Increased cardiovascular risk in HIV-infected patients may relate to arterial inflammation

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The elevated risk of cardiovascular disease seen in patients infected with HIV appears to be associated with increased inflammation within the arteries, according to a study that will appear in a special issue of *JAMA* published in conjunction with the International AIDS Conference. The report from Massachusetts General Hospital (MGH) found that levels of inflammation within the aortas of HIV-infected individuals with neither known cardiovascular disease nor elevated traditional risk factors were comparable to those of patients with established cardiovascular disease.

"Several recent studies, including ones that we've done, have found that HIV-infected patients have about twice the risk of heart attack and stroke as non-infected individuals do," says Steven Grinspoon, MD, director of the MGH Program in Nutritional Metabolism and a member of the Neuroendocrine Unit, the study's principal investigator. "These new data suggest a plausible mechanism through which increased arterial inflammation related to activation of the immune system may increase the risk of cardiovascular events in these patients."

While traditional risk factors – such as accumulation of abdominal fat, smoking, high blood pressure and elevated cholesterol levels – have been thought to contribute to the increased cardiovascular risk in HIV-infected patients, investigators also have theorized that inflammation may play a role as well. Previous evidence suggesting an association was based on measurements of inflammatory markers like C-reactive protein

in the bloodstream, but the current study is the first to provide direct evidence of increased inflammation in the arterial walls of patients with HIV.

The investigators, including Ahmed Tawakol, MD, co-director of the MGH Cardiac MR-PET-CT Program, analyzed the results of PET and CT scans of 81 participants: 27 HIV-infected individuals without known cardiovascular disease, all receiving antiretroviral therapy; 27 non-infected controls without atherosclerosis, matched with the HIV group in terms of age, gender and traditional cardiovascular risk factors; and 27 non-infected controls known to have atherosclerosis, matched by gender with the HIV group. All of the PET scans used a radiopharmaceutical called FDG, which accumulates in areas of inflammatory activity. Imaging data for both control groups were selected prospectively from a database of patients who had been scanned for clinical diagnosis of non-HIV related conditions.

The FDG PET scans revealed that levels of inflammation in the aortas of the HIV-infected participants were higher than those seen in control participants without atherosclerosis and were actually comparable to levels seen in control participants with cardiovascular disease. Levels of arterial inflammation in the HIV group were not affected by traditional risk factors or the type of antiviral treatment they received, and increased inflammation was even seen in patients whose viral levels were at undetectable levels. Measurement of circulating inflammatory markers found that levels of soluble CD163, a marker of monocyte activation, were elevated in the HIV group; but no differences were seen in markers of generalized inflammation.

"Activated monocytes – part of the innate immune system – may be attracted to plaque lesions in the arteries, where they become activated macrophages that release substances contributing, over time, to plaque rupture and heart attack," Grinspoon explains. "Activated macrophages

also can release chemical signals that attract more monocytes, setting up a vicious cycle. We previously showed that increased CD163 levels were associated with noncalcified plaque, which is more susceptible to rupture. Our new findings that levels of CD163, but not other inflammatory markers, are related to inflammation signified by the uptake of FDG – even among patients without detectible virus – suggest that soluble CD163 could be a useful marker of risk-associated inflammation in HIV patients."

A professor of Medicine at Harvard Medical School, Grinspoon stresses that these results do not imply that modification of traditional risk factors is not important in HIV-infected patients but that nontraditional risk factors such as arterial inflammation should also be considered and potentially targeted by new therapies. While FDG-PET scanning would not be appropriate for mass screening of patients, measurement of inflammatory markers like CD163 levels should be explored. His team is currently investigating whether statin treatment might reduce arterial inflammation among HIV-infected patients, the majority of whom demonstrate only modest increases in cholesterol levels.

"Our data also suggest that targeting monocyte activation may be a unique strategy to reduce arterial inflammation in these patients, have implications about the pathogenesis of cardiovascular disease in other inflammatory conditions, and emphasize a new way to look at risk in such patients," Grinspoon adds.

Provided by Massachusetts General Hospital