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The essential monthly primary care update

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Alendronate: How Much of a Good Thing?

Source: Black DM, et al. *JAMA*. 2006;296:2927-2938

THE MOST POPULARLY USED pharmacotherapy for prevention and/or treatment of osteoporosis (OSPS) is bisphosphonate (BIS), specifically alendronate and risedronate. Once an appropriate treatment candidate is identified, therapy is usually employed on an “indefinite” basis, since an optimum duration of treatment remains to be elucidated. Black, et al compared 5 years vs 10 years of BIS in a large population of patients (n = 1,099) by following all patients on BIS for 5 years, and then discontinuing BIS in half of the population and following the entire group for an additional 5 years.

As might be intuitively obvious, subjects who discontinued BIS during the second 5-year phase of the study did show declines in BMD (bone mineral density) and increases in markers of bone turnover compared with persons continuing BIS. More importantly, there was NOT an increase in fracture occurrence amongst persons who discontinued BIS after 5 years. All in all, even with 5 years of BIS treatment followed by 5 years with no active agent, BMD remained better than at baseline.

Long term use of BIS is generally considered safe, and the optimum duration of treatment remains unknown. This data suggests that for persons who have convincing rationale to discontinue BIS (eg, expense, inconvenience, intolerance), a hiatus of as long as 5 years may not increase risk of osteoporotic fracture. ■

Early Localized Prostate Cancer: Does Intervention Make a Difference?

Wong, et al. *JAMA*. 2006;296:2683-2693

PSA SCREENING IS UTILIZED BY most clinicians for men at age 50 and beyond. As a result, the distribution of prostate cancers discovered in middle-aged men has evolved to include a disproportionate number of early, localized tumors. There have been conflicting data about the impact on survival of intervention (radiation therapy or radical prostatectomy) in persons with localized disease.

The SEER database (Surveillance, Epidemiology, and End Results) provides observational data on US cancer registry patients representing 14% of the US population. From this database, men age 65-80 (n=111,640) with a new diagnosis of prostate cancer in the 1991-1999 time period were classified as either receiving active intervention or observation.

At the end of a 12-year study period, the hazard ratio for death was 31% greater in men in the observation group (p = <0.05) than in men who received active intervention. Active intervention was associated with increased frequency of incontinence and erectile dysfunction compared to observation, although the latter population had more obstructive voiding symptoms.

Observational data cannot provide conclusive answers to questions about outcomes related to particular interventions. Results from randomized interventional trials to more conclusively address the question of whether active treatment improves outcomes in senior men with localized prostate cancer are pending. ■

CV Biomarkers: The More Is Not Always the Merrier

Source: Wang TJ, et al. *N Engl J Med*. 2006;355:2631-2639.

INITIATED IN 1948, THE FRAMINGHAM Heart Study is the longest ongoing epidemiologic study in the United States. Thanks to reports stemming from this observational data set, we have come to recognize “conventional” risk factors for cardiovascular disease (CVD): smoking, hypertension, and cholesterol. Although attributable risk for CVD from these risk factors is substantial, emerging biomarkers—eg, CRP, brain natriuretic peptide (BNP), plasma rennin, homocysteine, urinary albumin-to-creatinine ratio—might provide greater risk prediction.

Wang, et al followed 3,209 Framingham Heart Study participants who were free of known cardiovascular disease at baseline for 7.4 years (mean) to evaluate the relationship between 10 biomarkers (individually and in aggregate) and CVD.

After adjustment for conventional risk factors, each individual biomarker was associated with an incremental increase in CVD risk, most prominent of which was BNP (hazard ratio = 1.25). However, even though biomarkers did independently predict risk for CVD, the incremental amount added in addition to conventional risk factors was reported to be only “modest.” Although biomarkers are associated with CVD risk, conventional risk factors are responsible for the majority of attributable risk. ■

BNP: Not Just for Heart Failure

Source: Bibbins-Domingo K, et al. *JAMA*. 2007;297:169-176.

ELEVATED LEVELS OF BRAIN NATRIURETIC peptide (BNP) reflect cardiac ventricular wall stress, and correlate well with the presence and severity of heart failure. Similarly, BNP levels at hospital discharge for heart failure predict prognosis. Indeed, BNP levels can discriminate between heart failure and pulmonary etiologies amongst dyspneic patients presenting to an acute care setting.

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The Heart and Soul Study is comprised of approximately 1000 patients with stable coronary heart disease (CHD) residing in Southern California who are followed to evaluate the relationship between psychological factors and outcomes in persons with existing CHD.

Bibbins-Domingo report on data evaluating the relationship between BNP and CHD in patients with stable heart disease, without evidence of exercise intolerance (patients must be able to walk one block).

Over a 3.7 year period of observation, a linear relationship between BNP and cardiovascular events/death was noted. This relationship was not altered by the presence of an abnormal ejection fraction. Individuals in the uppermost quartile of BNP experienced 8 times the rate of cardiovascular events compared to those in the lowest BNP quartile.

BNP is a potent prognostic marker, not only in acute and recently treated heart failure, but also in ambulatory patients with stable coronary artery disease. ■

Like Everything Else, The Brain is Use It or Lose It

Willis S, et al *JAMA*. 2006;296:2805-2814.

COGNITIVE DECLINE (CGD) HAS effects that spill over into impaired activities of daily living (ADL). Cognitive training has been used to remediate CGD, and has been shown to produce significant improvements in cognitive function; whether this cognitive improvements translates into favorable effects upon ADL has not been studied.

Adult senior citizens (n=2,832) were invited to join a 5 year study investigating the impact of 3 areas of training (memory, reason, and processing speed) on both ADL and cognitive abilities. Subjects were randomized to receive either 10 sessions of training at baseline, followed by booster sessions at 1 year and 3 years, or no intervention.

The training in reasoning resulted in less decline in ADL than no cognitive training. Training for processing and memory did show prompt positive effects on each of those specific cognitive components, and these effects were quite durable, since they remained measurably different 5 years later. However, only reasoning training impacted ADL. Cognitive training favorably affects cognitive decline. Of the cognitive training interventions, this study suggests that cognitive reasoning training also reduces decline in ADL. ■

High Vitamin D Levels are Associated with Reduced Risk of MS

Source: Munger KL, et al. *JAMA*. 2006;296:2832-2838.

ALTHOUGH THE CAUSE OF MS remains uncertain, prevailing opinion suggests that it is an autoimmune disorder. Epidemiologic data shows that geography is associated with MS: increasing distance from the equator (north or south) is associated with greater incidence of MS. One explanation for the observation that increasing latitude is associated with increased MS is that Vitamin D status at increasing latitude is progressively less optimal. For example, in Boston during the winter, little UV-B light penetrates the atmosphere, producing inadequate vitamin D generation.

To study the relationship between Vitamin D status and MS, serum samples from active duty US military (n = 7 million) were assayed for 25-hydroxyvitamin D (25HD). Persons with MS had their 25HD levels compared with persons without MS.

Using the lowest 25HD quintile for comparison, higher quintiles of 25HD were associated with 40-60% lower incidence of MS, but only in the Caucasian population. No relationship between 25HD and MS was seen in black or Hispanic subjects. There may be a relationship between MS and 25HD. ■