Height and Incidence of Cardiovascular Disease in Male Physicians

Patricia R. Hebert, PhD; Janet W. Rich-Edwards, MPH; JoAnn E. Manson, MD, DrPH; Paul M. Ridker, MD; Nancy R. Cook, ScD; Gerald T. O'Connor, ScD; Julie E. Buring, ScD; Charles H. Hennekens, MD, DrPH

Background. An inverse association between height and risk of coronary heart disease (CHD) has been reported in several case-control and cohort studies, but the reasons for the association remain uncertain. We evaluated this association among 22,071 male physicians, a population homogeneous for high educational attainment and socioeconomic status in adulthood.

Methods and Results. The study population was comprised of participants in the Physicians' Health Study, a randomized, double-blind, placebo-controlled trial of low-dose aspirin and \( \beta \)-carotene in the primary prevention of cardiovascular disease and cancer among US male physicians, aged 40 to 84 years, in 1982. Participants were classified into five height categories at study entry, from shortest to tallest, and were followed an average of 60.2 months to determine the incidence of myocardial infarction (MI), stroke, and death from cardiovascular disease. Men in the tallest (≥73 in. or 185.4 cm) compared with the shortest (<67 in. or 170.2 cm) height category had a 35% lower risk of MI (relative risk, 0.65; 95% confidence interval, 0.44 to 0.99; \( P = .04 \)), after adjusting for known cardiovascular risk factors. Further, a marginally significant inverse trend (\( P \) trend = .05) across the height categories was observed. Although the relationship was not strictly linear, for every inch of added height, there was an approximate 2% to 3% decline in risk of MI. In contrast, men in the tallest compared with the shortest height category had only small and nonsignificant decreases in risk of stroke and cardiovascular death. While no significant trend in risks of these end points across the height categories was observed, the numbers of events for these end points were far less than for MI, and thus the confidence intervals were wide.

Conclusions. These data indicate that height is inversely associated with subsequent risk of MI. At this time, a few mechanisms are plausible, but none are convincing. Other epidemiological and basic research efforts are needed to explore the association between height and cardiovascular disease.

Key Words • height • coronary disease • myocardial infarction

An inverse association between height and risk of coronary heart disease (CHD) has been reported in several analytic studies, both case-control1-3 and cohort.4-7 Height may be an independent risk factor or a marker for some other variable. For example, heterogeneity of social class may be a confounding factor and has not been adequately addressed in previous studies. The early termination of the randomized aspirin component of the US Physicians' Health Study provided an opportunity to test the association between height and risk of cardiovascular disease in a large cohort of 22,071 male physicians, a population homogeneous for high educational attainment and socioeconomic status in adulthood.

Methods

The subjects and methods of the Physicians' Health Study have been described in detail elsewhere.8,9 Briefly, 22,071 US male physicians, aged 40 to 84 years at entry and free from prior myocardial infarction (MI), stroke, or transient cerebral ischemia, were assigned at random, using a 2x2 factorial design, to one of four treatment groups: aspirin (325 mg every other day), \( \beta \)-carotene (50 mg on alternate days), both active agents, or both placebos.

Every 6 months for the first year, and annually thereafter, participants were sent brief questionnaires about their compliance with their assigned regimen and the occurrence of any relevant events. At baseline, participants reported their height to the nearest inch. Information was also obtained on a number of known cardiovascular risk factors, including weight, smoking, systolic and diastolic blood pressures, hypertension, diabetes mellitus, elevated cholesterol, angina pectoris, parental history of MI prior to age 60, use of alcohol,
and exercise frequency. On each follow-up questionnaire, participants were asked whether they had experienced any cardiovascular disease (CVD) event since the return of the last questionnaire.

For all reported CVD events, consent from participants or, in the case of death, from the next of kin was requested to obtain relevant medical records. Reported diagnoses were confirmed after examination of medical records and other available information by an end points committee of physicians that included two internists, a cardiologist, and a neurologist, all blinded to treatment assignment. Diagnoses of nonfatal MI were confirmed on the basis of the World Health Organization criteria.\textsuperscript{10} Nonfatal stroke was defined as a typical neurological deficit, sudden or rapid in onset, lasting more than 24 hours and attributable to a cerebrovascular event.\textsuperscript{11} Death from cardiovascular disease was documented by convincing evidence of a cardiovascular mechanism on the basis of all available information, including death certificates, hospital records, and—for deaths outside the hospital—observers’ impressions.\textsuperscript{9} When corroborating information could not be obtained, a reported MI, stroke, or CVD death was not considered to be confirmed. Records were available for review for 95.6% of reported MIs, 95.2% of strokes, and 94.8% of all deaths. All analyses are based on confirmed events.

