Clinical Briefs in Primary Care™

Evidence-based updates in primary care medicine

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Long-Term Payoff of Bariatric Surgery

Source: Arterburn DE, et al. *JAMA* 2015; 313:62-70.

The benefits of bariatric surgery are gaining new levels of respect as long-term evidence of favorable outcomes — other than cosmetic — continue to accrue. Indeed, in the population of obese diabetics, bariatric surgery is one of the only interventions documented to improve all-cause mortality.

New support for the positive impact of bariatric surgery comes from a retrospective cohort study of patients (n = 2500) who had undergone bariatric surgery in Veteran's Administration (VA) hospitals throughout the United States in the interval from 2000-2011. Survival in these patients was compared with a control group matched for age, body mass index (BMI), and type 2 diabetes. The mean pre-surgical BMI in the BAR group was 47, and mean age was 52 years.

In the follow-up intervals from years 1-5 and, years later, 5-14, there was a distinct advantage favoring bariatric surgery patients, who enjoyed a greater than 50% lower all-cause mortality than matched controls.

Because this study is retrospective, it cannot be regarded as definitive in proving that bariatric surgery reduces mortality. Additionally, because these data were collected from VA hospitals, the patient population was disproportionately male (74%). Nonetheless, the accumulating evidence consistently points to favorable effects of bariatric surgery upon mortality. ■

Colon Cancer Screening By Stool DNA Testing

Source: *JAMA* 2014;312:2566-2567.

Recent guidelines issued by the American Cancer Society and American Society of Gastroenterology recommend colonoscopy as the preferred screening method for colon cancer, but wisely include the philosophy, "The best colon cancer screening test is the test you can get done!" — reflecting the relative reticence shown by many Americans to undergo colonoscopy. Computed tomography colonography compares very favorably to colonoscopy, yet many insurers are not willing to pay for it.

Stool DNA testing (trade name Cologuard) is based on the observation that colon cancers consistently shed cells that contain cancer markers in the stool (example names of such markers include KRAS, NDRG4, BMP3). In the most recent iteration of stool DNA testing kits, an assay for human hemoglobin is also included (eliminating the need for dietary restriction prior to stool testing).

The process if fairly simple: a collection kit is sent to the patient's home, the specimen is mailed back, and if either the colon cancer markers or the human hemoglobin test return positive, the patient needs follow-up colonic evaluation (e.g., colonoscopy). Some patients (and clinicians) may feel so reassured by negative stool DNA testing that they feel comfortable to stop screening at that point. Unfortunately, even though stool DNA testing is very sensitive for colon cancer compared to colonoscopy (sensitivity = 92%), it is much less sensitive for precancerous lesions. Additionally, some false-positives occur with stool DNA testing.

Despite these limitations, stool DNA testing provides a viable way to do colon cancer screening for persons unwilling to undergo other screening methods. Negative stool DNA screening will be so reassuring to some patients that they will elect not to pursue further, more definitive screening. ■

Intracranial Hemorrhage Risk: Are Novel Oral Anticoagulants Meaningfully Better Than Warfarin?

Source: Vespa PM. *JAMA* 2015;312: 2562-2563.

Clinicians have commonly overestimated the risk of intracerebral hemorrhage (ICH) during anticoagulant therapy. Indeed, such misapprehensions have sometimes led to failure to employ warfarin (and probably other agents) when indicated for atrial fibrillation. There is little dispute that novel oral anticoagulants (apixiban, dabigatran, rivaroxaban) are simpler to use, since they do not require monitoring and are essentially free of food interactions. Clinical trials with novel oral anticoagulants (NOACs) have consistently documented that NOACs are associated with a lesser risk of intracerebral hemorrhage (ICH), which is certainly a good thing — but how much of a good thing?

First, it may come as a surprise that in the modern era, large clinical trials of warfarin treatment in atrial fibrillation

demonstrate ICH events consistently below 1% per year. Since the risk of thrombotic stroke in atrial fibrillation — even at a CHADS score of 1 — is approximately 3% per year, the risk:benefit ratio is strongly in favor of anticoagulation.

