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Adult height associates with angiographic extent of coronary artery disease

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A B S T R A C T

Background and aims: Shorter stature is an established risk factor for coronary artery disease (CAD), but less is known about its association with extent of the disease.
Methods: We assessed the relationship between self-reported height and angiographic findings in 7706 men and 3572 women identified from a nationwide coronary angiography registry in Iceland.
Results: After adjustment for traditional cardiovascular risk factors, a standard deviation decrease in height associated with a greater likelihood of significant CAD (defined as ≥50% luminal diameter stenosis) both in men (adjusted odds ratio [OR_{adj}]: 1.24, 95% confidence interval [CI]: 1.18, 1.31; $p = 3.2 \times 10^{-16}$) and women ($OR_{adj} = 1.10$, 95% CI: 1.02, 1.18; $p = 0.012$). In partial proportional odds logistic regression models, a standard deviation decrease in height was associated with higher odds of having greater extent of CAD in men ($OR_{adj} = 1.19$, 95% CI: 1.15, 1.25; $p = 1.5 \times 10^{-16}$) and women ($OR_{adj} = 1.09$, 95% CI: 1.02, 1.16; $p = 0.014$). When limited to patients with significant CAD, the association was statistically significant in men ($OR_{adj} = 1.08$, 95% CI: 1.03, 1.14; $p = 0.0022$) but not in women ($p = 0.56$).
Conclusions: Our findings show that shorter stature is associated with greater extent of coronary atherosclerosis in a large unselected population of individuals undergoing coronary angiography. This relationship appears to be sex-dependent, with stronger effects in men than in women.

1. Introduction

Coronary artery disease (CAD) is one of the most common causes of death and disability worldwide [1]. Large epidemiological studies have shown that shorter stature is associated with higher risk of developing CAD [2–6]. Although height is a well-established risk factor for CAD, less is known about its association with the extent and severity of coronary atherosclerosis. To our knowledge, two studies have assessed this relationship in individuals undergoing coronary angiography [7,8]. These studies have suggested an inverse correlation between height and the extent of coronary disease in men [7,8], but not in women [8]. These findings were based on relatively modest sample sizes and have not been replicated in other cohorts. Here, we sought to investigate the relationship between height and angiographic findings in a nationwide study of more than 11,000 individuals who underwent coronary angiography in Iceland.

2. Materials and methods

2.1. Study population

We identified all individuals who underwent coronary angiography for clinical indications in Iceland from January 1, 2007 to June 30, 2015, using data from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR). The SCAAR database has been described in detail [9,10]. Clinical and procedural data on all individuals undergoing coronary angiography in Iceland have been recorded in SCAAR since January 1, 2007 [11]. A total of 11,419 unique individuals were identified. For individuals with multiple procedures, we used the earliest record. Clinical characteristics of the individuals and angiographic findings were recorded as documented in the SCAAR database. Height was self-reported. We excluded those with missing data on height (N = 115), recorded

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height below 140 cm (N = 13) or missing angiographic data (N = 13), leaving 11,278 individuals in the final analysis. The study was approved by the National Bioethics Committee and the Data Protection Authority in Iceland.

2.2. Coronary angiography

Coronary angiograms were scored by an interventional cardiologist at the time of procedure. Individuals were classified as having significant CAD if ≥ 50% luminal diameter stenosis was found in a major epicardial coronary artery (left anterior descending, circumflex or right coronary artery) or in the left main coronary artery. We quantified the extent of CAD as the number of diseased coronary arteries using the Coronary Artery Surgery Study (CASS) score [12]. Individuals with significant CAD were classified as having one-, two- or three-vessel disease on the basis of the number of major epicardial coronary arteries with ≥50% diameter stenosis. Patients with left main disease (≥50% stenosis) were classified as having two-vessel disease, irrespective of other coronary stenosis. Thus, possible scores ranged from zero (individuals with normal coronary arteries or non-significant CAD) to three diseased coronary arteries.

2.3. Statistical analyses

We used binary and ordinal logistic regression models to test whether a decrease of one standard deviation (SD) in height associates with the extent of CAD. First, we performed the analyses for the total group and then repeated the analysis for the subgroup of patients with significant CAD (at least one-vessel disease). We also performed the analyses for men and women separately, as sex is the major determinant of adult height.