Although the β-carotene component of the trial is ongoing, the Data Monitoring Board recommended early termination of the blinded aspirin component, primarily due to the emergence of a statistically extreme (44%) reduction in risk of a first MI.\textsuperscript{8} Thus, the data for this analysis include all incident CVD events as of January 25, 1988, the date physicians were unblinded to their aspirin treatment assignment. At that time, participants had been followed for an average of 60.2 months (range, 46 to 77 months). Of the survivors, a total of 99.7% were still providing information on morbidity, and the vital status of all 22,071 physicians was known.

Height was used both as a continuous variable (in inches) as well as an ordinal scale variable. The mean height in this population was 70.1 in. (178.1 cm) with a standard deviation of 3.0 in. Because height was reported to the nearest inch, its distribution was not strictly continuous. An attempt was made to form categories as close to quintiles as possible (Table 1). The shortest and tallest groups were 67 in. (170.2 cm) or less and 73 in. (185.4 cm) or more, respectively, which fell 1 SD below and above the mean. These represented 16.2% and 17.3% of the study population. Three middle categories were formed from the remaining 5 in. The largest category was comprised of men 70 and 71 in. in height, which included the mean and median height of all men in the study. Thus, the five categories of height were ≤67 in. (170.2 cm), 68 to 69 in. (172.7 to 175.3 cm), 70 to 71 in. (177.8 to 180.3 cm), 72 in. (182.9 cm), and ≥73 in. (185.4 cm).

Baseline characteristics were first compared across the height categories. Age-adjusted means and prevalence rates were obtained by the method of direct standardization to the overall age distribution by 5-year categories.\textsuperscript{12} Outcome measures included total MI (fatal plus nonfatal), total stroke (fatal plus nonfatal) and death from cardiovascular disease. Incidence rates were calculated by dividing the numbers of events by person-time of follow-up for men in each category of height. Relative risks were calculated as the ratio of the incidence rate in each of the height categories compared with that of the shortest, which served as the referent group. To control simultaneously for the effects of known cardiovascular risk factors, multivariate relative risks (RRs) were derived from proportional-hazards models.\textsuperscript{13}

For each RR, the 95% confidence interval and two-sided P values were calculated. The P values for trend over height categories and risks of various outcomes were calculated by treating height as an ordinal variable (categories 1 to 5) in the proportional-hazards model. In addition, various functional forms of height were considered, including log, square, and cubic forms. All models controlled for age (in years) and aspirin and β-carotene assignments. Additional analyses also controlled for body mass index (continuous variable), smoking (current, past), history of hypertension (yes, no), diagnosis of diabetes (yes, no), history of elevated cholesterol (yes, no), history of angina pectoris (yes, no), parental history of MI prior to age 60 (yes, no), alcohol use (daily, weekly), and exercise at least weekly (yes, no).

## Results

The mean height (70.1 in or 178.1 cm) of the study participants is taller than the average of 68 to 69 in. (172.7 to 175.3 cm) of all US men of similar age.\textsuperscript{14} As expected, shorter men were older than taller men (P trend < .001) (Table 2). Other baseline cardiovascular risk factors, adjusted for age, also varied across the five height categories. A greater proportion of shorter men were overweight (P trend < .001), and they had a higher body mass index (P < .001 for the shortest versus other height categories). Although there was a positive association between height and systolic blood pressure (P trend < .001), no trend was seen for diastolic blood pressure and a higher proportion of shorter men reported hypertension (P trend < .001). Similarly, the reported prevalences at baseline of elevated cholesterol (P trend < .001) and diabetes mellitus (P trend = .02) were inversely related to height. Taller men exercised more frequently (P trend < .001) and were more likely to drink alcohol (P trend < .001). Specifically, 28.4% of those in the tallest category reported daily alcohol use compared with 20.6% in the shortest. There were no

## Table 1. Distribution of Heights in 22,069 Participants in the Physicians’ Health Study

<table>
<thead>
<tr>
<th>Height Categories</th>
<th>Height (In.)</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≤67</td>
<td>3571</td>
<td>16.2</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>2316</td>
<td>10.5</td>
</tr>
<tr>
<td>3</td>
<td>69</td>
<td>2391</td>
<td>10.8</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>3502</td>
<td>15.9</td>
</tr>
<tr>
<td>5</td>
<td>≥73</td>
<td>3819</td>
<td>17.3</td>
</tr>
</tbody>
</table>

