

Clinical Briefs in Primary Care

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Evidence-based updates in primary care medicine

Online Supplement to *Clinical Cardiology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Integrative Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports*

Volume 20, Number 8

August 2015

We're Going to Be Hearing a Whole Lot More About Nonalcoholic Fatty Liver Disease

SOURCE: Rinella ME. Nonalcoholic fatty liver disease: A systematic review. *JAMA* 2015;313:2263-2273.

Epidemiologic insights about disease prevalence might sometimes be perceived as belaboring the obvious. After all, who doesn't know that obesity has become an epidemic, that diabetes prevalence continues to rise unabated, and that hepatitis C is currently the most common cause of end-stage liver disease. Nevertheless, new epidemiologic sirens may sometimes awaken our motivation to address what might otherwise remain silent health burdens, with nonalcoholic fatty liver disease (NAFLD) being an excellent case-in-point.

Even the moniker "NAFLD" presumes we might automatically consider alcohol to be the default cause of fatty liver disease. While that might have been the case decades ago, the dual burdens of obesity and diabetes — both of which are direct antecedents to NAFLD — have changed the map of fatty liver disease on a global basis.

NAFLD portends important downstream consequences. Up to 30% of people with NAFLD have steatohepatitis, among whom approximately 20% will ultimately progress to cirrhosis. Since as many as 75 million to 100 million U.S. adults have NAFLD, this presents an epidemiologically compelling burden. Lifestyle intervention, when it leads to weight loss, is successful in improving liver pathology. There is some suggestion that independent of weight loss, a Mediterranean diet may have particular advantage.

Although no medication has been FDA approved to treat nonalcoholic steatohepatitis, some clinical data is supportive of pioglitazone (30 mg/d) or vitamin E (800 IU/d).

Clinicians should maintain vigilance as recommendations for identification and management of NAFLD evolve. ■

Dietary Fat Used to Be the 'Bad Guy'

SOURCE: Mozaffarian D, Ludwig DS. The 2015 U.S. Dietary Guidelines: Lifting the ban on total dietary fat. *JAMA* 2015;313:2421-2422.

In March 2015, the Dietary Guidelines Advisory Committee (DGAC) released its report for review by the secretaries of Agriculture and Health and Human Services. The 2015 Dietary Guidelines for Americans will be derived from the DGAC report, and some clinicians may be surprised at new directions suggested by the DGAC.

For instance, dietary cholesterol has been eliminated as a "nutrient of concern" based on recent data clarifying the lack of a relationship between dietary cholesterol and cardiovascular (CV) events. Similarly, previous guidance suggested an upper limit on total dietary fat consumption; in contrast, the current DGAC report neither restricts dietary fat nor lists fat as a "nutrient of concern," based on the observation that reducing total fat has not been shown to improve CV outcomes.

Earlier guidance, which suggested limiting fat in the diet, often resulted in substitutions with increased amounts of carbohydrates, resulting in dietary modifications that commonly contained highly processed carbohydrates (such as added sugar.)

The new report includes advice that

Americans consume excessive amounts of refined grain produces, such as white bread chips, white rice, crackers, and bakery goods. The U.S. populace has had more than a decade to ingrain the concept that dietary fats are "the bad guy." It will likely take a substantial amount of additional effort to clarify that replacement of fats with refined carbohydrates is not a healthful tradeoff. ■

Risks of Digoxin Use in Atrial Fibrillation

SOURCE: Washam JB, et al. Digoxin use in patients with atrial fibrillation and adverse cardiovascular outcomes: A retrospective analysis of the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF). *Lancet* 2015;385:2363-2370.

Beta-blockers, calcium channel blockers, and digoxin are among the commonly used choices for rate control in patients with atrial fibrillation (AF). The role of digoxin is based on limited data, most of which is not recent. Large clinical trials of novel anticoagulants for patients with AF have been completed within the last decade. Since a substantial minority of patients enrolled in AF anticoagulant trials were receiving digoxin as part of their therapeutic regimen, these data provide a window of observation about associations of digoxin with outcomes.

The Rivaroxaban Once Daily Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET-AF) enrolled more than 14,000 patients with AF to compare rivaroxaban with warfarin. More than 5000 AF patients were being treated with digoxin at baseline

(37% of total ROCKET-AF participants).

At a median follow-up of approximately 2 years, digoxin treatment was associated with increased all-cause mortality (17% relative increase), vascular death (19% relative increase), and sudden death (36% relative increase).

