POEMs

Patient-Oriented Evidence That Matters

Thromboembolism Recurrence Likely; Consider It a Chronic Disease

Clinical Question

After stopping anticoagulation for venous thromboembolism (VTE), what is the likelihood of a subsequent VTE over 10 years?

Bottom Line

Perhaps it is time to start thinking about VTE as a chronic disease. Approximately one in 10 patients that have a VTE will have a second VTE over the next 12 months and almost four in 10 will have a second VTE over 10 years. The risk of developing deep venous thrombosis is 6.2% over one year and 25.1% over 10 years. The risk for pulmonary embolism is 3.3% over one year and 11.2% over 10 years. (Level of Evidence = 1a–)

Synopsis

Researchers assembled 18 studies involving 7,515 patients by searching three databases for studies in any language that reported follow-up data on patients with a first, unprovoked VTE who were treated for at least three months and then followed up for at least nine months (range = two to 10 years). The authors included observational and intervention trials. All studies were evaluated as being high quality. Over the first year following discontinuation of treatment, 10.3% of patients had a second VTE, 6.2% developed deep venous thrombosis, and 3.3% developed pulmonary embolism. Over 10 years, the cumulative incidence of VTE was 36.1% (95% CI, 27.8 to 45.0), deep venous thrombosis was 25.1% (95% CI, 17.2 to 33.7), and pulmonary embolism was 11.2% (95% CI, 5.9 to 18.4). The confidence intervals for the 10-year figures are wide (and therefore the estimate is inexact) because only three studies of 1,975 patients followed patients for 10 years, with dropouts along the way. There was some significant heterogeneity among the studies for some of the outcomes that could not be explained by initial VTE site, sex, or use of aspirin following anticoagulant treatment.

Study design: Meta-analysis (other)

Funding source: Government

Setting: Various (meta-analysis)

Reference: *Khan F, Rahman A, Carrier M, et al.; MARVELOUS Collaborators. Long term risk of symptomatic recurrent venous thromboembolism after discontinuation of anticoagulant treatment for first unprovoked venous thromboembolism event: systematic review and meta-analysis.* BMJ. *2019;366:l4363.*

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Linagliptin and Glimepiride Equally Effective for Adults with Type 2 Diabetes Mellitus

Clinical Question

Is linagliptin (Tradjenta) noninferior to glimepiride (Amaryl) in adults with poorly controlled type 2 diabetes mellitus?

Bottom Line

This study found that linagliptin is noninferior to glimepiride for reducing the risk of cardiovascular death, myocardial infarction, and stroke in adults with type 2 diabetes at an increased risk of cardiovascular disease. Although hypoglycemic events occurred significantly more often in patients treated with glimepiride, study-targeted levels of A1C (mean 7.2%) were consistent with levels previously shown to unnecessarily increase the risk of severe hypoglycemia and premature mortality. The Good Rx price (www.goodrx.com; accessed September 19, 2019) for a one-month supply of linagliptin is $378 vs. $3 for glimepiride. (Level of Evidence = 1b)

Synopsis

Clinicians have many options for second-line treatment to metformin monotherapy in adults with poorly controlled type 2 diabetes. The investigators identified adults with type 2 diabetes, an A1C of 6.5% to 8.5%, and high cardiovascular risk (e.g., established cardiovascular disease, multiple risk factors including hypertension, smoking, hyperlipidemia, age greater than 69 years, evidence of microvascular complications). Eligible patients randomly received (concealed allocation assignment) linagliptin (5 mg per day) or glimepiride

(1 to 4 mg per day, titrated to achieve a target A1C of less than 7.5%). Additional medications were added as needed for persistent hyperglycemia. Individuals masked to treatment group assignment assessed all outcomes. Complete follow-up occurred for 96% of participants for a mean of 6.3 years.

Using intention-to-treat analysis, no significant difference occurred between the groups treated with linagliptin vs. glimepiride in the primary end point of cardiovascular death, myocardial infarction, or stroke (11.8% vs. 12.0%, respectively). There was also no significant difference between the two groups in all-cause mortality or study drop-out rates due to adverse events. Weight gain was significantly higher in the glimepiride group (3.4 lb [1.54 kg]). Rates of hypoglycemia, including severe events, were also increased in the glimepiride group (number needed to harm = 3 to 4 for at least one episode).

