

Height as marker of cardiometabolic risk; a combined analysis of two cohorts. Height and CVD risk factors

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Abstract

Aim: To investigate the association of height with cardiometabolic risk.

Methods: Standing adult height of the ATTICA study participants (n=1,128) and the Greek Caucasian MEDIS study participants (n=2,221), were investigated in relation to combined cardiometabolic risk (i.e., history of hypercholesterolemia, diabetes, hypertension and obesity)

Results: Increase in height was inversely associated with cardiometabolic risk, history of hypercholesterolemia (p<0.001) and diabetes (p<0.05), after adjusting for various confounders.

Conclusion: Among older people, increased standing height seems to be a determinant of cardiometabolic risk.

Key words: Cardiovascular Diseases; standing height; height; elderly

SUBMISSION: 10/09/2018 | ACCEPTANCE: 03/10/2018

Citation

Gkouvas CK, Foscolou A, Panagiotakos D. Height as marker of cardiometabolic risk; a combined analysis of two cohorts. Height and CVD risk factors. *Hell J Atheroscler* 2018; 9: 70-79

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1. Introduction

Cardiovascular disease (CVD) has received great attention in the literature the past decades. There are a plethora of articles trying to describe this complex phenomenon and propose possible mechanisms and, independent and interacting biological, anthropometric, clinical, behavioural, and lifestyle factors that contribute to its development across aging [1-4]. Regarding CVD, many anthropometric indices, indirect indicators of metabolic profile, have already been used [5]. However, one factor that has not, yet, received much attention, whereas there were several research findings in the past underlying its triggering role in cardiovascular system patho-physiology, is standing height. In one of the first papers published in early 1990s using data from the participants in the Physicians' Health Study, the investigators concluded that height was inversely associated with subsequent risk of myocardial infarction. At that time the mechanisms were limited and less convincing. Till then, there are few studies that have also revealed an association of increased height with lower risk of CVD [6-8]. Moreover, results from a recently published meta-analysis showed that 6.5 cm increase of height was associated with 10% lower risk for coronary heart disease [9]. Investigators tried to go further and study the potential mechanisms. Some explanations of these findings include larger vessels' diameters that are affected in lesser degree from atherosclerosis [10] and higher level of insulin sensitivity in taller individuals, as a result of early life over nutrition, which has as a consequence lower fat content in liver and lower risk for diabetes and CVD [11].

It is clear from all the aforementioned that the evidence regarding the associations between height and cardiometabolic disease are well founded. In that context, the aim of the present work was to investigate the association of height with several cardiometabolic risk markers simultaneously (i.e., history of hypercholesterolemia, diabetes, hypertension and obesity) among apparently healthy men and women who participated in two large-scale, population-based studies in Greece.

2. Methodology

Study sample

The working sample consisted of $n = 3,349$ individuals aged 50 years old and older, from the ATTICA ($n =$

1,128) and the MEDIS ($n = 2,221$) epidemiologic studies. In brief, the ATTICA is an observational study, carried out in the greater metropolitan Athens area in Attica region, Greece, during 2001-2002. The principal goal of the study was to investigate the prevalence of cardiovascular disease (CVD) risk factors and their associations with various socioeconomic, lifestyle and psychological characteristics. The total sample consisted of 3042 participants (>18 years old), randomly selected from all Attica region areas and were free of CVD and other chronic diseases, as assessed through a detailed clinical evaluation by the study's physicians (in the present analysis a sub-sample of study's sample, of $n = 1,128$ individuals over 50 years old were studied). More information about ATTICA study may be found elsewhere [12]. The MEDIS (Mediterranean Islands) study, was carried out in a variety of Mediterranean islands; during 2005-2017 a total of 3,128 older people (>50 years) from 26 Mediterranean islands, of 5 countries, were enrolled. Individuals who resided in assisted-living centers, had a clinical history of CVD or cancer, or had left the island for a considerable period of time during their life (i.e., >5 years) were excluded. In the present work, a sub-sample of $n = 2,221$ individuals who were living in Greek islands only, were studied. More information about MEDIS study may be found elsewhere [13].

