POEMs

Patient-Oriented Evidence That Matters

Limited Data: Deprescribing Is Safe, But at the Risk of Symptom Recurrence

Clinical Question

Is deprescribing long-term medication safe and effective?

Bottom Line

The limited rigorous data on deprescribing suggest that many patients can safely stop unnecessary medication, but symptom relapse is significant. (Level of Evidence = 1a–)

Synopsis

The authors searched PubMed and EMBASE for randomized trials that compared deprescribing (i.e., the process of withdrawing unnecessary medications) with placebo or usual care. Two authors independently assessed the inclusion of studies and the risk of bias for each study. Although they reviewed the reference lists of the included studies, the authors do not describe a formal search or formal assessment of the potential of publication bias. They included 27 studies, each of which included between 20 and 2,471 patients. Sixteen of the studies used placebo and 11 used usual care as the comparator. The studies evaluated a wide range of drug classes, including antihypertensives, antipsychotics, corticosteroids, and so forth. The authors reasonably decided against pooling data because of the marked variability in the target drugs, target group (mean age varied between 50 and 89 years of age), and follow-up duration (four weeks to five years). Only 10 of the studies were of low risk of bias. The rate of successful deprescribing varied from 20% to 100%; in 19 of the studies the rate of successful deprescribing exceeded 50%. Sixteen of the studies reported on symptom relapse or resumption of deprescribed medications (range 0% to 80%). Among the nine placebo-controlled studies reporting on relapse, five found significantly greater relapse in the intervention groups (rate difference ranged from 14% to 50%). The included studies found that adverse events were infrequent.

Study design: Systematic review

Funding source: Self-funded or unfunded

Setting: Outpatient (any)

Reference: *Thio SL, Nam J, van Driel ML, Dirven T, Blom JW. Effects of discontinuation of chronic medication in primary care: a systematic review of deprescribing trials.* Br J Gen Pract. *2018;68(675): e663-e672.*

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Simple Clinical Prediction Rule Determines Risk of Heart Failure with Preserved Ejection Fraction

Clinical Question

Which patients with unexplained dyspnea are more likely to have heart failure with preserved ejection fraction (HFPEF [diastolic heart failure]) as the cause?

Bottom Line

A simple clinical prediction rule using noninvasive data can identify patients at low, moderate, and high risk for HFPEF. Although validated in a separate group of patients, the validation group was from the same center, so prospective validation should still be performed in a separate

population by another group of investigators. (Level of Evidence = 2b)

Synopsis

The authors identified patients who had been referred to the Mayo Clinic for unexplained dyspnea and underwent invasive testing. The reference standard was right-sided coronary catheterization, with measurement of pressures at rest and, if necessary, during exercise. Predictors were ascertained by chart review. This is ordinarily a red flag, but in this case the predictors were relatively unambiguous (e.g., body mass index, number of medications for hypertension) and the chart review was done in parallel by two investigators using clear prespecified definitions for each variable. The derivation population consisted of 414 consecutive patients, 64% of whom had HFPEF. The validation population was 100 consecutive patients at the same center, with a prevalence of HFPEF of 61%. The mean age of participants was 56 years for those with noncardiac dyspnea and 68 years for those with HFPEF; 60% were women. Logistic regression was used to identify independent predictors, and points were assigned to each predictor based on the beta-coefficient. The independent predictors were body mass index greater than 30 kg per m^2 (2 points), taking two or more antihypertensive drugs (1 point), paroxysmal or persistent atrial fibrillation (3 points), Doppler echocardiogram with pulmonary artery systolic pressure greater than 35 mm Hg, 60 years or older, and Doppler echocardiogram showing an E/e ratio of more than nine. In the validation group, the observed proportion with HFPEF ranged from 0% with 0 points to more than 90% with at least 6 points. The authors suggest that the diagnosis can be provisionally ruled out for patients with 0 or 1 point, ruled in for patients with more than 5 points, and that further testing is needed for those with 2 to 5 points.

Study design: Decision rule (validation)

Funding source: Government

Setting: Outpatient (specialty)

Reference: *Reddy YN, Carter RE, Obokata M, Redfield MM, Borlaug BA. A simple, evidence-based approach to help guide diagnosis of heart failure with preserved ejection fraction.* Circulation. *2018;138(9):861-870.*

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Risk of GI Bleeding Highest with Rivaroxaban, Lower with Apixaban, and Lowest with PPI Cotherapy

Clinical Question

Which oral anticoagulants have the highest risk of causing upper gastrointestinal (GI) tract bleeding, and does cotherapy with a proton pump inhibitor (PPI) lower that risk?

