

Clinical Briefs in Primary CareTM

The essential monthly primary care update

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Lose-Dose Abdominal CT for Appendicitis

Source: Kim K, et al. *N Engl J Med* 2012; 366:1596-1605.

RADIATION EXPOSURE FROM CT IS QUITE substantial. A “typical” abdominal CT (AB-CT) examination exposes a patient to X-radiation equivalent to more than 500 chest X-rays. The dose-response relationship between diagnostic/therapeutic radiation and untoward consequences is uncertain; nonetheless, the magnitude of radiation from imaging — combined with the ever-increasing frequency with which high-dose diagnostic imaging is used — prompts concern. Perspicacity for wise use of radiation is imperative, especially in younger persons, in whom the lag time for adverse impact of radiation is most pertinent and in whom the likelihood of additional radiation exposure is increased.

When appendicitis is suspected, AB-CT has become the diagnostic imaging of choice. Standard-dose AB-CT exposes the patient to approximately 500 mGy/cm of radiation. Low-dose AB-CT exposes the patient to approximately 100 mGy/cm, but it is not widely used because of uncertainty about its accuracy (compared to standard AB-CT).

Kim et al randomized young adult patients with suspected appendicitis (n = 891) to low-dose or standard-dose AB-CT. The primary outcome of the study was the number of appendectomies performed that did *not* demonstrate appendicitis.

The negative appendectomy rate did not differ significantly between the two groups (3.2% vs 3.5%). Statistical crite-

ria were satisfied that low-dose AB-CT is noninferior to standard dose AB-CT. Clinicians may wish to ascertain the radiation dose used in AB-CT for appendicitis at their institutions. ■

Degludec, a New Ultra-long-acting Basal Insulin for Diabetes

Source: Garber AJ, et al. *Lancet* 2012; 379:1498-1507.

THE ADVENT OF BASAL INSULINS THAT DO not have a prominent peak plasma level — so-called “flat” pharmacodynamic activity — was a welcome addition to diabetes management, since their predecessor, NPH, was often limited by problematic hypoglycemia. Utilization of glargine and detemir insulins, the two basal insulin analogs most recently available in the United States, has mushroomed in response to their superior tolerability compared to NPH insulin: a reduction of about 20% in hypoglycemic episodes and less weight gain. Degludec has recently been submitted to the FDA for approval. It is considered an ultra-long-acting basal insulin.

Garber et al performed a controlled trial in type 2 diabetic patients (n = 972) to compare degludec with glargine as part of a basal-bolus regimen. The primary endpoint of the trial was achieved A1c, but rates of hypoglycemia were also compared.

Both insulins achieved similar A1c improvement, and the overall rate of hypoglycemia was low in both groups. However, the degludec patients experienced almost 20% fewer hypoglycemic

episodes (defined as glucose < 56 mg/dL) than the glargine group.

Degludec insulin, if FDA approved, may provide a superior hypoglycemia risk profile than insulin glargine while achieving a similar level of A1c reduction. ■

Prevention Benefits of Aspirin: Cancer, Vascular, or Both?

Source: Rothwell PM, et al. *Lancet* 2012; 379:1602-1612.

AMERICAN CLINICIANS HAVE TYPICALLY thought of aspirin as a preventive (primary and secondary prevention) for cardiovascular (CV) events. Recently, the role of aspirin for primary prevention of CV events has been embattled because although clinical trial data indicate reduction in CV events, total mortality has not been convincingly favorably impacted.

Aspirin appears to have at least two favorable effects upon cancer. It appears to decrease the incidence of colon cancer, and — as a consequence of what otherwise might appear to be an adverse effect — enhances detection rates of existing colon cancer by increasing their proclivity to bleed.

Rothwell et al performed an analysis of trial data from 51 randomized, controlled aspirin prevention trials. Among almost 70,000 participants, risk of cancer death was reduced by approximately 15%, and incidence of cancer was reduced by about one-fourth. Although there is a reduction in vascular events with the use of aspirin, bleeding events induced by aspirin tend to balance this out in the earliest years of aspirin use.

Since cancer is well-entrenched as the No. 2 cause of death in America (and is inching into the No. 1 slot), when we think of the preventive benefits of aspirin, it is time to reframe our thinking into appreciation of the combined benefits of cancer mortality reduction in addition to CV event reduction. ■

UTI in Long-Term Care Facilities Among Older Adults

Source: Genao L, Buhr GT. *Ann Long-Term Care: Clin Care Aging* 2012;20:33-38.