In both studies, a group of health scientists (cardiologists, general practitioners, physicians, dietitians, public health nutritionists and nurses) with field experience collected all required information using standard, validated questionnaires and clinical procedures.

Bioethics

The ATTICA study was approved by the Institutional Ethics Board of First Cardiology Clinic (Athens University Medical School) and was carried out in accordance to the Declaration of Helsinki (1989) of the World Medical Association. Similarly, the Bioethics Committee of Harokopio University approved the MEDIS study (16/19-12-2006). Participants of both studies were informed about the aims and procedures and gave their informed consent prior to their enrollment.

Measurements

Socio-demographic and lifestyle data

Age (years), gender (men/women), smoking, finan-

cial and education status were assessed. Regarding financial status, participants were asked to self-characterize their income during the previous three years as low, i.e., inadequate to cover daily expenses, medium, i.e., trying hard to cover daily expenses, good, i.e., adequate to cover daily expenses, or very good, i.e., very adequate to cover daily expenses), while education level was described with school years. Current smokers were defined as those who smoked at least one cigarette or any type of tobacco per day at the time of the interview. Former smokers were defined as those who previously smoked but had quit within the previous year. Current and former smokers were combined as ever smokers. The remaining participants were defined as non-smokers.

Physical activity was assessed through a translated version of the validated "International Physical Activity Questionnaire" (IPAQ) [14], suitable for assessing population levels of self-reported physical activities, taking into consideration frequency (times per week) and duration (at least 10 minutes) of walking, moderate and vigorous activities, as well as sedentary activity. Participants who did not report any physical activities were defined as physically inactive. The evaluation of dietary habits in the ATTICA study was based on a semi-quantitative food-frequency questionnaire (FFQ) that was provided by the Unit of Nutrition of Athens University Medical School [15]. All participants were asked to report the average intake (per week or day) of several food items that they consumed (during the last 12 months). Similarly, dietary habits in the MEDIS study were assessed through a similar semi-quantitative, validated, and reproducible FFQ [16]. The frequency of consumption of various food types (i.e., meat and meat products, fish and seafood, milk and other dairy products, fruits, vegetables, greens and salads, legumes, cereals, pasta, olive oil and alcohol) on a daily, weekly or monthly basis, was assessed. To evaluate the level of adherence to the Mediterranean diet, the Med-DietScore (theoretical range 0–55) was used [17], with higher values indicating greater adherence.

Anthropometric characteristics

In both studies, standing height, weight, waist and hip circumferences, were measured using standard procedures, with people in light clothing and without shoes;

Waist circumference was measured in the middle between the lowest rib and the iliac crest using an inelastic measuring tape to the nearest 0.5 cm, hip circumference was measured at the level of the largest extension of the hips in a horizontal plane. Waist-to-hip ratio, waist-to-height ratio and Body Mass Index (BMI, as weight / height squared (kg/m^2), were also calculated.

Clinical characteristics

Type 2 diabetes mellitus was determined using American Diabetes Association diagnostic criteria (at least two measurements of fasting blood glucose ≥ 126 mg/dL or the use of anti-diabetic medication). Participants who were diagnosed as having blood pressure levels $\geq 140/90$ mmHg or used antihypertensive medications were classified as hypertensive. Hypercholesterolemia was defined as total serum cholesterol levels of at least two measurements > 200 mg/dL or the use of lipid-lowering agents according to the National Cholesterol Education Program Adult Treatment Panel III guidelines [18].

Then, a cumulative score (range 0–4) indicating the overall burden of participants' history of 4 major cardiometabolic risk factors (i.e., hypercholesterolemia, diabetes, hypertension and obesity) was also calculated, and used as a proxy of overall cardiometabolic risk (participants having none of the aforementioned risk factors received a score of 0, having one factor received score of 1, etc.).