Study design: Randomized controlled trial (double-blinded)

Funding source: Industry

Allocation: Concealed

Setting: Outpatient (primary care)

Reference: *Rosenstock J, Kahn SE, Johansen OE, et al.; CAROLINA Investigators. Effect of linagliptin vs glimepiride on major adverse cardiovascular outcomes in patients with type 2 diabetes: the CAROLINA randomized clinical trial.* JAMA. *2019;322(12):1155-1166.*

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Fewer Severe Exacerbations in Patients with Mild to Moderate Asthma Treated with As-Needed Budesonide Plus Formoterol Compared with Maintenance Budesonide

Clinical Question

Is as-needed use of a long-acting beta-agonist plus corticosteroid as effective as maintenance, low-dose corticosteroids in preventing severe exacerbations in patients with mild to moderate asthma?

Bottom Line

Patients with mild to moderate asthma only need relief treatment. In this study, patients taking the combination of budesonide/formoterol (Symbicort) as needed had slightly fewer severe exacerbations than patients treated with twice daily budesonide (Pulmicort). A recent POEM (https://www.essentialevidenceplus.com/content/poem/210808) reached similar conclusions. (Level of Evidence = 2b)

Synopsis

The researchers recruited adults with self-reported mild asthma who were taking only reliever therapy, either short-acting beta-agonists (SABAs) alone or SABAs plus low to moderate doses of inhaled corticosteroids, in the 12 weeks before randomization. They randomized patients (not concealed) to receive either relief therapy alone with one puff of budesonide 200 mcg/formoterol 6 mcg per inhalation (n = 437) or maintenance therapy with one puff twice daily of budesonide 200 mcg per inhalation (n = 447) and for rescue to use two puffs as needed for terbutaline 250 mcg per inhalation. Everyone except the statistician knew what interventions were assigned. The researchers evaluated the patients six times over a year. At baseline, the participants in each group were similar. Consistent with recruiting patients with mild asthma, the primary outcome, the number of exacerbations rarely occurred in either group. The researchers used standard criteria for determining if an exacerbation was severe: at least three days of systemic corticosteroids, or hospital admission or emergency department visit requiring systemic corticosteroids. Over the course of a year, the patients treated only as needed experienced fewer exacerbations (0.12 per year) compared with the maintenance-treated patients (0.17 per year). Although the difference was statistically significant, this does not look like an important difference. Roughly one-third of patients in each group also reported nasopharyngitis.

Study design: Randomized controlled trial (nonblinded)

Funding source: Government

Allocation: Unconcealed

Setting: Outpatient (any)

Reference: *Hardy J, Baggott C, Fingleton J, et al.; PRACTICAL study team. Budesonide-formoterol reliever therapy versus maintenance budesonide plus terbutaline reliever therapy in adults with mild to moderate asthma (PRACTICAL): a 52-week, open-label, multicentre, superiority, randomised controlled trial.* Lancet. *2019;394(10202):919-928.*

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Guideline for Chronic Diarrhea: Screening for IBD and Celiac Disease Is In, Screening for Ova and Parasites Is Out

Clinical Question

What workup should be considered for patients with chronic diarrhea?

Bottom Line

Although an algorithm to guide the workup is not offered, the American Gastroenterological Association suggests the following tests for patients with chronic diarrhea (i.e., watery diarrhea for at least four weeks): fecal calprotectin or fecal lactoferrin to screen for inflammatory bowel

disease (IBD), and testing for giardiasis, celiac disease, and bile acid diarrhea. They do not recommend screening for ova and parasites unless the patient has come from a high-risk area. They also recommend against using erythrocyte sedimentation rate (ESR) and C-reactive protein to screen for IBD. (Level of Evidence = 5)

Synopsis

This guideline was developed by a team comprising two gastroenterologists, a primary care physician, and a methodologist, but no patient representative. They performed a systematic review and graded the level of evidence using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) methodology. One team member reported financial relationships with companies that make diagnostic or treatment products for gastrointestinal disorders. In patients with chronic diarrhea, the group suggests screening for IBD using fecal calprotectin or fecal lactoferrin, but not ESR or C-reactive protein (conditional recommendation based on low-quality evidence). They also recommend testing for *Giardia* (strong recommendation based on high-quality evidence), but recommend against testing for ova or other parasites unless the patient is from or has traveled to a high-risk area (conditional recommendation based on low-quality evidence). They also suggest testing for celiac disease (strong recommendation based on moderate-quality evidence) and testing for bile acid diarrhea by assay or by an empiric trial of a bile acid binder (conditional recommendation based on low-quality evidence). The group does not recommend a specific order of testing.

Study design: Practice guideline

Funding source: Foundation

Setting: Various (guideline)

Reference: *Smalley W, Falck-Ytter C, Carrasco-Labra A, et al. AGA clinical practice guidelines on the laboratory evaluation of functional diarrhea and diarrhea-predominant irritable bowel syndrome in adults (IBS-D).* Gastroenterology. *2019;157(3):851-854.*

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