

Body mass index and thrombogenic factors in newly menopausal women

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Although having a high body mass index (BMI) is a known risk factor for cardiovascular disease, researchers are only beginning to understand how BMI affects the physiological processes involved in the development of the disease. Now, a study of a subset of women in the Kronos Early Estrogen Prevention Study (KEEPS), suggests that as BMI increases, so do platelet reactivity and thrombogenic microvesicles and activated protein C in the blood—all of which contribute to the formation of atherothrombosis and associated cardiovascular events. Moreover, as BMI increases, so do traditional established cardiovascular risk factors such as blood pressure, blood glucose, total cholesterol, LDL cholesterol, triglycerides, and high-sensitive C-reactive protein.

Muthuvel Jayachandran, Assistant Professor of Physiology in the Mayo Clinic's Department of Physiology and Biomedical Engineering in Rochester, Minn., is the lead author of the study which is entitled, "[Body Mass Index](#) and Thrombogenic Factors in Newly [Menopausal Women](#)." He will present his team's findings at the 2010 American Physiological Society (APS) conference, Inflammation, Immunity, and Cardiovascular Disease, in Westminister Colorado, August 25-28.

The Study

The Mayo researchers assessed cardiovascular risk factors in 118 women newly enrolled in the KEEPS, an ongoing multicenter study designed to evaluate the effectiveness of [hormone replacement therapy](#) in preventing

cardiovascular disease in newly post-menopausal women aged 42 to 58. All women in the study had their final menstrual period less than 36 months prior to enrollment.

The Mayo subset study is a baseline study that determined cardiovascular risk parameters in women before they were randomized to receive hormone replacement therapy or placebo in the KEEPS. The researchers divided the 118 women into three groups according to BMI, with women in the low, moderate, and high groups having BMIs of less than 25, 25 to 29.9, and 30 to 34.9 respectively. The researchers assessed conventional [cardiovascular risk factors](#) such as blood pressure, cholesterol, triglycerides, fasting [blood glucose](#), and liver function. They also analyzed the women's blood for platelet count, platelet reactivity, populations of activated cell membrane-derived thrombogenic microvesicles, and the amount of high-sensitive C-reactive protein and activated protein C. Finally, the women underwent computer tomography scans to test for the presence of calcium in their coronary arteries, an indicator of cardiovascular disease.

Results

Although most of the conventional risk factors were in the normal range in all of the women, the researchers found that these parameters were significantly greater in the moderate and high BMI groups compared to the low BMI group. For example, the mean blood pressure in the low BMI group was 115/72 mmHg, but 124/77 mmHg and 127/78 mmHg in the moderate and high BMI groups, respectively. Likewise, mean fasting blood glucose was 89 mg/dL in the low BMI group, but 92 mg/dL and 95 mg/dL in the moderate and high BMI groups. The exception was LDL, which was normal in the low BMI group with a mean of 122 mg/dL, but borderline high in the moderate and high BMI groups, each having a mean of 138 mg/dL and 140 mg/dL, respectively.

The researchers found elevated levels of platelets, thrombogenic microvesicles, high-sensitive C-reactive protein, and activated protein C in the moderate and high BMI groups. The mean platelet count in the low BMI group was $220 \times 10^3/\mu\text{L}$, but $233 \times 10^3/\mu\text{L}$ and $255 \times 10^3/\mu\text{L}$ in the moderate and high BMI groups, respectively. Mean high-sensitive C-reactive protein in the low group was 1 pg/mL, but 2 pg/mL in the moderate BMI group and 4 pg/mL in the high BMI group. Mean activated protein C was 0.6 ng/mL in the low group, but 1 ng/mL in both the moderate and high BMI groups.

Finally, researchers assessed the risk of developing coronary artery calcium according to the number of women in each group who tested positive for it. Women in the low BMI group had an 8% risk, but women in the moderate and high BMI groups had a 17% and 14% risk, respectively

Implications

According Dr. Jayachandran, the upward trend in risk parameters among women in the moderate and high BMI groups should be taken seriously. "It indicates that there may be more risk for cardiovascular disease. Early menopause is a time to address life style changes that will reduce BMI and therefore, cardiovascular risk," he said.

He added that studies like KEEPS will be pivotal in clearing up the controversy surrounding menopausal hormone therapy and cardiovascular risk. Previous studies, such as the Women's Health Initiative and the Heart and Estrogen/Progestin Replacement Study, did not show any cardiovascular benefit, but the demographics in those studies were different.

"Those studies examined women with a mean age of 62 years. They were further away from their menopause before starting treatment, and

the hormones may not reduce existing atherosclerosis," Dr. Jayachandran said. "We want to know how the hormone treatments might work early on to prevent the development of cardiovascular disease."

Provided by American Physiological Society

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