Statistical analysis

Continuous variables are presented as means \pm standard deviation (SD) and categorical variables as frequencies. For better interpretation, height was divided into the following categories: ≤ 165 cm, 166–170 cm, 171–175 cm and > 170 cm, for men, and ≤ 150 cm, 151–155 cm, 156–160 cm, 161–165 cm and > 165 cm, for women. Multi-way analysis of variance (MANOVA) was applied to evaluate individual's characteristics in relation to height categories, accounting for age and sex of the participants. Ordinal logistic analysis was also used in order to evaluate the association of standing height, as a continuous variable (per centimeter), with overall cardiometabolic risk factors score and each risk factor individually, after adjusting for various clinical and socio-demographic char-

acteristics. Results are presented as b-coefficients and 95% confidence interval. The STATA software, version 14 (MP & Associates, Sparta, Greece) was used for all statistical analyses.

3. Results

In **Table 1**, baseline socio-demographic, lifestyle and clinical characteristics of the ATTICA and MEDIS stud-

ies' participants, categorized by standing height, are presented. Shortest individuals (i.e., ≤ 165 cm for men and ≤ 150 cm for women) had higher burden of cardiometabolic risk factors than those with higher stature (p 's <0.001).

Moreover, in **Figure 1** a clear decreasing trend of cardiometabolic cumulative risk factors score and participants' height is illustrated, in both men and women.