Two participants were excluded because no information on height was available; one of these had a nonfatal myocardial infarction during follow-up.
TABLE 2. Age-Adjusted Prevalence of Potential Cardiovascular Risk Factors at Baseline by Categories of Height

<table>
<thead>
<tr>
<th>Height Categories</th>
<th>Mean age, y *†</th>
<th>Mean body mass index, kg/m² *†</th>
<th>Overweight, %‡</th>
<th>Mean systolic blood pressure, mm Hg †</th>
<th>Mean diastolic blood pressure, mm Hg †</th>
<th>Reported hypertension, %§</th>
<th>Smoking, %</th>
<th>Assigned to active aspirin, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (shortest) ≤67 in (n=3571)</td>
<td>54.1 (10.5)</td>
<td>25.8 (4.1)</td>
<td>21.0</td>
<td>125.7 (11.3)</td>
<td>79.1 (7.7)</td>
<td>15.4</td>
<td>38.3</td>
<td>50.1</td>
</tr>
<tr>
<td>2 68-69 in. (n=4707)</td>
<td>54.2 (9.7)</td>
<td>24.8 (2.7)</td>
<td>11.5</td>
<td>125.8 (11.1)</td>
<td>78.6 (7.4)</td>
<td>14.3</td>
<td>39.3</td>
<td>50.5</td>
</tr>
<tr>
<td>3 70-71 in. (n=6629)</td>
<td>53.4 (9.4)</td>
<td>24.8 (2.7)</td>
<td>12.2</td>
<td>126.0 (11.3)</td>
<td>78.8 (7.5)</td>
<td>14.1</td>
<td>39.7</td>
<td>49.9</td>
</tr>
<tr>
<td>4 72 in. (n=3343)</td>
<td>52.4 (9.0)</td>
<td>24.8 (2.7)</td>
<td>13.7</td>
<td>126.4 (11.0)</td>
<td>78.9 (7.3)</td>
<td>12.5</td>
<td>38.6</td>
<td>48.3</td>
</tr>
<tr>
<td>5 (Tallest) ≥73 in. (n=3819)</td>
<td>51.6 (8.6)</td>
<td>24.8 (2.8)</td>
<td>12.2</td>
<td>126.5 (11.3)</td>
<td>78.9 (7.4)</td>
<td>12.9</td>
<td>41.1</td>
<td>50.5</td>
</tr>
</tbody>
</table>

*Crude age. †Mean (SD). ‡Body mass index >27.8 kg/m². §Hypertension is defined as systolic blood pressure >160 mm Hg or diastolic blood pressure >95 mm Hg or currently treated with antihypertensive medication. ¶MI denotes myocardial infarction, occurring in either parent before age 60.

Differences across the height categories in the proportion of men who reported angina at baseline (P trend=.43). There also were no differences in the proportion of men assigned to active aspirin (P trend=.69), nor was height a predictor of compliance with the active aspirin regimen.

During an average of 60.2 months of follow-up, there were 377 total MIs (fatal and nonfatal), 217 total strokes (80% of which were ischemic), and 164 total CVD deaths.

In Table 3, the RRs are shown for risk of MI by height categories, beginning with crude estimates (adjusted for age, aspirin-assignment, and β-carotene treatment assignment only) and adding first body mass index alone and then all covariates to the model. As would be expected since shorter men, in general, had less favorable cardiovascular risk profiles at entry into the study, the protective effect of taller stature on risk of MI became less pronounced as covariates were added to the model. Initially, in the crude analysis, men in the tallest compared with the shortest height category had a 47% reduction in risk of MI, and the P value for trend across the height categories was .0002 (see Table 2). When body mass index was added to the model, the reduction in risk comparing the extremes of height was slightly less (41%), and the P value for trend was increased to .002.

The inverse association, however, although weaker, persisted after control for all covariates in the full multivariate model (Table 3 and Figure). Men in the tallest height category had an approximate 35% decrease in risk of total MI compared with those in the shortest category (RR=.65; 95% confidence interval, 0.44 to 0.99 P=.04), after adjusting for age, aspirin assignment, β-carotene assignment, body mass index, smoking, history of hypertension, diagnosis of diabetes, history of elevated cholesterol, history of angina pectoris, parental history of MI prior to age 60, alcohol use, and exercise frequency. Further, a marginally significant inverse trend (P=.05) across height categories persisted. For every added inch of height, there was an approximate 2% to 3% decrease (P=.16) in risk of MI over the 5 years of follow-up.

