News in Brief

PRESENCE OF CAROTID BRUIT MAY IDENTIFY PATIENTS AT HIGH CARDIOVASCULAR RISK

A meta-analysis from the Walter Reed Army Medical Center indicates that the presence of carotid bruits doubled the risk of myocardial infarction (MI) and almost tripled the risk of cardiovascular death. When the analysis was limited to studies that allowed direct comparison between patients with and without bruits, the risk of MI and cardiovascular death in those with bruits was still twice as high.

The authors concluded that atherosclerotic changes causing carotid bruits might reflect systemic vascular pathological changes, including changes of the coronary arteries. They added that auscultation of the carotid should be used in every patient who might be at risk for coronary heart disease, to aid in assessment of cardiac risk.

Currently, the implication of a carotid bruit has been on cerebro-vascular events. However, the authors note that carotid bruit has only weak predictive accuracy for cerebro-vascular events in asymptomatic patients. The authors suggested that patients with carotid artery disease are more likely to die from cardiovascular than from cerebro-vascular disease.

Data from 22 studies (with a total of 17,295 patients and 62,413.5 patient-years of follow-up) was analysed. The median duration of follow-up was four years. Patients with bruits had an MI rate of 3.69 per 100 patient-years, versus 1.86 per 100 patient-years in those without bruits. The yearly rate of cardiovascular death was 2.85 versus 1.11 per 100 patient-years (with and without bruits, respectively). Four trials allowed direct comparisons of patients with and without bruits. Patients with bruits had a two times greater risk of MI (OR 2.15, 95% CI 1.67 to 2.78) and cardiovascular death (OR 2.27, 95% CI 1.49 to 3.49).

The meta-analysis has several limitations. One third of the study participants had pre-existing cardiovascular disease. The influence of a bruit on secondary prevention is unclear. The prognostic value of a bruit was not compared with cardiovascular risk scores. Patients without bruits could have other signs that could have similar prognostic significance. Prospective studies on asymptomatic patients are needed to study the prognostic value of a combination of simple clinical signs, like neck and groin auscultation, pulse palpation, heart rate, pulse pressure, or blood-pressure difference between arms. These studies could narrow the indications of cardiovascular imaging techniques and make them more cost effective.

(Source: Pickett CA, et al. Carotid bruits as a prognostic indicator of cardiovascular death and myocardial infarction: A meta-analysis. Lancet 2008 May 10; 371(9624):1587-94.)

HORMONE THAT DRIVES THE URGE TO EAT MAY WORK BY MAKING FOOD MORE DESIRABLE

A McGill University study of a very small number of patients appears to suggest that a gut hormone may play a role in eating behaviour by stimulating pleasure responses in the brain. Infusion of ghrelin into healthy volunteers heightened

Page 33 ►

◀ Page 32 – News in Brief

activation of the brain's reward centres in response to pictures of food, as captured by MRI. The authors said that their findings indicate that after ghrelin infusion, people seemed to actually see food pictures better and remembered food pictures better. This might provide a possible clue to weight management.

The authors said that eating behaviour has both homeostatic and hedonic (pleasure-driven) components. Homeostatic feeding is thought to be regulated by hypothalamic hormones. Hedonic feeding involves brain regions associated with reward and motivation.

Ghrelin has widespread effects in the brain. It is a peptide hormone secreted by the gut, and stimulates hunger and food consumption. However, the mechanisms are unclear. To try to understand the mechanisms better, the researchers studied 20 non-obese healthy volunteers. Three hours after eating a standardised meal, the participants viewed a series of pictures of food and scenery and subjectively rated their appetites and moods, and the participants' recall of the pictures was examined. Twelve participants received ghrelin by intravenous infusion and eight received a placebo infusion. All participants underwent functional brain MRI and then viewed the same pictures again.

Participants in the ghrelin group showed a significant increase in hunger assessment and recall of food pictures ($P = 0.01$), but hedonic ratings did not differ between the two viewings of the pictures. In the placebo group, neither picture recall nor subjective responses differed between the two viewings.

Brain MRI after ghrelin infusion (versus placebo) showed a heightened neural response in the amygdala, orbito-frontal cortex, anterior insula and striatum. The authors said that these regions encode the "salience and the hedonic and incentive value of visual cues".

However, the study has several limitations. Ghrelin causes increased secretion of growth hormone, ACTH, cortisol, and prolactin, all of which may act on the brain. The number of participants was very small, and all of them were males.

(Source: Malik S, et al. Ghrelin modulates brain activity in areas that control appetitive behavior. Cell Metabol 2008; 7: 400-409.)

SMOKING CESSATION LEADS TO EARLY AND LATE MORTALITY BENEFITS IN WOMEN

According to the Nurses' Health Study (Harvard School of Public Health), within five years of stopping smoking, a woman's excess vascular

risk virtually disappeared, but lung mortality remains elevated for 15 additional years. After 22 years of follow-up, stopping smoking reduced the risk of every cause-specific mortality outcome evaluated. The full mortality benefit of smoking cessation accrued over 20 years, but over a variable timeframe.