Because these results have been obtained from a post-hoc analysis of a clinical trial, they cannot be regarded as definitive. Nonetheless, the results should prompt reconsideration of the various choices available for rate control in AF, and hopefully will stimulate performance of a randomized trial to provide more conclusive evidence. ■

Oral Nutritional Supplementation for Hospitalized COPD Patients Pays Off

SOURCE: Snider JT, et al. Effect of hospital use of oral nutritional supplementation on length of stay, hospital cost, and 30-day readmissions among Medicare patients with COPD. *Chest* 2015;147:1477-1484.

In contrast to many of the other top 10 causes of death in the United States, chronic obstructive pulmonary disease (COPD) deaths are increasing, such that COPD is now the third most common cause of

CLINICAL BRIEFS IN PRIMARY CARE™

is published monthly by AHC Media, LLC. Copyright © 2015 AHC Media, LLC.

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death. Although a variety of pharmacologic interventions are available to improve symptoms and decrease exacerbations, none has been shown to reduce mortality.

COPD is associated with increased risk for malnutrition, which may lead to further respiratory function compromise and immune dysfunction. Might nutritional supplementation of patients admitted for COPD improve outcomes?

Snider et al utilized the Premier Research Database, which contains hospitalization information from 460 U.S. hospitals and 46 million hospitalizations. The authors compared outcomes in persons > 65 years of age admitted for COPD (n = 378,419) who received oral nutritional supplementation (n = 10,322) vs those who did not. Outcomes of interest were length of hospital stay, hospitalization costs, and readmission rates.

Oral nutritional supplementation was associated with numerous favorable results: Length of stay was reduced by 21.5%, readmission rate was reduced by 7%, and even the cost of hospitalization was reduced by 12.5%. Overall, the results suggested that for every dollar spent on oral nutritional supplementation, the hospital saved \$18.

It is clear oral nutritional supplementation has been employed in a small minority of COPD admissions (10,322 out of 378,419 admissions). These favorable results should prompt reconsideration of the value — health wise and economic — of oral nutritional supplementation in patients admitted for COPD. ■

An Unrecognized Relationship Between Asthma and Obesity

SOURCE: Pakhale S, et al. Effects of weight loss on airway responsiveness in obese adults with asthma: Does weight loss lead to reversibility of asthma? *Chest* 2015;147:1582-1590.

The prevalence of asthma is increasing, although the reasons behind this are not entirely clear. There may be an important link between asthma and obesity.

For instance, incident asthma is almost 50% more common in obese persons. Each increment of three units in body mass index (BMI) is associated with a 35% increase in asthma. Even the degree of airway hyperreactivity — the hallmark of asthma — is directly related: For each one-unit increase in BMI (e.g., a BMI change from 30 to 31 kg/m²), there is a 3% increase in airway hyperreactivity.

Whether treatment of obesity might benefit patients with asthma has received little attention in the literature. Pakhale et al performed a prospective controlled trial in

obese adults (mean BMI = 45 kg/m²) with asthma to compare metrics of pulmonary function and airway hyperreactivity in subjects who participated in a weight loss program vs control. The intervention group received lifestyle intervention to enhance dietary weight loss and exercise.

The metric for airway hyperreactivity was the PC20 — the amount of methacholine necessary to produce a bronchoconstrictive effect enough to reduce FEV₁ by 20% (the more methacholine it takes, the less hyperreactive your airways are).

At the end of the 3-month trial, the intervention group had lost a mean of approximately 17 kg, but the control group had a gain of approximately 1 kg. The intervention group enjoyed improvements in pulmonary function (improved FEV₁), asthma quality of life, and PC20. Weight reduction may be an overlooked tool for asthma management. ■

Sound Stimulation in Alzheimer's Patients

SOURCE: Clements-Cortes A, Bartel L. Sound stimulation in patients with Alzheimer's disease. *Annals Long-Term Care* 2015;23:10-16.

Music therapy can be a helpful and pleasurable experience for patients with Alzheimer's disease (AD). Although clinical trials on the subject are not large or plentiful, the favorable results obtained appear promising. For instance, one clinical trial looked at the impact of music therapy among persons with agitation and AD. A 45-minute session of music therapy reduced agitated and disruptive behaviors (like swearing or yelling). Whether music therapy provides long-term benefits has not been well studied.

For most, if not all of us, music has deep-rooted emotional links. Background music has been shown to improve cognitive performance throughout the adult lifespan, including college students, older adults, and patients with AD. Interestingly, those brain areas responsible for processing music are commonly preserved in patients with AD, despite their loss of other cognitive functions. At a less macroscopic level, exposure to music has been shown to increase levels of IgA and decrease cortisol.

Whether clinicians want to consider supporting the use of recreational environmental music (simple background music for patients) or the formal structure of music therapy provided by a trained therapist, music may provide meaningful clinical improvements in AD patients, as well as an enhanced quality of life. ■