Atrial fibrillation mega trials (each > 10,000 patients) have been completed with the three FDA-approved NOACs. Each agent demonstrated a reduction in ICH compared to warfarin, with an overall odds ratio of 0.49 — essentially half the risk of ICH with NOACs compared to warfarin. ICH is a devastating consequence of anticoagulation, and although more than 99% of patients treated with warfarin for atrial fibrillation per year will not suffer ICH, the ability to reduce risk for such a dreaded event is an important consideration. ■

Metformin: Have We Been Overcautious in CKD?

Source: Inzucchi SE, et al. *JAMA* 2014;312: 2668-2675.

Boundaries devised by regulatory agencies around the world for safe use of metformin differ from FDA labelling in the United States; many other nations allow more liberal use of metformin, indicating it is safe at lower levels of renal function than the boundaries you and I are used to: creatinine ≥ 1.5 md/dL for men, ≥ 1.4 mg/dL for women, or an eGFR < 60 mL/min/1.73 m^2. The observation that metformin has been used in patients with chronic kidney disease (CKD) beyond these boundaries safely, and the relative rarity of lactic acidosis related to metformin in the United States, have stimulated a reappraisal of the recommendations for patients with CKD. Metformin is cleared by the kidneys, but the original dosing and safety recommendations put into place more than 20 years ago are reportedly based on potential administration of metformin at doses up to 3 g/d, which of course is substantially above the usual maximum dose actually used in the United States (2000-2550 mg/d).

Inzucchi et al reviewed the literature in reference to studies that evaluated metformin, kidney disease, and lactic acidosis. Several trials even included plasma metformin measured at eGFR levels as low as < 30 mL/min. The authors opine that — contingent on regular monitoring — metformin might be safely used in diabetics with CKD down to an eGFR as low as 30 mL/min. ■

Reduction in Prostate Cancer Mortality with Screening

Source: Schroder FH, et al. *Lancet* 2014;384: 2027-2035

The pendulomic swing in enthusiasm for prostate cancer screening from strong endorsement to disenchantment resulted from a huge clinical trial database that included two mega trials that enrolled more than 250,000 men. One trial, the European Randomised Study of Screening for Prostate Cancer ([ERSPC] n = 182,160), demonstrated a reduction in prostate cancer-related mortality at 9-years follow-up, but no reduction in total mortality. Since all-cause mortality was not reduced, policymakers rightly questioned the propriety of advising large-scale screening if the overall rate of death was not altered.

The ERSPC now has data on up to 13 years of follow-up that remain concordant with their findings at 9 and 11 years: a reduction in prostate cancer mortality (rate ratio 0.79 or a 21% reduction), but again, no reduction in all-cause mortality.

Although a 21% relative reduction in prostate cancer mortality might seem impressive, the absolute risk reduction is much less so: avoidance of one prostate cancer death per 781 men screened. Based on the recommendations of the United States Preventive Services Task Force, most primary care clinicians have minimized screening of average-risk adult men for prostate cancer. These results confirm the rationale for that clinical posture. ■

Doing the Right Thing for Acute Bronchitis in Healthy Adults: Antibiotics NOT

Source: Smith S. *JAMA* 2014;312: 2678-2679.

The scenario is commonplace, evokes sympathy, and might even make you feel a little uncomfortable: Your third patient of the morning comes in with an apparent viral bronchitis, with the chief complaint, "I need some antibiotics." While an antibiotic prescription might seem to be the path of least resistance, the literature does not provide support that it is the wisest path.

Most cases of acute bronchitis in healthy individuals are viral. A review of seven randomized trials found that antibiotic treatment provided a short-term benefit of a half-day shorter duration of cough than placebo. This modest benefit needs to be weighed in comparison to the many adverse effects associated with antibiotic administration. Concordant with these observations, the National Institute for Care Excellence (United Kingdom) Guidelines have suggested that antibiotics not be used for healthy persons in the absence of pneumonia.

While some patients will be disappointed if antibiotics are not dispensed, an explanation of the risk:benefit ratio will often assuage them. Despite increasing awareness of the limited benefits of antibiotics, over-prescribing remains commonplace. ■

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