Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 56, No. 23, 2010
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2010.04.067

Erectile Dysfunction and Later Cardiovascular Disease in Men With Type 2 Diabetes

Prospective Cohort Study Based on the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) Trial

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Objectives The aim of this study was to examine the relationship between erectile problems in men and cardiovascular disease (CVD) mortality.

Background Although there are plausible mechanisms linking erectile dysfunction (ED) with coronary heart disease (CHD) and stroke, studies are scarce.

Methods In a cohort analysis of the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) trial population, 6,304 men age 55 to 88 years with type 2 diabetes participated in a baseline medical examination when inquiries were made about ED. Over 5 years of follow-up, during which study members attended repeat clinical examinations, the presence of fatal and nonfatal CVD outcomes, cognitive decline, and dementia was ascertained.

Results After adjusting for a range of covariates, including existing illness, psychological health, and classic CVD risk factors, relative to those who were free of the condition, baseline ED was associated with an elevated risk of all CVD events (hazard ratio: 1.19; 95% confidence interval: 1.08 to 1.32), CHD (hazard ratio: 1.35; 95% confidence interval: 1.16 to 1.56), and cerebrovascular disease (hazard ratio: 1.36; 95% confidence interval: 1.11 to 1.67). Men who experienced ED at baseline and at 2-year follow-up had the highest risk for these outcomes.

Conclusions In this cohort of men with type 2 diabetes, ED was associated with a range of CVD events. (J Am Coll Cardiol 2010; 56:1908–13) © 2010 by the American College of Cardiology Foundation

Erectile dysfunction, the inability to achieve and maintain a penile erection for satisfactory sexual performance (1), can be highly prevalent, with some estimates as high as 80% in elderly men with comorbidities such as diabetes (2). Originally thought to be psychogenic or neuropathic in origin, several lines of evidence now suggest that the predominant etiology is

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Manuscript received September 24, 2009; revised manuscript received April 15, 2010, accepted April 30, 2010.

vascular (3–5). Thus, risk factors for erectile dysfunction (ED) (e.g., smoking, raised blood pressure, obesity) appear to be the same as those for cardiovascular disease (CVD) (3), and the occurrence of erectile dysfunction rises monotonically with a progressive clustering of these indexes.

Erectile dysfunction appears to be associated with increased risk for clinical events of CVD (6,7), coronary heart disease (CHD) (8–10), and stroke (9), but prospective cohort studies, which provide the best observational evidence of a relationship are very scarce. We address this paucity of evidence by using data from cohort analyses of a large, well-characterized, randomized controlled trial.

Abbreviations and Acronyms

CHD = coronary heart disease

CVD = cardiovascular disease

ED = erectile dysfunction

Methods

The ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) trial, described in detail elsewhere (11), was designed to investigate the separate effects of routine blood pressure lowering and intensive blood glucose control on vascular outcomes in patients with existing type 2 diabetes. In brief, from 2001 to 2003, 12,877 men and women age 55 to 88 years with type 2 diabetes and histories of major macrovascular or microvascular disease, or at least 1 other cardiovascular risk factor, were recruited from 215 centers in 20 countries. After an initial "run-in" phase, 11,140 subjects (6,407 men) were randomized using a factorial design to perindopril-indapamide or placebo and to intensive blood glucose control on the basis of gliclazide modified release or to standard blood glucose control. The flow of patients through the study is depicted in Figure 1. For the purposes of the present study, data from the trial were analyzed on the basis of a prospective cohort study design, as we have done previously (12). Approval to conduct the trial was obtained from the ethics committee of each study center; all participants provided written informed consent.

Baseline examination. At study induction, participants responded to questionnaire inquiries and took part in a medical examination. Glycosylated hemoglobin, blood cholesterol (and fractions), blood pressure, resting heart rate, and serum creatinine were measured using standard protocols. Height and weight were used to derive body mass index (kg/m^2). Nurses administered a series of questions regarding ethnicity, educational attainment, physical activity, alcohol intake, cigarette smoking habit, major chronic

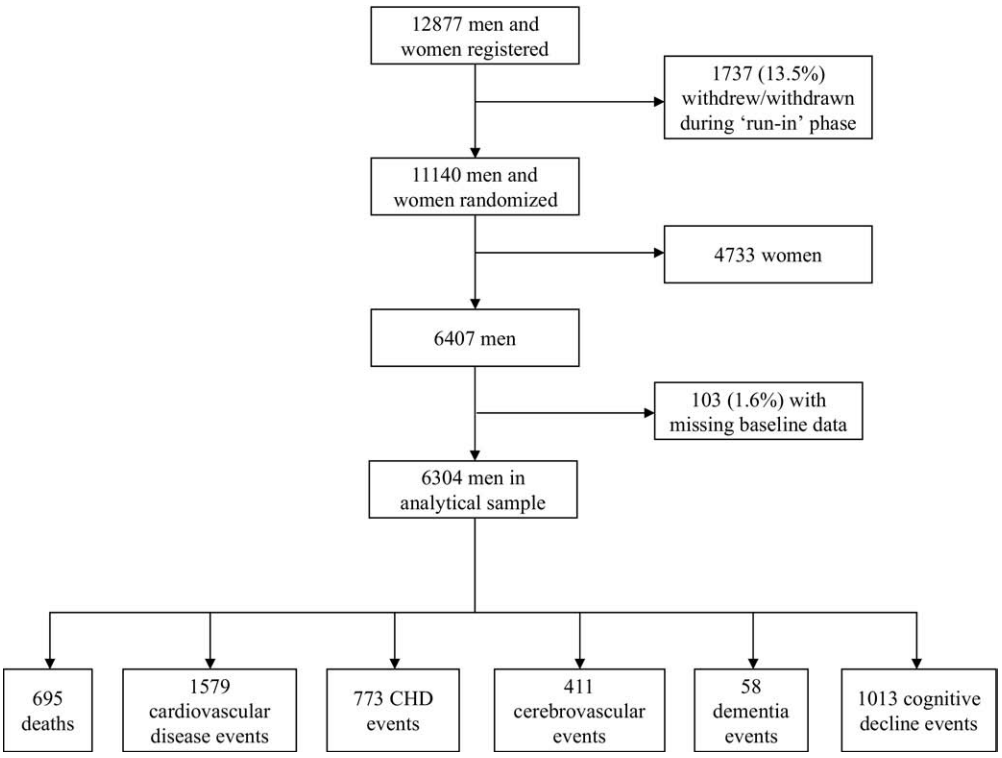

Figure 1 Flow of Study Participants Through the ADVANCE Trial

Flow of participants into the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) trial, focusing on men who reported their erectile function and who had complete covariate data at baseline. The causes and numbers of deaths and events in these men after 5 years of follow-up are provided in the last row. CHD = coronary heart disease.