バイオマーカーカテプシン Sにより死亡リスクが上昇する

カテプシン Sと心血管疾患およびがんによる死亡リスクとの関連性が発見された

Association found between cathepsin S and risk of death from cardiovascular disease and cancer

蛋白バイオマーカーカテプシン Sの血中レベルの高い高齢男女は死亡リスクが高いとのスタディ結果がEuropean Society of Cardiology学会において発表されJAMAオンライン版に掲載された。研究者らは2つの独立した地域ベースのコホート（ウプサラ成人男性長期スタディ（ULSAM；対象1,009人；平均年齢：71歳；経過観察期間中央値：12.6年間）およびウプサラ高齢者血管系前向き調査（PIVUS；対象987人；平均年齢：70歳；経過観察期間中央値：7.9年間）のデータを使用した。ULSAM群では413人が死亡した（心血管死131人、癌死148人）。PIVUSスタディでは100人が死亡した。年齢、収縮期血圧、糖尿病、喫煙、ボディマスインデックス、総コレステロール、高密度リポ蛋白コレステロール、降圧治療、脂質低下療法、および心血管疾患歴で補正した結果、カテプシン Sは死亡リスク上昇と関連があった。PIVUSコホートでは血清中カテプシン Sレベルが最も高い人々では最も低い人々と比較し死亡リスクが2倍（200%）であった。ULSAMコホートでは、このバイオマーカーレベルが最も高い人々は心血管死亡リスクが1.6倍（60%）高く、癌死のリスクも高かった。

Full Text

In an analysis of data from two separate study groups, elderly men and women who had higher levels of the protein biomarker cathepsin S in their blood had an increased risk of death, according to a study in JAMA. This biomarker might have a relationship with the development of cardiovascular disease and cancer. The study is being published early online to coincide with its presentation at the European Society of Cardiology Congress.

Cathepsin S is a cysteine protease involved in intracellular and extracellular proteolysis. Higher circulating levels of cathepsin S have been shown to be associated with increased inflammatory activity. "Experimental studies suggest that cathepsin S activity is involved in the development of cardiovascular disease via promotion of atherosclerotic plaques and destabilization of advanced plaques. Moreover, cathepsin S activity has been implicated in the development of cancer via stimulation of cancer cell migration and tumor angiogenesis," according to background information in the article. Based on these previous reports, the authors hypothesized that circulating levels of cathepsin S would be a marker for an increased mortality risk. There has been a lack of prospective data regarding this potential association.

Elisabeth Jobs, M.Sc., of Uppsala University, Uppsala, Sweden, and colleagues investigated the association between serum levels of cathepsin S and the risk of mortality in a community-based sample of elderly men and women. The researchers used data from two independent community-based cohorts, the Uppsala Longitudinal Study of Adult Men (ULSAM; n = 1,009; average age: 71 years; baseline period: 1991-1995; median follow-up: 12.6 years; end of follow-up: 2006) and the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS; n = 987; 50 percent women; average age: 70 years; baseline period: 2001-2004; median follow-up: 7.9 years; end of follow-up: 2010). Serum samples were used to measure cathepsin S.

In the ULSAM group, 413 participants died during follow-up. There were a total of 131 deaths due to cardiovascular disease and 148 deaths due to cancer. During follow-up with the PIVUS cohort, 100 participants died. The researchers found that in multivariable models adjusted for age, systolic blood pressure, diabetes, smoking status, body mass index, total cholesterol, high-density lipoprotein cholesterol, antihypertensive treatment, lipid-lowering treatment, and history of cardiovascular disease, higher serum cathepsin S was associated with an increased risk for death.

In the PIVUS cohort, participants with the highest levels of serum cathepsin S had about double (200 percent) the risk of death compared to participants with the lowest levels. The authors also found that in the ULSAM cohort, participants with the highest levels of the biomarker had an approximately 1.6 times (60 percent) increased risk for cardiovascular mortality, and an increased risk for death from cancer.

"Our community-based data confirm and extend previous experimental research that suggest that cathepsin S activity is involved in the pathological processes leading to cardiovascular disease, cancer, and death," the researchers write.

"Given its putative role in atherogenesis and tumorigenesis, cathepsin S has been put forward as a possible target of pharmaceutical intervention and the development of selective cathepsin S inhibitors is ongoing. Some of these inhibitors are being evaluated in various phases of clinical trials. If these drugs are found to be effective, tools for identification of target groups and monitoring of treatment need to be developed. Our study suggests that it is possible to assess serum levels of cathepsin S in large populations. Future intervention trials are needed to evaluate whether cathepsin S inhibition is a safe and effective pharmacological target for these diseases."

The authors add that "further research is needed to determine the utility of cathepsin S measurements in clinical settings."

Conference News