The Hypertriglyceridemic Waist: A Simple Clinical Marker for Cardiometabolic Risk

A simple and inexpensive risk assessment tool that incorporates waist circumference and triglyceride level may help to identify patients who are at increased risk of coronary artery disease (CAD), according to new findings from the European Prospective Investigation into Cancer (EPIC)-Norfolk cohort study. Benoit Arsenault, PhD, Université Laval, Québec, Canada, described findings from the EPIC-Norfolk study and the emerging role of the hypertriglyceridemic waist phenotype as a marker for CAD risk.

Abdominal Obesity as a Risk Factor for CVD

Obesity is increasingly recognized as an important risk factor for cardiovascular disease (CVD). As a common measure of obesity, body mass index (BMI) predicts CVD risk. However, not every individual with an elevated BMI carries excess visceral adipose tissue, which appears to be the most important source of risk factors, such as insulin resistance, elevated triglycerides, low high-density lipoprotein (HDL) levels, and hypertension. At any given BMI, greater levels of accumulated visceral fat are associated with a worse cardiometabolic risk profile and increased mortality risk.

Researchers have proposed the hypertriglyceridemic waist phenotype as a potential risk assessment tool that accounts for abdominal obesity and its associated metabolic changes. For men, the hypertriglyceridemic waist phenotype is defined as a waist circumference of 90 cm (35.4 inches) or more and a triglyceride level of 2.0 mmol/l (177 mg/dL) or more. For women, the criteria for the hypertriglyceridemic waist phenotype are a waist circumference of at least 85 cm (33.5 inches) and a triglyceride level of at least 1.5 mmol/l (133 mg/dL).

In the current study, Prof. Arsenault and colleagues examined the association between the hypertriglyceridemic waist phenotype and CAD risk and whether the phenotype could improve risk prediction beyond traditional CVD risk factors. The EPIC-Norfolk cohort analysis included 21,787 men and women aged 45 to 79 years who were followed for a mean of 9.8 years [Arsenault BJ et al. *CMAJ* 2010].

The Hypertriglyceridemic Waist Phenotype and CAD Risk

Patients with the hypertriglyceridemic waist phenotype had an altered cardiometabolic risk profile compared with men and women with normal waist and/or triglyceride measures. In particular, the hypertriglyceridemic waist phenotype was associated with:

- Higher systolic blood pressure levels ($p<0.001$)
- Higher apolipoprotein B levels ($p<0.001$)
- Higher C-reactive protein levels ($p<0.001$)
- Lower HDL levels ($p<0.001$)
- Lower apolipoprotein A-I levels ($p<0.001$)
- Smaller low-density lipoprotein particles ($p<0.001$)

Increased waist circumference and elevated triglyceride levels significantly predicted risk of CAD. Men with the hypertriglyceridemic waist phenotype were more than twice as likely to develop CAD as men who did not have the phenotype (HR, 2.40; 95% CI, 2.02 to 2.87). The risk for CAD increased more than 3-fold for women with the hypertriglyceridemic waist

Peer-Reviewed
Highlights from the

2nd International Congress on Abdominal Obesity

International Chair on Cardiometabolic Risk

phenotype compared with women who did not have the phenotype (HR, 3.84; 95% CI, 3.20 to 4.62).

Compared with normal values, the presence of either an increased waist circumference or hypertriglyceridemia reduced the probability of survival without CAD among both men and women. However, the presence of both an increased waist circumference and an elevated triglyceride level was associated with the worst disease-free survival ($p<0.001$) for both men and women.

By providing additional information about excess abdominal adiposity and associated metabolic abnormalities, the hypertriglyceridemic waist phenotype could have the potential to improve traditional CVD risk assessment tools. In the current analysis, Prof. Arsenault and colleagues evaluated the risk of coronary heart disease (CHD) according to Framingham risk scores and the hypertriglyceridemic waist phenotype. Even among men and women with the lowest Framingham risk score (≤10%), those with the hypertriglyceridemic waist phenotype were at greater risk of CHD than those without the phenotype.

Even though the hypertriglyceridemic waist phenotype is a robust marker of abdominal obesity, it can not be used on its own to fully assess a patient's risk of CAD, Prof. Arsenault said. Instead, the phenotype should be used together with existing CVD risk prediction algorithms, such as the Framingham risk score, to provide a better assessment of global cardiometabolic risk.

Multiple Targeted Therapy is Critical for Reducing Cardiometabolic Risk

Obesity is associated with a range of adverse metabolic consequences, including endothelial dysfunction, systemic inflammation, and insulin resistance. Therefore, to provide effective protection against the development of atherosclerosis and heart disease, obese patients require combination drug regimens that target several cardiometabolic risk factors.

Kwang Kon Koh, MD, Gachon University Gil Hospital, Incheon, Korea, described the rationale for multiple targeted therapy in patients with abdominal obesity.

Adipose tissue acts as a complex endocrine organ that secretes both atherogenic cytokines, such as leptin and high-sensitivity C-reactive protein (hsCRP), and anti-atherogenic hormones, such as adiponectin. As individuals gain weight, the accumulation of visceral adipocytes leads to macrophage infiltration, increased release of atherogenic cytokines, and decreased secretion of adiponectin. Together, these pathologic mechanisms promote the development of atherosclerosis.

Moderate weight loss, defined as a loss of 5% to 10% of total body weight and 15% to 30% of visceral adipose tissue, improves cardiometabolic risk profile by lowering low-density lipoprotein (LDL) and triglyceride levels and improving glycemic control [Roberts CK et al. *J Appl Physiol* 2006]. However, weight loss goals are difficult to achieve. In a study of obese patients following 1 of 4 popular weight loss programs, the drop-out rate ranged from 35% to 50% after 12 months [Dansinger ML et al. *JAMA* 2005]. Among patients who remained in the program, the mean weight loss ranged from 4.7 to 7.1 lbs. Therefore, although moderate weight loss is an effective tool for reducing cardiometabolic risk, many obese patients will require additional interventions.

Statin-based Combination Therapy

Combination drug therapy can be tailored to address the related mechanisms that underlie obesity, diabetes, dyslipidemia, hypertension, atherosclerosis, and coronary heart disease (CHD). Statins and renin-angiotensin-aldosterone system blockers, such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), have beneficial vascular and metabolic effects in patients with multiple risk factors. For instance, in a randomized, double-blind, placebo-controlled study of 47 patients with hypertension and hypercholesterolemia, combination therapy with simvastatin 20 mg/day and losartan 100 mg/day improved vasomotor function and reduced inflammatory markers to a greater extent than statin or ARB monotherapy [Koh KK et al. *Circulation* 2004]. In another randomized, double-blind, placebo-controlled study of 50 patients with type 2 diabetes, combination treatment with simvastatin 20 mg/day and ramipril 10 mg/day provided a greater reduction in hsCRP levels and a greater improvement in endothelium-dependent dilation than either statin or ACE inhibitor therapy alone [Koh KK et al. *Hypertension* 2005].

Not all statin therapies have similar metabolic effects in patients with elevated LDL levels. Prof. Koh and colleagues showed that despite providing similar reductions and LDL levels and similar improvements in endothelium-dependent dilation, simvastatin and pravastatin had different effects on adipocytokine levels and glucose metabolism. In a study of 43 patients with hypercholesterolemia, treatment with pravastatin 40 mg/day significantly increased plasma adiponectin levels by 10% ($p=0.012$) and insulin sensitivity by 6% ($p=0.008$) compared with baseline. In contrast, treatment with simvastatin 20 mg/day significantly