Original article

# Height and risk of sudden cardiac death: the Atherosclerosis Risk in Communities and Cardiovascular Health Studies

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ABSTRACT

*Purpose:* Sudden cardiac death (SCD) is an important cause of mortality in the adult population. Height has been associated with cardiac hypertrophy and an increased risk of arrhythmias but also with decreased risk of coronary heart disease, suggesting a complex association with SCD.
*Methods:* We examined the association of adult height with the risk of physician-adjudicated SCD in two large population-based cohorts: the Cardiovascular Health Study and the Atherosclerosis Risk in Communities study.
*Results:* Over an average follow-up time of 11.7 years in Cardiovascular Health Study, there were 199 (3.6%) cases of SCD among 5556 participants. In Atherosclerosis Risk in Communities study, over 12.6 years, there were 227 (1.5%) cases of SCD among 15,633 participants. In both cohorts, there was a trend toward decreased SCD with taller height. In fixed effects meta-analysis, the pooled hazard ratio per 10 cm of height was 0.84; 95% confidence interval, 0.73–0.98; $P = .03$. The association of increased height with lower risk of SCD was slightly attenuated after inclusion of risk factors associated with height, such as hypertension and left ventricular hypertrophy. The association appeared stronger among men than women in both cohorts.
*Conclusions:* In two population-based prospective cohorts of different ages, greater height was associated with lower risk of SCD.

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## Introduction

Sudden cardiac death (SCD), with an estimated incidence of between 180,000 and 450,000 cases in the United States [1] and a global incidence of 4–5 million people per year [2], is a major public health issue. Although SCD can result from multiple pathologic processes, the major cause for SCD is ventricular tachyarrhythmias, including ventricular tachycardia and fibrillation. Left ventricular

(LV) mass, which has been associated with risk of both ventricular fibrillation and SCD [3,4], is also associated with increased height [5]. Based on this association, many investigators have suggested the need to index LV mass to body stature, although the specific manner of this adjustment remains uncertain [6]. Implicit in these adjustments is the concept that height itself is not associated with SCD, such that by adjusting for it, one is able to more clearly identify the "pathologic" increase in LV mass. However, if height itself is associated with SCD, then depending on the nature of this association, such an adjustment might be counterproductive. Indeed, we recently demonstrated this phenomenon for the association of height with atrial fibrillation [7].

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Analysis of the causes of SCD is complicated by the multiple pathologic mechanisms that can lead to ventricular tachyarrhythmias (and other causes of SCD, such as asystole). Myocardial ischemia can cause ventricular fibrillation itself. This mechanism is well described, with approximately 80% of cases of SCD [8] being associated with coronary artery disease. To complicate matters, height is inversely associated with risk of coronary heart disease (CHD) [9], emphasizing that the overall association of height and SCD, with potentially both adverse (via LV mass) and beneficial (via CHD) pathways, requires formal study.

To address these issues, we examined this association in two large prospective cohort studies that span a range of ages and include formal adjudication of cases of SCD.

## Materials and methods

In both cohorts, all study procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2004.

### The Atherosclerotic Risk in Communities study

The Atherosclerosis Risk in Communities (ARIC) study [10] is a multicenter prospective cohort study investigating the etiology of atherosclerotic disease in a middle-aged biracial population. Participants at baseline (1987–1989) included 15,792 men and women aged 45–64 years, recruited from four communities in the United States: Forsyth County, NC; Jackson, MS (African Americans only); the northwest suburbs of Minneapolis, MN; and Washington County, MD.

The ARIC study protocol was approved by the institutional review board of each participating center. After obtaining written informed consent, participants underwent a baseline clinical examination and were re-examined in 1990–1992, 1993–1995, and 1996–1998. Of the original study population, 159 subjects were excluded due to missing data, leaving an analysis size of 15,633 participants.

Risk factors examined in this analysis were ascertained at the baseline examination and were followed through December 31, 2001. Participants reported information on smoking status, education, history of cardiovascular disease, use of medications, and underwent examination that included standard height and weight measurements. Other prevalent risk factors examined included diabetes mellitus, resting blood pressure or use of antihypertensives, prevalent heart failure (HF) [11], CHD [11], and stroke.

