Erectile Dysfunction and Mortality

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[Correction added after online publication 15-Jun-2009: Dr. Ganz's name has been updated.]

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ABSTRACT

Introduction. Erectile dysfunction (ED) and cardiovascular disease (CVD) share pathophysiological mechanisms and often co-occur. Yet it is not known whether ED provides an early warning for increased CVD or other causes of mortality.

Aim. We sought to examine the association of ED with all-cause and cause-specific mortality.

Methods. Prospective population-based study of 1,709 men (of 3,258 eligible) aged 40–70 years. ED was measured by self-report. Subjects were followed for a mean of 15 years. Hazard ratios (HR) were calculated using the Cox proportional hazards regression model.

Main Outcome Measures. Mortality due to all causes, CVD, malignant neoplasms, and other causes.

Results. Of 1,709 men, 1,284 survived to the end of 2004 and had complete ED and age data. Of 403 men who died, 371 had complete data. After adjustment for age, body mass index, alcohol consumption, physical activity, cigarette smoking, self-assessed health, and self-reported heart disease, hypertension, and diabetes, ED was associated with HRs of 1.26 (95% confidence interval [CI] 1.01–1.57) for all-cause mortality, and 1.43 (95% CI 1.00–2.05) for CVD mortality. The HR for CVD mortality associated with ED is of comparable magnitude to HRs of some conventional CVD risk factors.

Conclusions. These findings demonstrate that ED is significantly associated with increased all-cause mortality, primarily through its association with CVD mortality. **Araujo AB, Travison TG, Ganz P, Chiu GR, Kupelian V, Rosen R, Hall SA, and McKinlay JB. Erectile dysfunction and mortality. J Sex Med 2009;6:2445–2454.**

Key Words. Aging; Erectile Dysfunction; Cardiovascular Disease; Longitudinal Studies; Men; Mortality

Introduction

Erectile dysfunction (ED) affects approximately 18 million men aged 20 years or older in the United States [1]. With aging of the United States and worldwide population, a considerable increase in the prevalence of ED is projected [2]. The factors that increase risk of ED include older age, depression, diabetes, and cardiovascular disease (CVD) risk factors [3–7]. The relationship between ED and CVD has received substantial attention. The prevailing notion supported by relatively scant data is that ED may serve as a sentinel marker for CVD [8–18]. This is based largely on shared pathophysiological mechanisms (e.g., endothelial dysfunction, arterial occlusion, systemic inflammation) [8,11,14,19–24] and risk factors [4,6,11,25–28], the high co-prevalence of both conditions [5,13,15,29,30], and the reasonable premise that progressive occlusive disease should manifest earlier in the microvasculature than in larger vessels [14,31]. Prospective studies examining ED as a sentinel for CVD are rare, but recent data from the placebo arm of the Prostate Cancer Prevention Trial (PCPT) [32], the Olmstead County Study [33], as well as others [34,35] provide some support, although not for the most meaningful end points of cardiovascular and overall mortality. Any link between ED and mortality would have important clinical implications in light of the observation that sudden death may be the first manifestation of CVD [36–38].

To our knowledge, PCPT is the only study to examine the association between ED and mortality

risk [32]. In that study, death from any cause was unrelated to prevalent or incident ED. The number of deaths in PCPT, however, was relatively small, and follow-up was short at 7 years. Our objective was to examine the association of ED with all-cause and cause-specific mortality in a well-characterized cohort of men who were followed over a mean of 15 years. We tested the hypothesis that ED predicts all-cause mortality, primarily through its association with CVD mortality.

Methods

Sample

The Massachusetts Male Aging Study (MMAS) is a prospective observational cohort study of aging, health, and endocrine and sexual function in a population-based random sample of men between ages 40–70 years [39]. A total of 1,709 respondents (52% of 3,258 eligible) completed the baseline (1987–1989; baseline) protocol. MMAS subjects were observed again in 1995–1997 (n = 1,156, 77% response rate) and 2002–2004 (n = 853, 65% response rate). These response rates were expected, given the requirements for early-morning phlebotomy and extensive in-person interviews. Participants received no financial incentive at baseline, and $50 and $75 remunerations at the first and second follow-ups, respectively.

Protocol

Extensive details on the MMAS have been published elsewhere [39]. The core field protocol for MMAS remained the same between throughout the study. A trained field technician/phlebotomist visited each subject at home, administered a health questionnaire, and obtained two nonfasting blood samples. Anthropometrics (height, weight, hip, and waist circumference) and blood pressure were directly measured according to standard protocols developed for large-scale fieldwork [40]. Two nonfasting blood samples were drawn, and serum was pooled for analysis. High-density lipoprotein (HDL) cholesterol was measured at a Centers for Disease Control–certified lipid laboratory (Miriam Hospital, Providence, RI). The following information was collected via interviewer-administered questionnaire: demographics, psychosocial factors, history of chronic disease, self-assessed general health status, tobacco and alcohol use, nutritional intake, and physical activity/energy expenditure during the past seven days. MMAS received institutional review board approval, and all participants gave written informed consent.

Covariates

A common set of variables was used to control for confounding in multivariate statistical models. Age and body mass index (BMI) were input as continuous variables. In addition, the following categorical variables were included: alcohol consumption (<1, 1, and 2+ drinks/day), calories expended in physical activity (none, <200 kcal/day and ≥200 kcal/day), current cigarette smoking, self-assessed health (excellent, very good, good, fair/poor), and self-reported chronic disease (heart disease, hypertension, and diabetes).

ED

At the end of the interview, the subject was given a 23-item questionnaire on sexual activity to be completed in private and returned in a sealed envelope [41]. The questionnaire included 13 items related to ED: e.g., "During the last six months have you ever had trouble getting an erection before intercourse begins?" The 13 items were combined in a discriminant-analytic formula to assign a degree of erectile function to each subject [42]. The same discriminant formula was used at both baseline and follow-up.

Calibration data for the discriminant formula were taken from an additional single-question, subjective self-assessment of ED, included in the follow-up questionnaire in response to recommendations of the NIH Consensus Panel [3]. Impotence was defined as "being able to get and keep an erection that is rigid enough for satisfactory sexual activity." The subject rated himself as completely impotent ("never able to get and keep an erection . . ."), moderately impotent ("sometimes able . . ."), minimally impotent ("usually able . . ."), or not impotent ("always able . . ."). In random subsets of the follow-up samples, the self-assessment was validated [43] against two established ED measures, the International Index of Erectile Function [44] ($r = 0.71$, n = 254) and the Brief Male Sexual Function Inventory [45] ($r = 0.78$, n = 251), as well as an independent urologic assessment [46]. As we have done in previous analyses [4,5,47], we analyzed both the four-category ED status variable, and also a binary ED status variable (absence/presence), which was defined as moderate or complete ED.