Binary logistic regression was used to test the association with significant CAD (at least one-vessel disease *vs.* no significant stenoses) and multivessel CAD (at least two-vessel disease *vs.* one-vessel disease or no significant stenoses). We adjusted for potential confounders in two separate models: one with adjustment for age and sex, and one with further adjustment for body mass index (BMI), smoking, diabetes mellitus, hypertension and use of lipid-lowering medication. Quintile analyses were performed separately for men and women, using the tallest quintile as the reference.

Ordinal logistic regression [13] was used to assess the association with the extent of CAD considered as four ordered categories: $0 < 1 < 2 < 3$ diseased coronary arteries. The assumption of a constant effect of each independent variable across various thresholds of the outcome (proportional odds assumption) was tested in each model. As this assumption did not hold in most cases, we employed partial proportional odds models, in which the constraint of proportional odds is relaxed for variables that violate this assumption [14]. In all models, the proportional odds assumption was met for height. The odds ratios derived from these models represent the estimated impact of height on the odds of greater versus lesser extent of CAD across the categories. We used the *gologit2* program in Stata software, version 13.0 (StataCorp, Texas, USA), to fit partial proportional odds models [15]. All other statistical analyses were performed with R software, version 3.1 (R Foundation for Statistical Computing, Vienna, Austria), and a two-sided *p* value of less than 0.05 was considered to be statistically significant.

3. Results

Table 1 shows the characteristics of the individuals. A total of 11,278 individuals who underwent coronary angiography were identified: 7706 (68%) men and 3572 (32%) women. The average height of men was 178.4 cm (range: 146 cm–204 cm, SD = 6.5 cm) and 164.9 cm for women (range: 144 cm–193 cm, SD = 5.8 cm).

In the overall sample, shorter stature associated with greater likelihood of having significant CAD (at least one-vessel disease) with an adjusted odds ratio (OR_{adj}) of 1.28 (95% confidence interval [CI]: 1.21, 1.36), adjusting for traditional cardiovascular risk factors (Table 2). The effect was stronger in men (OR_{adj} = 1.24, 95% CI: 1.18, 1.31) compared to women (OR_{adj} = 1.10, 95% CI: 1.02, 1.18) (*p* for interaction = 0.0070). Compared to the tallest quintile, men and women in the shortest quintile were 1.69 (95% CI: 1.43, 1.98) and 1.32 (95% CI: 1.03, 1.68) times more likely to have significant CAD, respectively (Fig. 1). Shorter individuals were more likely to have multivessel disease (at least two-vessel disease) in the overall sample (OR_{adj} = 1.25, 95% CI: 1.17, 1.32; Table 2); this association was evident among men (OR_{adj} = 1.20, 95% CI: 1.14, 1.26) but was not statistically significant in women (OR_{adj} = 1.08, 95% CI: 0.99,

Table 1
Characteristics of the individuals.

Characteristic	All (N = 11,278)		Men (N = 7706)		Women (N = 3572)		*p* value[b]
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	
Age, years	64.8 (11.2)		63.7 (11.2)		67.0 (10.9)		<0.001
Height, cm	174.1 (8.9)		178.4 (6.5)		164.9 (5.8)		<0.001
Body mass index (BMI)[a]	28.4 (4.9)		28.5 (4.6)		28.1 (5.3)		<0.001
Diabetes mellitus		12.9		13.4		11.6	0.007
Hypertension		61.7		59.2		67.1	<0.001
Lipid-lowering medication		59.9		59.9		60.1	0.83
Current smoker		21.2		21.9		19.6	0.006
Previous history of							
Myocardial infarction		13.3		15.3		9.0	<0.001
Coronary artery bypass grafting		5.8		7.2		2.8	<0.001
Percutaneous intervention		10.6		12.2		7.1	<0.001
Angiographic findings							
No significant stenosis		37.5		30.6		52.4	<0.001
One-vessel disease		26.1		26.9		24.2	0.002
Two-vessel disease		15.4		17.4		11.1	<0.001
Three-vessel disease		13.2		15.8		7.6	<0.001
Left main disease		7.8		9.3		4.6	<0.001
No. of diseased coronary arteries	1.12 (1.06)		1.28 (1.06)		0.79 (0.97)		<0.001

[a] Weight (kg)/height $(m)^2$.
[b] *p* values are for the comparison between men and women. *t*-tests were used for continuous variables and chi-squared tests for categorical variables.

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