Participants underwent a standard supine digitally recorded 12-lead electrocardiogram (ECG) with classification according to the Minnesota Code [12]. Left ventricular hypertrophy was defined electrocardiographically based on Cornell criteria [13].

### Determination of SCD in ARIC

All participants were contacted annually by phone and all hospitalizations and deaths in the previous year were identified. For deaths, we obtained death certificates. If the death occurred out-of-hospital, we also sought next of kin interviews and physician, coroner, and autopsy information about the death. To classify SCD, all events classified as having fatal CHD (definite fatal myocardial infarction, definite fatal CHD, or possible fatal CHD, in- and out-of-hospital) were reviewed again and adjudicated by a committee of physicians, funded through the Johns Hopkins University Donald W. Reynolds Cardiovascular Research Center. SCD was defined as a sudden pulseless condition from a cardiac origin in a previously stable individual. After review of data available, cases were classified as "definite" sudden arrhythmic death, "possible" sudden arrhythmic death, "not" sudden arrhythmic death, or unclassifiable.

### The Cardiovascular Health Study

The design and objectives of the Cardiovascular Health Study (CHS) have been previously described [14]. In brief, CHS is a longitudinal study of men and women aged 65 years or older, randomly selected from Medicare lists in Pittsburgh, PA; Forsyth County, NC; Sacramento County, CA; and Washington County, MD. The original cohort of 5201 participants was enrolled in 1989–1990; a second cohort of 687 African Americans was recruited in 1992–1993. Except where specified otherwise, both cohorts were used in this analysis, providing a total of 5888 participants. The institutional review board at each center approved the study, and each participant gave informed consent.

The baseline examination included a standardized questionnaire assessing a variety of risk factors, including smoking, alcohol intake, history of stroke, CHD, and HF, self-reported health status, and medication use on enrollment. Methods of determining prevalent cardiovascular disease were previously validated [15]. The examination included measurements of standing height, weight, and seated blood pressure (measured with a random-zero sphygmomanometer) [15], as well as a resting 12-lead ECG.

Of the initial 5888 individuals in the study population, we excluded 332 participants missing data on height, leaving a total of 5556 individuals for the analysis (Table 1).

Participants were contacted every 6 months for follow-up, alternating between a telephone interview and a clinic visit for the first 10 years and by telephone interview only thereafter. Participants were followed from baseline until June 30, 2006, or death from other causes. The maximum follow-up was 16 years (median 12.5 years).

### Determination of SCD in CHS

Death certificates, inpatient records, nursing home or hospice records, physician questionnaires, interviews with next-of-kin, and autopsy reports, where available, were reviewed to determine the cause of death. SCD was defined as a sudden pulseless condition, presumed to be due to a cardiac arrhythmia, in a previously stable individual that occurred out of the hospital or in the emergency room. For unwitnessed deaths, the participant must have been seen within 24 hours of the arrest in a stable condition and without evidence of a noncardiac cause of cardiac arrest. SCD cases could not be under hospice or nursing home care or have a life-threatening noncardiac comorbidity.

### Analysis

Analyses were performed separately for each cohort and then combined in a prespecified meta-analysis. We examined *definite* SCD as the primary end point, with *total* SCD (includes both definite and possible) used as validation. For individual cohort analyses, a baseline model was used using Cox proportional hazards regression with adjustment for age, sex, race, study location, smoking status, and highest level of education achieved. If death during follow-up was due to other causes than SCD, the individual was censored at that time. We chose to include smoking status given the likelihood that achieved height and smoking status are markers of early life socioeconomic status [16]. A second model was examined with inclusion of potential mediators (risk factors) of SCD potentially influenced by height and included waist circumference, hypertension, resting heart rate, diabetes, prevalent HF, stroke, or CHD, and left ventricular hypertrophy as defined by ECG criteria [12,17]. These analyses were also repeated with stratification by sex and race. We tested multiplicative interactions between height and sex, prevalent CHD, and race. In a subanalysis, we examined any incident nonfatal CHD as a time-varying covariate in the two models,