcg twice daily, significantly reduces the likelihood that patients with early COVID-19 will require emergency department evaluation or hospitalization (number needed to treat [NNT] = 7 to 8). This is a widely available, relatively inexpensive drug with the potential for great benefit. There are seven other trials underway looking at inhaled budesonide or ciclesonide (Alvesco); the results are urgently awaited. (Level of Evidence = 1b–)

Synopsis

From previous randomized trials, we know that oral corticosteroids such as methylprednisolone are only helpful in more severely ill patients with COVID-19, and there was a trend toward worse outcomes in those with mild disease, perhaps by suppressing immune function systemically. Observational studies have shown an association between inhaled corticosteroids and better outcomes in patients with mild disease.

The researchers identified adults with less than seven days of cough, and either fever or anosmia or both (N = 146). They randomized the patients to receive budesonide using 400-mcg actuations, with two actuations twice daily, or usual care. A nurse did a swab for SARS-CoV-2, which was positive for 94% of patients. Groups were balanced at randomization. Four patients withdrew consent before receiving the allocated intervention, one in each group needed urgent care before they could be swabbed, and one withdrew because they found the inhaler too burdensome, leaving a per-protocol population of 139 patients. Patients in the budesonide group were told to stop using the inhaler when they had recovered (median = seven days), and all patients were followed up for 28 days.

It does not appear that outcomes were assessed in a masked manner, and the study was stopped early because of the large benefit. In the entire population, the primary outcome of urgent emergency department visits or hospitalization occurred less often in the budesonide group using an intention-to-treat analysis (3% vs. 15%; P = .009; NNT = 8). The magnitude of benefit was similar in the per-protocol population (1% vs. 14%; NNT = 7). Time to recovery was also approximately one day faster in the budesonide

group, and symptom resolution was more rapid. Adverse events (sore throat [four patients] and dizziness [one patient]) were minor and self-limited. The open-label design, early trial shutdown, and failure to mask outcome assessment are limitations, but the magnitude of benefit was large enough that this treatment should be considered for all patients with mild symptoms of COVID-19.

Study design: Randomized controlled trial (single-blinded)

Funding source: Industry and government

Allocation: Concealed

Setting: Emergency department

Reference: *Ramakrishnan S, Nicolau DV Jr., Langford B, et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial [published online April 9, 2021].* Lancet Respir Med. *Accessed June 4, 2021. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00160-0/fulltext*

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Tighter Blood Pressure Control Does Not Increase the Likelihood of Orthostatic Hypotension

Clinical Question

Are lower blood pressure goals associated with a higher likelihood of orthostatic hypotension?

Bottom Line

Orthostatic hypotension, a drop of 20 mm Hg systolic or 10 mm Hg diastolic after moving from sitting to standing, was not associated with more intensive treatment of blood pressure and may be less likely to occur with intensive treatment. (Level of Evidence = 1a)

Synopsis

The authors assembled randomized trials from three databases, including Cochrane CENTRAL, that compared intensive goals with less intensive goals for blood pressure treatment. They included studies written in any language. Two investigators independently abstracted the articles and evaluated them for quality. All studies were open label, and there was a risk of detection bias because investigators were aware of the patients' treatments. The studies enrolled 18,466 patients. Intensive blood pressure treatment was associated with a lower risk for orthostatic hypotension, but not by much (odds ratio = 0.93; 95% CI, 0.86 to 0.99). The likelihood of orthostatic hypotension was not different with active treatment compared with placebo. The effect did not differ if the patient had (or did not have) orthostatic hypotension before randomization. The original studies did not evaluate for rates of lightheadedness, syncope, or falls.

Study design: Meta-analysis (randomized controlled trials)

Funding source: Government

Setting: Various (meta-analysis)

Reference: *Juraschek SP, Hu J-R, Cluett JL, et al. Effects of intensive blood pressure treatment on orthostatic hypotension: a systematic review and individual participant-based meta-analysis.* Ann Intern Med. *2021;174(1):58-68.*

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