Obesity, hypertension and the metabolic syndrome

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The prevalence of obesity in both developed and developing countries has increased dramatically in recent years. Many people who are obese develop metabolic changes that increase the risk of diabetes mellitus and adverse cardiovascular outcomes. Obesity leads to the development of insulin resistance, lipid abnormalities and increased blood pressure. The metabolic syndrome was designated as a way to easily identify individuals that tend to have a clustering of cardiovascular risk factors. Central obesity is one of the main determinants of the metabolic syndrome and is essential for the definition of metabolic syndrome according to the recent International Diabetes Federation worldwide definition of metabolic syndrome.

The association between obesity and hypertension has been well documented by multiple cross-sectional studies and weight gain has been shown prospectively to lead to the development of hypertension. Hypertension associated with obesity is characterized by sodium and volume retention and increased stroke volume with normal peripheral vascular resistance. Adipose cells are metabolically active and release many cytokines into the circulation including tumor necrosis factor, interleukins, plasminogen activator inhibitor-1, adiponectin and components of the renin-angiotensin system including angiotensinogen. These cytokines may contribute to the development of endothelial dysfunction, increased blood pressure and insulin resistance.

Patients with the metabolic syndrome typically fall within the moderate risk group for adverse cardiovascular events. Data from the National Health and Nutrition Examination Survey in the United States indicates about a 2-fold increased risk for a myocardial infarction and stroke in individuals with metabolic syndrome. The metabolic syndrome is associated with insulin resistance and impaired fasting glucose is a component of the criteria for the syndrome. There is a nearly 9-fold increased risk of developing diabetes mellitus in patients with the metabolic syndrome. Once diabetes is present, patients are considered to be in a high risk group for having future coronary events.

Since diabetes and insulin resistance are clearly linked to an increased cardiovascular risk, it is important to identify this subgroup of patients early and begin aggressive risk reduction therapy. The designation of the metabolic syndrome is one way to help identify this cohort of patients. The prevalence of the metabolic syndrome can be as high as one out of four individuals, however, and a large number of metabolic syndrome patients will not have developed insulin resistance at diagnosis. It would be helpful to easily identify the highest risk subset of insulin resistant patients within the metabolic syndrome group.

In the December 2005 issue of the Journal of Geriatric Cardiology, Nguyen et al. report a study of lean and overweight hypertensive patients from Vietnam. The overweight patients were more likely to have insulin resistance as measured by the Homeostasis Model Assessment (HOMA) formula. HOMA evaluations are not readily available, however, since fasting insulin and glucose values are needed for the calculation. Skin fold thickness measurements at the level of the abdomen correlated well with the HOMA calculation allowing the development of a simple formula that accurately predicted the insulin resistance index. The skin fold thickness measurement at the abdomen correlated best with insulin resistance supporting the use of waist circumference as a surrogate for insulin resistance in the metabolic syndrome. This may prove to be a simple clinical method for identifying a higher risk subgroup of patients with insulin resistance and high risk of developing diabetes.

Nguyen’s study is a small study and needs to be verified in a larger population to determine how useful skin fold thickness measurements will be in determining risk. In addition, it should be determined if skin fold measurements add incremental risk assessment beyond the simple classification of metabolic syndrome. Finally, it is important to use ethnic specific values for waist circumference as delineated by the International Diabetes Federation consensus to determine if a patient has metabolic syndrome and a higher likelihood of being insulin resistant.

The prevalence of insulin resistance was increased in the overweight hypertensive individuals in this study. This supports the fact that the majority of hypertensive patients are likely to have additional cardiovascular risk factors. To reduce cardiovascular risk in hypertensive patients it is necessary to treat both the hypertension and the additional risk...
factors. The Anglo Scandinavian Cardiac Outcomes Trial evaluated two different blood pressure regimens in hypertensive patients with multiple risk factors. A subset of the study group was randomized to lipid lowering therapy with atorvastatin versus placebo. The lipid-lowering arm of the study was stopped early because of a significant reduction in cardiovascular outcomes in the lipid-lowering arm. The average LDL-cholesterol levels were not significantly elevated in this study. Despite this finding, lipid-lowering proved to give substantial benefit to a hypertensive population of patients.

Patients with the metabolic syndrome are likely to benefit from reduction of multiple risk factors. Treatment goals should include a reduction in cardiovascular risk as well as a reduction in the development of diabetes. A lifestyle modification program with weight reduction and an exercise program is the cornerstone of therapy for the metabolic syndrome. The Diabetes Prevention Program used lifestyle modification in a group of individuals with impaired fasting glucose and showed a substantial reduction in the development of diabetes mellitus. Pharmacological therapy can then targeted to the lipid abnormalities, increased blood pressure and insulin resistance. Ongoing studies will help clarify the treatments that are best to reduce cardiovascular risk and the development of diabetes in this cohort of patients.

References