The Nurses' Health Study was started in 1976, and originally involved 121,700 female US registered nurses, ages 30 to 55. Participants gave detailed information (biennial questionnaires) about their medical history, and risk factors for cancer, heart disease, and other conditions. In 1980, 28% of the participants were smokers, 26% former smokers and 46% were never smokers. By 2002, 8% of surviving participants were smokers.

After 12 years of follow-up, current smoking and starting at a younger age increased the risk of all-cause and cause-specific mortality. With an additional 10 years of follow-up, the study had enough statistical strength to characterise the effect of smoking on deaths related to respiratory disease and malignancy.

In the study, there were 12,483 deaths: 4,485 (35.9%) among never-smokers, 3,602 (28.9%) among smokers and 4,396 (35.2%) among former smokers. The deaths consisted of 2,957 vascular deaths, 759 respiratory deaths, 1,237 lung cancer deaths, 2,104 smoking-related cancer deaths (including lung), 3,805 deaths

Page 34 ▶

◀ Page 33 – News in Brief

due to other types of cancer and 2,858 deaths due to other causes.

Current smokers had almost a three times greater mortality risk compared with never-smokers (HR 2.81, 95% CI 2.68 to 2.95). There was a similar difference for major cause-specific mortality.

Risks increased significantly with the number of cigarettes smoked daily. Former smokers had a 23% excess mortality risk. Smokers had a seven times greater risk for smoking-related cancer deaths (HR 7.25, 95% CI 6.43 to 8.18) and a 60% greater risk for other cancer deaths. The hazard ratios for former smokers were 2.33 (smoking-related cancer deaths) and 1.09 (other cancer deaths). For all respiratory causes of death, smoking increased the risk 10 times compared with never-smokers. Former smokers had a four times greater risk. Smokers had more than a three times greater risk of vascular death compared with never-smokers. Most of the excess risk had disappeared in former smokers (HR 1.32 versus never-smokers).

(Source: Kenfield SA, et al. Smoking and smoking cessation in relation to mortality in women. JAMA 2008; 299: 2037-2047.)

PATIENTS WITH TYPE 2 DIABETES AND NON-ALCOHOLIC FATTY LIVERS MAY DEVELOP CHRONIC KIDNEY DISEASE

An observational study, from the Universities of Verona and Colorado, found that white patients with type 2 diabetes and nonalcoholic fatty liver disease were at risk for developing chronic kidney disease. The risk for chronic kidney disease was 69% higher than for diabetic patients without fatty liver.

The study included 1,760 outpatients with type 2 diabetes, and with normal or near-normal kidney function and without overt proteinuria. Patients were followed for 6.5 years for the occurrence of chronic kidney disease (defined as overt proteinuria and/or estimated GFR 60 ml/min per 1.73 m2). The participants were recruited from the Valpolicella Heart Diabetes Study cohort, a prospective observational study to evaluate associations between diabetes and chronic vascular complications. Patients with common causes of fatty liver (alcohol abuse, chronic viral hepatitis, use of potentially hepato-toxic medications) were excluded.

During follow-up, 547 participants developed chronic kidney disease, with a yearly risk of about 4.5%. Non-alcoholic fatty liver disease (diagnosed by ultrasound) was associated with a moderately increased risk for the chronic kidney disease (HR 1.69, 95% CI 1.3 to 2.6, P = 0.001). When adjustments were made for gender, age, BMI, waist circumference, blood pressure, smoking, diabetes duration, glycosylated hemoglobin, lipids, baseline estimated GFR, micro-albuminuria and medications (hypoglycemic, lipid-lowering, anti-hypertensive, or anti-platelet drugs), there was no significant change in the association (HR 1.49, 95% CI 1.1 to 2.2, P = 0.01).

The authors said that the underlying mechanisms by which fatty liver might increase the risk for chronic kidney disease in type 2 diabetes was poorly understood. The most obvious explanation is the coexistence of underlying known risk factors.

However, the authors said that their findings were independent of numerous baseline risk factors, and postulated that non-alcoholic fatty liver might confer an excess risk beyond known risk factors. The authors also suggested that fatty liver in diabetic patients might be involved in the pathogenesis of chronic kidney disease, via molecular mediators from the liver (e.g. advanced glycosylated end products, increased reactive oxygen species, C-reactive protein, TNF-α, TGF-β1, other pro-inflammatory cytokines). Several other studies have shown that these potential mediators of vascular and/or renal injury are much higher in diabetic or obese patients with fatty liver disease. Liver disease might also worsen whole-body insulin resistance and hyperglycemia, in turn contributing to progression of kidney disease.

The study has several limitations. An estimated GFR was used to define chronic kidney disease. Fatty liver diagnosis was based on ultrasound and exclusion of other causes, and was not confirmed by biopsy. The study population comprised white participants, and the reproducibility of the results in other ethnic groups is not known.

It is not known whether treating fatty liver disease will ultimately prevent progression to chronic kidney disease. However, interventions effective in preventing or delaying the progression of chronic kidney disease in diabetic patients (weight reduction, use of angiotensin receptor blockers) might also be effective for fatty liver disease. ■

(Source: Targher G, et al. Increased risk of CKD among type 2 diabetics with nonalcoholic fatty liver disease. J Am Soc Nephrol 2008; DOI: 10.1681/ ASN.2007101155.)