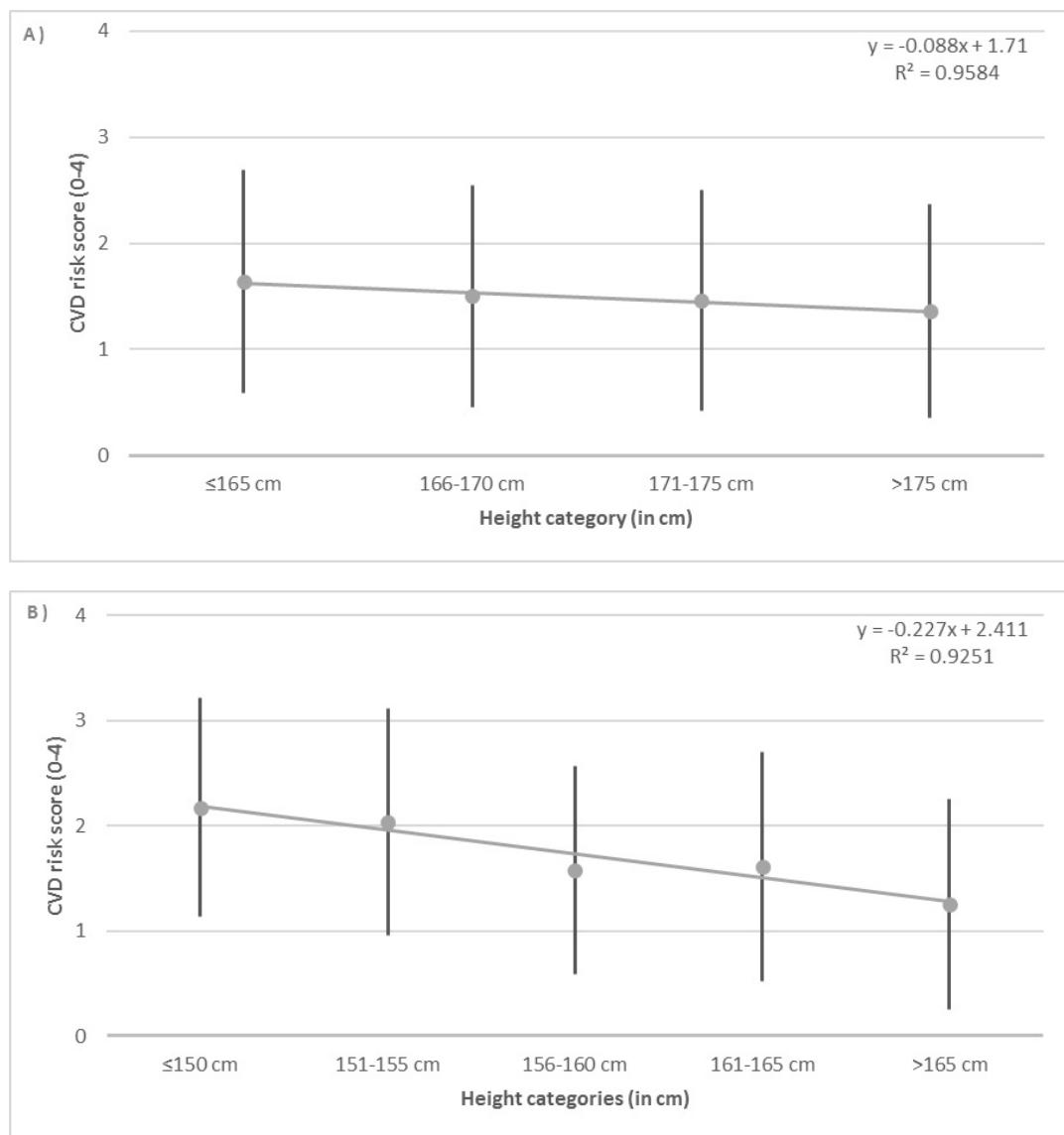


Figure 1. Mean CVD risk score by category of standing height, in (A) Men ($n=1751$) and (B) Women ($n=1598$) from the ATTICA and the MEDIS studies. CVD risk score is a cumulative score ranging from 0 to 4, depending on how many cardiometabolic risk factors (i.e., hypercholesterolemia, diabetes, hypertension and obesity) are present. Participants having none of the aforementioned risk factors received a score of 0, having one factor received score of 1, etc. CVD: Cardiovascular disease

Table 1: Prevalence (mean (SD) or %) of cardiometabolic risk factors by category of height, in n = 3,349 men and women of ATTICA and MEDIS studies.

Individuals' characteristics	Height categories in men (n=1751)					Height categories in women (n=1598)						p ¹
	All Men n = 1,751	≤ 165 cm (25%)	166-170 cm (28%)	171-175 cm (22%)	> 175 cm (25%)	All Women n = 1,598	≤ 150 cm (16%)	151-155 cm (19%)	156-160 cm (28%)	161-165 cm (20%)	> 165 cm (17%)	
Age (years)	70 ± 10	73 ± 10 ^{+x\$}	70 ± 10 ^{*\$}	68.7 ± 10 [*]	67 ± 11 ^{*+}	69 ± 10	74 ± 9 ^{+x\$#}	70 ± 9 ^{*\$#}	69 ± 10 ^{**}	67 ± 10 ^{*+}	65 ± 10 ^{*+x}	< 0.05
Weight (kg)	81 ± 13	74 ± 11 ^{+x\$}	80 ± 11 ^{**x\$}	83 ± 11 ^{*+†\$}	89.3 ± 14 ^{*+x}	72 ± 13	67 ± 14 ^{x\$#}	70 ± 11 ^{†\$#}	71 ± 12 ^{*\$#}	74 ± 12 ^{*+x#}	80 ± 12 ^{*+x\$}	< 0.001
Body Mass Index (kg/m ²)	27 ± 3.9	28.4 ± 4.1 ^{\$}	28.1 ± 3.7	27.6 ± 3.6	27.6 ± 3.9 [*]	28 ± 4.6	31 ± 6 ^{x\$#}	29 ± 5 ^{x\$#}	28 ± 5 ^{*+†#}	28 ± 5 ^{*+}	27 ± 4 ^{*+x}	< 0.05
Waist (cm)	102 ± 12	101 ± 12 ^{\$}	102 ± 13	103 ± 11	104 ± 14 [*]	96 ± 15	99 ± 14 ^{x\$#}	97 ± 14 [*]	95 ± 14 [*]	95 ± 15 [*]	95 ± 16 [*]	< 0.001
Hip (cm)	104 ± 10	102 ± 10 ^{x\$}	102 ± 11 ^{x\$}	105 ± 9 ^{*+†\$}	108 ± 9 ^{*+x}	107 ± 14	107 ± 13	108 ± 14	106 ± 12	107 ± 14	106 ± 16	< 0.001
Waist to hip ratio	0.98 ± 0.11	0.99 ± 0.08 ^{\$}	1.0 ± 0.14 ^{x\$}	0.9 ± 0.08 [†]	0.96 ± 0.11 ^{*+}	0.91 ± 0.36	0.93 ± 0.1	0.89 ± 0.1	0.88 ± 0.1	0.90 ± 0.5	0.96 ± 0.8	< 0.001
Waist to height ratio	0.6 ± 0.07	0.62 ± 0.07 ^{+x\$}	0.6 ± 0.08 ^{*\$}	0.59 ± 0.06 [*]	0.58 ± 0.08 ^{*+}	0.6 ± 0.09	0.67 ± 0.09 ^{+x\$#}	0.63 ± 0.09 ^{†x\$#}	0.6 ± 0.09 ^{*+†#}	0.58 ± 0.09 ^{*+}	0.56 ± 0.09 ^{*+x}	< 0.05
MedDietScore (0-55)	29 ± 7	29 ± 8	29 ± 7	29 ± 7	29 ± 7	29 ± 7	31 ± 7 ^{x\$#}	30 ± 7 [#]	29 ± 7 ^{*#}	29 ± 6 ^{*#}	27 ± 7 ^{*+x\$}	0.580
Smoking current (%)	32	26 ^{\$}	31	34	37 [*]	15	5 ^{x\$#}	9 [#]	16 ^{*#}	14 ^{*#}	32 ^{*+x\$}	< 0.001
Smoking past (%)	65	61 ^{\$}	63	66	70 [*]	20	8 ^{x\$#}	13 [#]	20 ^{*#}	21 ^{*#}	38 ^{*+x\$}	< 0.001
Physically active (%)	45	45	42	47	46	37	29 ^{\$}	40	37	41 [*]	37	< 0.001
Alcohol drinking daily (%)	68	67	64	67	70	27	23	24	26	29	33	< 0.001
Socioeconomic status (% high)	29	19 ^{+x\$}	24 ^{*\$}	35 [*]	41 ^{*+}	19	9	14	16	17	15	< 0.001

