

Does Serum Homocysteine Explain the Connection Between Sexual Frequency and Cardiovascular Risk?

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ABSTRACT

Background: Sexual activity correlates with various health issues, and homocysteine is considered an independent risk factor for cardiovascular events and atherosclerosis. Research on the relation of sexual activity to sexual frequency and homocysteine is sparse.

Aim: To examine the association between sexual frequency and homocysteine in the general population in the United States.

Methods: In total, 2,267 eligible participants 20 to 59 years old who had serum homocysteine data and completed a sexual behavior questionnaire were enrolled from the National Health and Nutrition Examination Survey of 2005 to 2006. The correlation between sexual frequency and serum homocysteine levels was analyzed using a linear regression model and an extended-model approach was performed for covariate adjustment.

Outcomes: Individuals, especially men, in the lower quartiles of sexual frequency had significantly higher serum homocysteine levels, and a sex difference was identified in subgroup analysis.

Results: In a model of quartile-based analysis after adjustment for age, sex, and race and ethnicity, the regression coefficient of the highest quartile of sexual frequency compared with the lowest quartile was -1.326 ($P = .012$). After further adjustment for multiple covariates, the inverse association between sexual frequency and serum homocysteine levels remained unchanged. Negative trends maintained statistical significance (P for trend $< .05$). In subgroup analysis by sex, a negative association between sexual frequency and serum homocysteine levels remained unchanged in men even after adjusting for multiple covariates, but not in women.

Clinical Implications: Clinical physicians in primary care should support patients' sexual activity, and there are implications for health promotion programs.

Strengths and Limitations: This is the first observational investigation stratified by sex to evaluate the correlation between sexual frequency and serum homocysteine levels. The study was a cross-sectional observational investigation and the causal relation should be evaluated in a follow-up study.

Conclusion: Decreased sexual frequency correlated with higher homocysteine levels in a nationally representative sample of US adults, especially men; this might increase the risk of cardiovascular disease or other atherothrombotic events. **Yang H-F, Kao T-W, Lin Y-Y, et al. Does Serum Homocysteine Explain the Connection Between Sexual Frequency and Cardiovascular Risk? J Sex Med 2017;XX:XXX–XXX.**

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INTRODUCTION

Sexual activity is an important component of quality of life in contemporary societies and has a substantial impact on health issues such as disability, mortality, and longevity.^{1,2} Sexual partnership, good-quality sex life, sexual frequency, and sexual interest are positively related to health in middle-age and elderly individuals in the United States.³ The Caerphilly cohort study reported that a higher frequency of orgasmic sexual intercourse was associated with lower mortality and death from coronary artery disease in men.⁴ Sexual frequency was negatively associated with mortality in men and the quantity of sex was noted to be important to men in the Duke First Longitudinal Study of Aging.² Men who engaged in sexual intercourse less than once per week developed erectile dysfunction (ED) at twice the rate as those who reported intercourse once per week and intercourse frequency seemed to predict the development of ED.⁵ In addition, ED and cardiovascular events share many risk factors, including atherosclerosis, smoking, diabetes mellitus, hypertension, and dyslipidemia, and their pathophysiology is mediated through endothelial dysfunction.⁶ In a systemic review and meta-analysis of eight observational studies composed of 12,067 participants, metabolic syndrome was associated with a 2.6-fold increase of ED, and patients with metabolic syndrome should be informed about this relation and encouraged to make lifestyle modifications to improve their general health and to limit cardiovascular risk and ED prevalence.⁷ A total of 740 participants from six clinical trials of lifestyle modification intervention or pharmacotherapy to decrease cardiovascular risk factors with a follow-up of at least 6 weeks showed statistically significant improvement in sexual function in men with ED.⁸ In the Massachusetts Male Aging Study, decreased sexual frequency was an independent cardiovascular risk factor in community-dwelling men and might be a useful method for screening cardiovascular risk.⁹ Corona et al¹⁰ reported that a higher frequency of sexual attempts was independently associated with a lower incidence of major adverse cardiovascular events even after adjusting for known cardiovascular risk factors from longitudinal data. Maintaining an active sexual life appears to have a protective effect on men's overall and cardiovascular health.

Homocysteine is a sulfur-containing amino acid that is an intermediary product in the normal biosynthetic conversion of methionine to cysteine. Homocysteine level is believed to be an independent risk factor for atherosclerosis and cardiovascular disease.¹¹ There are multiple potential mechanisms to explain the role of homocysteine in the development of cardiovascular disease, such as oxidative stress from free radicals,^{12,13} lipid peroxidation,¹⁴ and decreased antioxidant enzyme activity.¹⁵ Therefore, we hypothesized that decreased sexual frequency would be an early predictor of subsequent cardiovascular adverse events, probably through the actions of homocysteine. The aim of this study was to examine this hypothesis by investigating data from the National Health and Nutrition Examination Survey (NHANES) of 2005 to 2006.

METHODS

Study Populations

The NHANES is a continuing series of stratified, cross-sectional, and multistage population-based surveys to evaluate the health and nutritional status of non-institutionalized civilians in the United States. It was designed by the National Center for Health Statistics of the Centers for Diseases Control and Prevention. Extensive household interviews, laboratory tests, and physical examinations are performed to collect information in a specially equipped mobile examination center. Trained examiners gather pertinent information, including age, sex, race and ethnicity, medical history, and the results of medical and physical examinations. The NHANES database is an annual survey and has been released on the NHANES website, which is freely accessible for download and analysis, every other year since 1999.

Measurement of Sexual Frequency

Our data were extracted from the NHANES database of 2005 to 2006. We limited our study population to include participants who completed a sexual behavior questionnaire. A total of 3,285 participants 20 to 59 years old were initially eligible for inclusion for the sexual behavior questionnaire. During the physical examination, the sexual behavior questionnaire was completed in a private room of the mobile examination center using the Audio Computer Assisted Self Interview (ACASI) system. Respondents hear questions through earphones and read questions on the computer screen using the ACASI system. Subjects move at their own rate and point to their answer by touching the screen. Major items include age at first sexual intercourse, number of sexual partners, sexual frequency, sexual orientation, circumcision status (men), and history of sexually transmitted diseases. We focused our study on the question "In the past 12 months, about how many times have you had vaginal or anal sex?" and excluded individuals answering "refused" ($n = 8$), "don't know" ($n = 5$), or "missing" ($n = 1,005$). There were 2,267 persons enrolled in the final analysis.

Measurement of Serum Homocysteine Levels

The Abbott homocysteine assay, a fully automated fluorescence polarization immunoassay from Abbott Diagnostics (Abbott Park, IL, USA), measures serum homocysteine levels. Conversion of homocysteine to S-adenosyl-homocysteine is catalyzed by S-adenosyl-homocysteine hydrolase in the presence of added adenosine. In the subsequent steps, the fluorescence polarization immunoassay detection system uses a specific monoclonal antibody and a fluoresceinated S-adenosyl-homocysteine analogue tracer. Serum homocysteine levels were calculated by the Abbott AxSYM using a machine-stored calibration curve.

Assessment of Covariates

Demographic data and clinical information, including age, sex, race and ethnicity (including Mexican American,

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