RRs of MI by height categories were also calculated using the same model previously described but excluding the 286 participants with a history of angina at baseline. These risk estimates were similar to those from the original model (Table 3) and were from the shortest to tallest height categories in the full multivariate model 1.0, 0.76, 1.02, 0.61, and 0.66 (P trend=.06).

Because the relationship between height and MI did not appear to be strictly linear, various functional forms of height were explored in predicting risk of MI,
### Table 3. Relative Risks and 95% Confidence Intervals for Cardiovascular Disease by Categories of Height

<table>
<thead>
<tr>
<th>Events</th>
<th>1 (shortest) ≤67 in. (n=3571)</th>
<th>2 68-69 in. (n=4707)</th>
<th>3 70-71 in. (n=6629)</th>
<th>4 72 in. (n=3343)</th>
<th>5 (tallest) ≥73 in. (n=3819)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI (fatal plus nonfatal)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>82§</td>
<td>95§</td>
<td>121</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude RR (95% CI)*</td>
<td>1.0 (0.66-1.20)</td>
<td>0.89 (0.64-1.13)</td>
<td>0.85 (0.42-0.89)</td>
<td>0.61 (0.36-0.79)</td>
<td></td>
</tr>
<tr>
<td>Simple multivariate RR</td>
<td>1.0 (0.73-1.32)</td>
<td>0.98 (0.71-1.25)</td>
<td>0.94 (0.46-0.98)</td>
<td>0.67 (0.40-0.87)</td>
<td></td>
</tr>
<tr>
<td>(95% CI)†‡</td>
<td>1.0 (0.55-1.08)</td>
<td>0.77 (0.70-1.29)</td>
<td>0.95 (0.46-1.03)</td>
<td>0.68 (0.44-0.99)</td>
<td></td>
</tr>
<tr>
<td>Full model multivariate RR</td>
<td>1.0 (0.60-1.47)</td>
<td>0.94 (0.68-1.57)</td>
<td>1.03 (0.63-1.80)</td>
<td>1.07 (0.44-1.36)</td>
<td></td>
</tr>
<tr>
<td>(95% CI)‡‡</td>
<td>1.0 (0.38-1.27)</td>
<td>0.69 (0.57-1.65)</td>
<td>0.97 (0.80-2.65)</td>
<td>1.46 (0.44-1.70)</td>
<td></td>
</tr>
</tbody>
</table>

RR indicates relative risks; CI, confidence interval; and MI, myocardial infarction.
*Controlled for age (in years), aspirin assignment, and β-carotene assignment only.
†Controlled for age (in years), aspirin assignment, β-carotene assignment, and body mass index (continuous variable).
‡Controlled for age (in years), aspirin assignment, β-carotene assignment, body mass index (continuous variable), smoking (current, past), history of hypertension (yes, no), diagnosis of diabetes (yes, no), history of elevated cholesterol (yes, no), history of angina pectoris (yes, no), parental history of MI prior to age 60 (yes, no), alcohol use (daily, weekly), and exercise frequency at least weekly (yes, no).
§47 Mls occurred among those 68 in. and 48 Mls among those 69 in. tall.
||Notes for the table:
- Including log, square, and cubic transformations. The best fit for height as a continuous variable appeared to be using cube of height (P=.14 in the fully adjusted model). However, this relationship was still not as strong as when height was categorized into the five height groups (P trend=.05), suggesting that there may be a more complex relationship between height and MI. The height and MI relationship was also explored using an alternative approach to categorizing height. The same cutoff points for the ends of the distribution (67 in. or less and 73 in. or more) were maintained, but the intermediate height categories were comprised of each inch of height (eg, 68, 69, 70, 71, and 72 in.). In this case, the trend in RR estimates across the seven height categories (P trend=.09 in the fully adjusted model) was slightly weaker than that observed for the five height categories. This may be because this model is similar to considering height as a continuous variable and thus assumes a linear relationship, which, as previously noted, does not appear to be an optimum model. The RR estimates from shortest to tallest height categories were 1.0, 0.69, 0.86, 0.97, 0.93, 0.69, and 0.66.
- There was, in contrast, no evidence of an association between height and risk of stroke or CVD death. Men in the tallest compared with the shortest height category had only small and nonsignificant decreases in risk estimates of 23% and 13%, respectively, when controlled for known coronary risk factors in the full multivariate model (Table 3). However, there were fewer events in these categories, and thus the confidence intervals were wide. There were no significant trends in risk across the height categories for these end points.