UNLESS A DRAMATIC DEMOGRAPHIC SHIFT occurs, approximately one in four of us will reside in a long-term care facility (LTCF) during our lifetime. Among LTCF residents, 30-50% of antibiotic utilization is for urinary tract infections (UTIs), resulting in substantial expense, adverse drug reactions, and ever-growing populations of resistant bacteria.

The first guidelines for managing UTI in LTCF were issued in 1991. The McGeer criteria included fever, chills, dysuria, frequency, urgency, flank pain, suprapubic pain, change in urine character, worsening of mental or functional status, and new or increased incontinence. Unfortunately, these criteria (and their subsequent modification, known as the Loeb

guidelines) had a sensitivity of only 30%, a positive-predictive value of 57%, and negative-predictive value of 61%. Further modifications of the Loeb guidelines have evolved into an algorithm with major and minor symptoms that have been shown to reduce false-positive diagnoses by 30% and antibiotic use by 20%.

Genao and Buhr do not support treatment of asymptomatic bacteriuria in the LTCF setting for older adults. They remind us of the merit of urine dipstick testing because of its strong negative-predictive value: A dipstick urine test negative for leukocyte esterase and nitrate has an essentially 100% negative-predictive value for the presence of UTI. Although not yet in widespread use, other biomarkers of bacterial infection are gaining support. For instance, serum procalcitonin has been studied as a marker of bacterial infection (including UTI) in young adults, and might perform equally well in older adults. ■

Beyond Gluco-centricity: Nonglycemic Effects of Incretin-Based Therapy

Source: Brown NJ. *J Am Soc Hypertens* 2012;6:163-168.

ALTHOUGH GLUCOSE CONTROL IN DIABETES has been consistently demonstrated to improve microvascular outcomes, no randomized clinical trial has shown favorable effects on macrovascular disease (stroke, MI, overall mortality). Whether the failure to achieve macrovascular risk reduction is secondary to adverse effects like weight gain, hypoglycemia, catecholamine activation, or other factors remains to be determined. In the mean time, clinicians would like to use agents that have favorable effects on glucose/A1c, but — at worst — neutral effects on cardiovascular risk factors.

The incretin class of agents is currently comprised of GLP-1 agonists (e.g., exenatide, liraglutide) and DPP4 inhibitors (e.g., sitagliptin, linagliptin, saxagliptin). Although both subgroups blunt glucagon and induce glucose-dependent insulin secretion, only the GLP-1 agonists have sufficient potency to also increase satiety and slow gastric emptying. Incretins are

generally weight neutral (DPP4) or associated with weight loss (GLP-1). Accordingly, favorable lipid or blood pressure effects might be associated with incretins compared to other treatments that increase weight. The DPP4 enzyme has also been shown to be responsible for breakdown of some vasoactive peptides; hence, changes in blood pressure could be a direct effect of DPP4 inhibition. Because GLP-1 enhances endothelial function, any medication that augments GLP-1 would be anticipated to at least potentially favorably effect vascular function. We look forward to incretin clinical trials that will define the cardiovascular outcomes associated with this class of therapy. ■

Home BP Monitoring May Assist BP Goal Attainment in the Elderly

Source: Cushman WC, et al. *J Am Soc Hypertens* 2012;6:210-218.

ALTHOUGH CLINIC BLOOD PRESSURE (CBP) has been the primary standard by which the majority of major clinical hypertension (HTN) trials have been measured, home BP (hBP) and ambulatory blood pressure monitoring (ABPM) correlate more closely with outcomes and target organ damage. With the advent of reliable, inexpensive, validated devices for home oscillometric BP measurement, national and international agencies now recommend routine inclusion of home BP monitoring for patients with HTN.

Cushman et al report on a trial in elderly hypertensives (men and women > age 70) which compared hBP monitoring with cBP monitoring (n = 128) over 16 weeks. They determined that hBP measurements were consistent with cBP.

Adherence to HTN medications is sub-optimal. Utilization of hBP monitoring enables early detection of hypotension, facilitates dose titration (up or down), and may uncover otherwise unidentified insufficient durability of pharmacotherapy (i.e., nighttime measurements showing a waning of antihypertensive effect). As has been demonstrated in other populations, elderly patients can effectively and reproducibly use hBP, which may enhance long-term adherence. ■

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