Medical Xpress

HPV linked to cardiovascular disease in women

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Women with cancer-causing strains of human papillomavirus (HPV) may be at increased risk for cardiovascular disease (CVD) and stroke even when no conventional risk factors for CVD are present.

Researchers at the University of Texas Medical Branch (UTMB) at Galveston are the first to investigate a potential connection between CVD and HPV, one of the most common sexually transmitted infections in the U.S. Their findings are published in the November 1st issue of the Journal of the American College of Cardiology.

"Nearly 20 percent of individuals with CVD do not show any risk factors , indicating that other 'nontraditional' causes may be involved in the development of the disease. HPV appears to be one such factor among women," said lead author Dr. Ken Fujise, Director, Division of Cardiology at UTMB. "This has important clinical implications. First, the HPV vaccine may also help prevent heart disease. Second, physicians should monitor patients with cancer-associated HPV to prevent heart attack and stroke, as well as HPV patients already diagnosed with CVD to avoid future cardiovascular events."

Fujise and his colleagues believe the link may be due to HPV's role in inactivating two tumor suppressor genes, p53 and retinoblastoma protein (pRb) – the same process by which HPV causes cancer. p53 has been shown to be essential in regulating the process of atherosclerosis; the retinoblastoma gene plays a pivotal role in regulating cell proliferation.

"If this biological mechanism is proven, a drug compound that inhibits the inactivation of p53 could help prevent CVD in women already infected with HPV," said Fujise.

Identifying the HPV-CVD Link

The study analyzed nearly 2,500 women ages 20-59 using cross-sectional data from the 2003-2006 National Health and Nutrition Examination Survey (NHANES), which included HPV DNA examination, via self-collected vaginal swabs, and genotyping. Among the study participants, 44.6 percent (1,141) were positive for HPV DNA; 23.2 percent (573) had "oncogenic," cancer-causing types.

Additional NHANES data was used to compare women in three groups: those with oncogenic HPV, those with other HPV types and those who were not infected. The data, drawn from questionnaires, include: prior incidence of CVD; metabolic risks (e.g., blood pressure, body mass index; blood glucose, triglycerides and HDL cholesterol levels, hypertension, diabetes and other co-morbidities); and clinical factors (e.g., age, race, sexual behavior, smoking status and alcohol consumption).

"We found that oncogenic HPV types were strongly associated with CVD, but we did not observe a correlation between HPV and numerous other metabolic risks. Further, the link persevered after adjusting for cardiovascular risk burden and management, other medical conditions and health and sexual behaviors," said Dr. Hsu-Ko Kuo, co-author of the study. "With more research, improved understanding of HPV as an independent factor in CVD may lead to improved patient outcomes – a crucial advancement because heart disease is the number one killer of women."

Fujise and Kuo recommend several directions for future research:

- Reexamine data from randomized controlled clinical trials of HPV vaccines for cardiovascular outcomes.
- Conduct a clinical study to determine whether HPV immunization positively affects cardiovascular outcomes in women.
- Ascertain better understanding of the molecular pathway from HPV infection to atherosclerosis through studies focused on the interaction between HPV and p53/pRb. To date, such studies have focused primarily on only two HPV types although there are more than 100 strains.
- Conduct a follow-up study on cardiovascular outcomes in relation to status of HPV infection to prove a causal relationship between HPV in the development of CVD.
- Finally, because this analysis was limited to women, the association between HPV and CVD among men is still unknown.

Because HPV samples were self-collected, Fujise cautions that there may be errors leading to underreported infection. Similarly, the self-reporting of cardiovascular events or illness may not fully reflect actual disease prevalence, which may indicate an even stronger correlation between HPV and CVD than the researchers observed. "While we're not certain if there is a cause and effect relationship between the two, there is a clear-cut association – with serious public health significance."

Provided by University of Texas Medical Branch at Galveston