Successful Aging Index score (0-10)	3.3 ± 1.2	3.0 ± 1.26 ^{x\$}	3.2 ± 1.08 ^{x\$}	3.4 ± 1.13 ^{*†}	3.6 ± 1.03 ^{*†}	2.9 ± 1.3	2.2 ± 1.3 ^{+x\$#}	2.6 ± 1.3 ^{**x\$#}	3.1 ± 1.2 ^{*†#}	3.0 ± 1.2 ^{*†#}	3.4 ± 1.1 ^{*†x\$}	< 0.001
Cardiovascular disease risk factors score (0-4)	1.5 ± 1.0	1.6 ± 1.0 ^{\$}	1.5 ± 1.0	1.5 ± 1.0	1.4 ± 1.0 ^{*†}	1.7 ± 1.1	2.2 ± 1.0 ^{x\$#}	2.0 ± 1.1 ^{x\$#}	1.6 ± 1.0 ^{*†#}	1.6 ± 1.1 ^{*†#}	1.3 ± 1.0 ^{*†x\$}	< 0.001
Hypercholesterolemia (%)	48	48	48	49	46	58	63 ^{\$}	68 ^{x\$#}	56 [†]	55 [†]	49 ^{*†}	< 0.001
Diabetes (%)	22	26 ^{\$}	21	25 ^{\$}	17 ^{**x}	20	24 ^{\$}	24 [#]	17	21	13 ^{*†}	0.08
Hypertension (%)	93	94	94	90	94	90	96 ^{x#}	94 ^{x#}	87 ^{*†}	90	82 ^{*†}	< 0.05
Obesity (%)	26	31 ^{x\$}	27	22 [*]	21 [*]	34	53 ^{x\$#}	44 ^{x\$#}	29 ^{*†#}	28 ^{*†}	18 ^{*†x}	< 0.001

Data are presented as mean values and SD or frequencies.

