Metabolic Syndrome Ups PAD Risk in Women

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NEW ORLEANS — Women with metabolic syndrome have an increased risk of developing symptomatic peripheral artery disease, mediated mainly by the syndrome's associated inflammation and endothelial activation, according to a study of more than 27,000 women.

"The bottom line is if you account for the inflammation associated with the metabolic syndrome, there is no residual risk associated with the syndrome itself," Dr. Aruna D. Pradhan said at the annual scientific sessions of the American Heart Association.

She reported on 27,111 middle-aged female health professionals free of known cardiovascular disease when they enrolled in the Women's Health Study. At entry, one-quarter met criteria for the metabolic syndrome. At that time 28% of those with metabolic syndrome had diabetes, as did 1.8% of the others.

During a median 13.3 years of follow-up, 114 women developed symptomatic peripheral artery disease (PAD). In an unadjusted first-pass analysis, those with metabolic syndrome at baseline were 62% more likely that the others to develop PAD. For each additional metabolic syndrome–defining risk factor present beyond the requisite minimum three out of five, the risk of PAD increased by 26%.

But women with metabolic syndrome also were slightly older, less likely to exercise, more likely to smoke, and had a higher body mass index, as well as a high prevalence of diabetes. Upon adjustment for these factors, metabolic syndrome remained a significant risk factor for PAD. Women with metabolic syndrome had an adjusted 48% greater likelihood of PAD; this risk climbed by another 21% for each additional metabolic syndrome–defining trait, said Dr. Pradhan of Brigham and Women's Hospital, Boston.

But the nearly 7,000 women with metabolic syndrome also differed from the more than 20,000 others in another important way: They had markedly higher levels of biomarkers of systemic inflammation. The median plasma level of high-sensitivity C-reactive protein (hsCRP) among participants with metabolic syndrome at baseline was 3.98 mg/L, compared with 1.53 mg/L in women without metabolic syndrome. Levels of soluble intercellular adhesion molecule-1 (ICAM-1) averaged 374 ng/mL in the metabolic syndrome group and 333 ng/mL in the comparison arm. As the number of metabolic syndrome elements present increased from zero to five, median CRP increased from 1.0 to 5.9 mg/L and median ICAM-1 rose from 321 to 413 ng/mL.

When hsCRP and ICAM-1 levels were folded into the multivariate adjustment model, metabolic syndrome was no longer associated with a significantly increased risk of PAD, suggesting that systemic inflammation is the driving force in the development of PAD, not the high triglycerides, low HDL, or other components of metabolic syndrome.

Session cochair Dr. William R. Hiatt said it's speculative as to whether these study findings apply to men, or to the development of asymptomatic PAD, which is far more prevalent than symptomatic disease.

Men have a higher incidence of symptomatic PAD than women, at least in clinical trials, noted Dr. Hiatt, professor of medicine at the University of Colorado, Denver. ■