Study in 7,000 men and women ties obesity, inflammatory proteins to heart failure risk

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Heart specialists at Johns Hopkins and elsewhere report what is believed to be the first wide-scale evidence linking severe overweight to prolonged inflammation of heart tissue and the subsequent damage leading to failure of the body's blood-pumping organ.

The latest findings from the Multiethnic Study of Atherosclerosis (MESA), to be published in the May 6 issue of the *Journal of the American College of Cardiology*, appear to nail down yet one more reason for the estimated 72 million obese American adults to be concerned about their health, say scientists who conducted the research.

"The biological effects of obesity on the heart are quite profound," says senior study investigator João Lima, M.D. "Even if obese people feel otherwise healthy, there are measurable and early chemical signs of damage to their heart, beyond the well-known implications for diabetes and high blood pressure."

He adds that there is "now even more reason for them to lose weight, increase their physical activity and improve their eating habits."

In the latest study, researchers conducted tests and tracked the development of heart failure in an ethnically diverse group of nearly 7,000 men and women, age 45 to 84, who were enrolled in the MESA study, starting in 2000.

Of the 79 who have developed congestive heart failure so far, 35 (44

percent) were physically obese, having a body mass index, or BMI, of 30 or greater. And on average, obese participants were found to have higher blood levels of interleukin 6, C-reactive protein and fibrinogen, key immune system proteins involved in inflammation, than non-obese adults.

A near doubling of average interleukin 6 levels alone accounted for an 84 percent greater risk of developing heart failure in the study population.

The researchers from five universities across the United States also found alarming links between inflammation and the dangerous mix of heart disease risk factors known as the metabolic syndrome. Its combined risk factors for heart disease and diabetes - high blood pressure, elevated blood glucose levels, excess abdominal fat and abnormal cholesterol levels, and particularly obesity - double a person's chances of developing heart failure.

"More practically, physicians need to monitor their obese patients for early signs of inflammation in the heart and to use this information in determining how aggressively to treat the condition," says Lima, a professor of medicine and radiology at the Johns Hopkins University School of Medicine and its Heart Institute.

All MESA study participants, who will be followed through to 2012, had no pre-existing symptoms of heart disease. Upon enrollment, they all underwent a physical exam, including weight and body measurements, blood analysis and an MRI scan to assess heart function.

"Our results showed that when the effects of other known disease risk factors - including race, age, sex, diabetes, high blood pressure, smoking, family history and blood cholesterol levels - were statistically removed from the analysis, inflammatory chemicals in the blood of obese

participants stood out as key predictors of who got heart failure," says Lima.

The chemicals are all known to be part of the body's defensive response to disease. They are well-recognized for producing symptoms that stem from the widening of small blood vessels, including redness and fever, and the release of immune system cells that make blood vessels leak fluid into surrounding tissue, causing swelling and cell death. The inflammatory process eventually leads to cell damage and the buildup of scar tissue near the damaged areas.

In obese participants, interleukin 6, a chemical that activates white blood cells and drives inflammation, was higher than in non-obese participants.

Similarly, a near tripling of average levels of C-reactive protein in study participants increased the chance of heart failure by 36 percent.

C-reactive protein levels are widely known to rise dramatically and speed up the early stages of inflammation when cells swell up with fluid, leading to widespread arterial damage.

One-fifth higher than average blood levels of fibrinogen, best known for its role in blood clotting but also a major player in muscle scarring, bumped up the risk of heart failure by 37 percent.

When the inflammatory protein levels were included in the scientists' statistical analysis, the heightened risk from obesity disappeared.

"What this tells us is that both obesity and the inflammatory markers are closely tied to each other and to
heart failure," says lead researcher Hossein Bahrami, M.D., M.P.H.

Each year, nearly 300,000 Americans die from heart failure.

Bahrami says study results also point to inflammation as a possible catalyst in metabolic syndrome. Increased blood levels of albuminuria, a chemical more known for its association with impaired kidney function and metabolic syndrome boosted risk of a progressively weakening heart nearly tenfold among MESA participants.

Bahrami, a senior cardiology research fellow at Hopkins, says “the basic evidence is building the case that inflammation may be the chemical route by which obesity targets the heart, and that inflammation may play an important role in the increased risk of heart failure in obese people, especially those with the metabolic syndrome.”

He notes that previous studies, also done at Hopkins, have shown that even moderate exercise to lose abdominal fat dramatically offsets the harmful effects of metabolic syndrome on heart function.

Bahrami says the team’s next steps are to determine how, over a longer timeframe, heart function changes with levels of inflammatory markers, and to see if alterations to the immune system proteins halts or speeds up disease.

Source: Johns Hopkins Medical Institutions