Bottom Line

Among patients using oral anticoagulants alone, the risk of hospitalization for upper GI tract bleeding is highest with rivaroxaban (Xarelto) and lowest with apixaban (Eliquis). Cotherapy with a PPI reduces the risk among patients using any oral anticoagulant. (Level of Evidence = 2b)

Synopsis

The risk of serious upper GI tract bleeding associated with individual anticoagulant drug choice (with or without PPI cotherapy) is uncertain. These investigators analyzed the U.S. Medicare beneficiary files of patients 30 years or older who initiated oral anticoagulation treatment with apixaban, dabigatran (Pradaxa), rivaroxaban, or warfarin (Coumadin). The primary outcome of interest was hospitalization for upper GI tract bleeding that is potentially preventable by PPI cotherapy, including esophagitis, peptic ulcer disease, and gastritis. Multiple analyses occurred to control for covariates, including cardiovascular disease, low-dose aspirin prophylaxis, frailty, alcohol abuse, liver disease, history of previous upper GI tract bleeding, current use of other medications that affect bleeding risk (e.g., nonsteroidal anti-inflammatory drugs), and age and other demographic factors.

A total of 1,643,123 patients had 1,713,183 new episodes of oral anticoagulant treatment from January 1, 2011, through September 30, 2015. The mean age of the patients was 76.4 years and the indication for anticoagulation was atrial fibrillation for 74.9% of them. In patients receiving anticoagulant treatment without PPI cotherapy, the adjusted incidence of hospitalization for upper GI tract bleeding was significantly higher in those who received rivaroxaban compared with those who received dabigatran, warfarin, or apixaban (144 per 10,000 person-years vs. 120, 113, and 73, respectively). For patients receiving anticoagulant treatment with PPI cotherapy, the adjusted incidence of severe upper GI tract bleeding was

lower than for patients not receiving cotherapy for all anticoagulants (76 per 10,000 per year vs. 115 per 10,000 per year; number needed to treat = 256), although still significantly highest with rivaroxaban.

Study design: Cohort (retrospective)

Funding source: Government

Setting: Outpatient (any)

Reference: *Ray WA, Chung CP, Murray KT, et al. Association of oral anticoagulants and proton pump inhibitor cotherapy with hospitalization for upper gastrointestinal tract bleeding.* JAMA. *2018;320(21):2221-2230.*

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FIT Has Similar Yield as Colonoscopy for Colorectal Cancer and Advanced Adenoma Over 10 Years

Clinical Question

What is the yield of a screening program based on fecal immunochemical testing (FIT) every two years for 10 years?

Bottom Line

Over a 10-year period, the rates of detection of colorectal cancer (CRC) and advanced adenomas using FIT are similar to those seen in studies of screening colonoscopy. This does not prove that FIT reduces morbidity and mortality due to CRC as effectively as colonoscopy. Modeling concludes that a FIT-based screening program will result in half as many colonoscopies as a program based on colonoscopy, a significant reduction in cost, burden, and harm of screening. (Level of Evidence = 2b)

Synopsis

The two most widely recommended strategies for CRC screening are FIT and colonoscopy. Several trials are currently underway to compare these approaches, with cancer-specific mortality as the primary outcome. Until then, we have to rely on observational studies and modeling to understand the benefit of each approach. Although colonoscopy is more sensitive than FIT, especially for the detection of advanced adenomas, what matters is the performance over a long-term screening program, not one-time accuracy. This study reports the results of five rounds of biennial FIT in a screening population 50 to 69 years of age in the Veneto region of northern Italy. The rate of detection of CRC was the highest in the first round of screening when prevalent lesions were detected (3.3 per 1,000 people), declining in subsequent rounds and stabilizing after the third round (approximately 1 per 1,000 people). Between rounds three and six, the CRC detection rate declined slightly from 0.95 to 0.84 per 1,000 people. A similar pattern was seen for advanced adenomas, declining from 15.9 per 1,000 people to approximately 10 per 1,000 people in subsequent rounds. Over the 10-year study period, the cumulative rate of positive FIT results was 25% for men and 17.6% for women. The cumulative rate for advanced adenoma was 60 per 1,000 people, and for CRC was 8.5 per 1,000 people. These rates are similar to those seen in studies of colonoscopy in Italy and the United States.

Study design: Cohort (prospective)

Funding source: Government

Setting: Population-based

Reference: *Zorzi M, Hassan C, Capodaglio G, et al. Long-term performance of colorectal cancer screening programmes based on the faecal immunochemical test.* Gut. *2018;67(12):2124-2130.*

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