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The essential monthly primary care update

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Effects of Losartan on Cardiovascular Morbidity and Mortality in Patients with Isolated Systolic Hypertension and LVH

Source: Kjeldsen SE, et al. *JAMA*. 2002;1491-1498.

Since the early 1990s it has been recognized that left ventricular hypertrophy (LVH) is an important prognostic indicator for cardiovascular morbidity and mortality. More recently, it has been suggested that angiotensin receptor blockers (ARBs) might exert a particularly favorable effect upon LVH, perhaps even independent of blood pressure (BP) effects. The LIFE (Losartan Intervention for Endpoint Reduction) study was designed to test the hypothesis that losartan (LSN) exerts preventive cardiovascular effects, beyond simply controlling BP. To this end, a randomized, controlled trial (n = 1326) of LSN vs atenolol (ATN) was initiated in persons with isolated systolic hypertension and LVH, with a primary composite end point of cardiovascular death, stroke, and MI.

Despite the fact that BP reduction was equal in both groups (28/9 mm Hg), there was a 25% relative risk reduction in the primary end point (CV death, stroke, MI) in favor of losartan. Additionally, LVH reduction was much more vigorously achieved by LSN than ATN. Stroke reduction was particularly favorably affected by LSN, in which a 40% reduction compared to ATN was seen. Lastly, LSN demonstrated a more favorable tolerability profile than ATN: discontinuations due to drug-related events were half as frequent in recipients of LSN than ATN. ■

Increase in Nocturnal Blood Pressure and Progression to Microalbuminuria in Type 1 Diabetes

Source: Lurbe E, et al. *N Engl J Med*. 2002;347:797-805.

It has been noted that among persons with type 1 diabetes (DM-1), hypertension (HTN) often develops concomitantly with occurrence of microalbuminuria (MAU). Closer investigation with ambulatory BP monitoring (ABPM) suggests that nocturnal blood pressure elevations (NBP) are particularly associated with MAU; however, whether the NBP causes the MAU (or they are concomitant) has been uncertain.

Lurbe and associates prospectively studied ABPM in adolescent DM-1 patients (n = 75) who were normoalbuminuric and normotensive at enrollment. Subjects were periodically monitored by ABPM and urinary albumin measurements for more than 5 years. MAU developed in 19% of study subjects, and was preceded by a modest elevation in BP, but it was only the NBP in which change was manifest. Over time, in the group that ultimately developed MAU, the NBP increased by 5 mm Hg compared to baseline; in the normoalbuminuric group, NBP did not change. The subtlety of these findings is reflected by the fact that neither office BP, nor mean daytime BP predicted MAU. Hence, ABPM may detect modest BP patterns, which lead to early prediction of target organ damage. ■

HRT, Lipid, and Glucose Metabolism in Diabetic and Nondiabetic Postmenopausal Women

Source: Crespo CJ, et al. *Diabetes Care.* 2002;25:1675-1680.

Like cardiovascular diseases, type 2 diabetes (DM-2) increases in postmenopausal women. Prospective randomized interventional trials have not shown a benefit for hormone replacement therapy (HRT) in improving cardiovascular outcomes. The effect of HRT upon lipids and glucose among diabetic populations has been little studied. Crespo and colleagues evaluated subjects (n = 2786) in the Third National Health and Nutrition Examination Survey (NHANES III) seeking the relationship between HRT, diabetes, and lipids.

In diabetic women, total cholesterol and non-HDL levels were significantly lower in women who used HRT than never users, but there was no difference in HDL levels. In contrast, in nondiabetic women HDL levels were higher in HRT users than

nonusers. Fasting glucose levels (FBS) in diabetic women were significantly lower in HRT recipients than never users (112 mg/dL vs > 150 mg/dL). Crespo et al conclude that menopausal HRT is associated with improved FBS, total cholesterol, and non-HDL in diabetics. The fact that these findings are observational in nature suggests cautious interpretation until their clinical relevance is ascertained through interventional trials. It may be that other, undetected factors in women who choose to use HRT are influencing lipid and glucose metabolism. ■

Effects of Long-Term Treatment With ACE Inhibitors in the Presence or Absence of Aspirin

Source: Teo Koon K, et al. *Lancet*. 2002;360:1037-1043.

Both angiotensin converting enzyme inhibitors (ACEI) and aspirin (ASA) have a proven valuable track record in a variety of cardiovascular preventive and therapeutic areas. One of the mechanisms by which ACEI are believed to confer benefit is the production of vasodilatory prostaglandins, including PGI-2 and PGE-3. Since ASA can blunt production of prostaglandins, it is conceivable that the combination of the 2 might "cancel out" beneficial effects. To date, evaluation of large clinical trials in which both ASA and ACEI were used have provided conflicting data. Hence, Teo and associates undertook a systematic review of long-term randomized trials in which ACEI and ASA were coadministered (n = 22,060) for meta-analysis.

ACEI treatment in these trials (including the SOLVD treatment, SOLVD prevention, SAVE, AIRE, TRACE, and HOPE studies) produced overall a 22% reduction in major clinical outcomes. Concomitant use of ASA was not associated with a statistically significant diminution of benefit. Based upon this information, Teo et al suggest that for persons who are receiving either ACEI or ASA, if the other agent is indicated, clinicians may feel confident that the combination will not reduce beneficial effects. ■

Long-Term Risks Associated with Atrial Fibrillation: 20-Year Follow-up of the Renfrew/Paisley Study

Source: Simon S, et al. *Am J Med*. 2002;113:359-364.

Most of the studies of atrial fibrillation (AF) that address cardiovascular (CV) consequences provide only short-term or intermediate-term insight (6 months-24 months). Long-term consequences of AF are much less studied. Simon and colleagues evaluated CV outcomes (including hospitalizations and deaths) over a 20-year follow-up in 15,000 persons enrolled in Renfrew and Paisley, Scotland. The population was middle-aged (45-64 years) at enrollment.

At entry enrollment (1972-1976), 100 persons had AF. During the extended follow-up, women manifest a 5-fold increase in cardiovascular hospitalization or death, and risk in men was 2-fold increased. Lone AF (AF in the absence of discernible cardiovascular disease) did not confer a statistically significant increase in cardiovascular risk. The increase in CV risk associated with AF was expressed primarily as stroke and heart failure. This new information indicates substantial long-term risk from AF. Simon and colleagues suggest that strategies to prevent CHF, as well as those already commonly practiced for stroke prevention, may be of benefit in persons with AF. ■

Olfactory Impairment in Older Adults

Source: Murphy C, et al. *JAMA*. 2002;288:2307-2312.

Despite widespread attention to the demographics and management of hearing and visual impairments in older adults, there has been little study of olfactory impairments (OLF). Olfactory impairment can results in aggravation of nutritional problems, inability to respond promptly to risk situations such as fire or gas leaks, and reduce quality of life. To better determine the prevalence of OLF, Murphy and colleagues examined data from participants in the Epidemiology of Hearing Loss Study (n = 2491), a cross-sectional study of adults aged 53-97.

Initially, self-report of OLF was assessed by asking the question, "Do you have a normal sense of smell (compared to other people)?" Then, testing for OLF was performed using the San Diego Odor Identification Test (SDOIT), which uses natural home odors such as coffee and chocolate. OLF was defined as inability to identify at least 6 of 8 odorants.

One fourth of the tested population manifested OLF by SDOIT. On the other hand, only 9.5% of the population self-reported deficits in smell. A multiple logistic regression model determined that smoking, nasal congestion, stroke history, and epilepsy were associated with increased risk of OLF. ■

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