### Discussion
In these prospective cohort study data from 22 071 male physicians, height was inversely associated with risk of MI, even after control for a large number of risk factors for cardiovascular disease. Our findings are
consistent with those of other studies, including both case-control\textsuperscript{1-3} and large prospective studies.\textsuperscript{4-7} despite the fact that many of the previously conducted studies did not control for many potential confounders, such as body mass index and socioeconomic status. The earliest case-control study\textsuperscript{1,2} controlled only for age and weight. Three prospective studies in men\textsuperscript{4-7} demonstrated inverse relationships, but none controlled for weight or body mass index, and only one\textsuperscript{6} adjusted for occupational status as a measure of social class. Finally, the most recently completed case-control study in women,\textsuperscript{3} which also showed an inverse association between stature and risk of MI, did control for body mass index and education as a measure of social class as well as other known risk factors for CHD. In studies of the general population, however, education alone may be an inadequate measure of social class. The consistency of our findings with these earlier studies suggests that uncontrolled confounding by body mass index and adult social class were not, in fact, explanations for previous results.

Whether there is also an inverse relationship of height to risk of other vascular events, such as stroke and cardiovascular death, is not yet clear. In our study, no statistically significant inverse association was demonstrated for stroke and CVD death, although comparisons of risk in men in the tallest relative to the shortest height category were in the same direction as that for MI. However, there were fewer events for stroke and CVD death, and thus the confidence intervals were wide. To date, no other studies have been published that have examined these other end points adequately. Such data could add to an elucidation of possible mechanisms, such as thrombogenesis versus effects more specific to the heart.

Several potential limitations of the present study must be considered. Height was self-reported by the physicians rather than measured directly. Such self-report could result in misclassification, such as, for example, shorter individuals possibly overestimating their height.\textsuperscript{13} However, since the information on height was collected prior to disease occurrence, any misclassification would be nondifferential with respect to the development of disease. Any such random misclassification could only result in an underestimate of the true association between height and MI.\textsuperscript{16}

There is, of course, the potential for residual confounding. There were a number of differences between the various height categories with respect to known coronary risk factors. Moreover, although there remained a statistically significant association between height and MI in our data, after control for these factors, the magnitude of the association was reduced. While social class in childhood was not assessed, the use of a study population of physicians has the advantage of minimizing confounding by educational attainment and adult socioeconomic status. Race was not assessed directly in this study, but virtually all participants were white. Even as late as 1990, blacks represented less than 5\% of admissions to US medical schools.\textsuperscript{17} Thus, it seems unlikely that confounding by unknown or unmeasured risk factors could explain to any substantial degree the inverse association observed between height and risk of MI.

There are a number of biologically plausible mechanisms that might explain an inverse relation of height to risk of MI, but, to date, these have not been fully evaluated. It may be that height acts as a marker for other physiological characteristics such as lung function or coronary artery lumen diameter or that retardation of fetal or infant growth may influence the risk of MI. Crude lung function is known to be correlated with height and other cardiovascular risk factors such as blood pressure and activity level\textsuperscript{18} as well as with subsequent risk of CVD death.\textsuperscript{19-22} In the British Regional Heart Study,\textsuperscript{7} height was associated overall with a decreased risk of MI, and this relationship disappeared after control for forced expiratory volume in 1 second (FEV\textsubscript{1}). These authors used FEV\textsubscript{1} unadjusted for height, which is a less clear physiological measure.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{plot.png}
\caption{Plots of relative risks and 95\% confidence intervals for myocardial infarction (fatal plus nonfatal events) by height categories. Left panel, controlled for age (in years), aspirin assignment, and \( \beta \)-carotene assignment. Right panel, Controlled for age (in years), aspirin assignment, \( \beta \)-carotene assignment, body mass index (continuous variable), smoking (current, past), history of hypertension, diagnosis of diabetes, history of elevated cholesterol, history of angina pectoris, parental history of myocardial infarction prior to age 60, alcohol use (daily, weekly), and exercise frequency at least weekly.}
\end{figure}
Acknowledgments

This investigation was supported by grant HL-34595 from the National Institutes of Health. J.R.-E. and P.R. are supported by Institutional Training Grant HL-07575 from the National Heart, Lung, and Blood Institute.

References