[†]p-values reflect the age-sex adjusted comparisons of individuals' characteristics between height categories, as derived from multi-adjusted analysis of variance (MANOVA) for the continuous variables or the Mantel-Haenszel chi-square test for the categorical variables. Within-height groups comparisons;

^{*}p-value < 0.05 for the comparisons vs. 1st group (i.e., ≤ 165 cm for men or ≤ 150 cm for women);

⁺p-value < 0.05 for the comparisons vs. 2nd group (i.e., 166-170 cm for men or 151-155 cm for women);

^xp-value < 0.05 for the comparisons vs. 3rd group (i.e., 171-175 cm for men or 156-160 for women);

^{\$}p-value < 0.05 for the comparisons vs. 4th group (i.e., > 175 cm for men or 161-165 cm for women); and

[#]p-value < 0.05 for the comparisons vs. 5th group (i.e., > 165 cm for women) after correcting for the inflation of Type-I error with the Bonferroni rule.

Table 2: Results from ordinal logistic models that evaluated standing height, as a continuous variable (per centimeter), in relation to the cumulative cardiometabolic risk factors score and each risk factor separately of the n = 3,349 older men and women (>50 years).

Independent variable	b-coefficient, 95%CI	p-value
CVD risk score	-0.04, -0.05 to -0.029	p<0.001
Hypercholesterolemia	-0.022, -0.033 to -0.01	p<0.001
Diabetes Mellitus	-0.015, -0.028 to -0.001	p<0.05
Hypertension	-0.016, -0.043 to 0.011	p=0.243
Obesity	-0.048, -0.061 to 0.035	p<0.001

All models were adjusted for age, sex, smoking habits, physical activity status, MedDietScore and socioeconomic status of the participants. CVD risk score is a cumulative score ranging from 0 to 4, depending on how many cardiometabolic risk factors (i.e., hypercholesterolemia, diabetes, hypertension and obesity) are present. Participants having none of the aforementioned risk factors received a score of 0, having one factor received score of 1, etc. CVD: Cardiovascular disease.

Height, anthropometric indices and cardiometabolic risk factors profile

However, residual confounding may exist, and the aforementioned relationships may be prone to selection bias. Thus, multi-adjusted analyses were performed. After controlling for age, sex, various lifestyle factors i.e., smoking habits, physical activity status, financial status, as well as adherence to the Mediterranean diet as evaluated through the MedDietScore, individuals' height showed a strong inverse association with cardiometabolic risk factors score (Table 2; p<0.001). To further explore the association of height with certain cardiometabolic disorders further analyses were also applied. Height seemed to have an inverse association with participants history of hypercholesterolemia, obesity (Table 2; p<0.001) and diabetes mellitus (Table 2; p<0.05), but there was no association of height with history of hypertension (Table 2; p=0.243). No height by sex or height by study (i.e., ATTICA or MEDIS) interactions on the aforementioned cardiometabolic risk factors were observed (all p's>0.50).

4. Discussion

The aim of the present work was to evaluate the asso-

ciation of standing height with cardiometabolic risk profile of over 50 years old men and women, offering more data to an overlooked subject and better understanding of the ever-going underlining processes of atheromatosis. It was revealed that higher height was associated with lower cardiometabolic risk factors profile, irrespective of sex or age. This association remained strong even after the adjustment for various factors such as financial status, dietary habits and physical exercise which early on were consider to be the key mediators of height's effect on CVD risk [8, 10]. Despite the limitations this observational study may carry, the presented findings are of significant importance since they give light to an underestimated area of research regarding the role of less used anthropometric indices on cardiovascular diseases' markers. Understanding the role of these markers may assist clinicians, as well as health care professionals, in better identifying the potential candidate for CVD or other related disorders, and, thus, reducing the burden of the disease at population level.

The association of height with CVD has not been well studied and understood. Although some researchers support that short stature offers many

prophylactic advantages against CVD [19], a number of prospective studies and meta-analysis have suggested that higher statures are more protected against atherosclerosis [7-11]. Given that taller individuals have lower risk of cardiovascular diseases [7-11] because they have lower BMI, lower non-HDL cholesterol [9], lower incidence of diabetes [11] and a tendency for a lower systolic blood pressure [9], we wanted to evaluate at the same time the impact of height with every component of our risk score, namely incidence of hypercholesterolemia, diabetes mellitus, hypertension and obesity. It is known that taller individuals enjoy better blood lipid profile and lower incidence of diabetes as compared to shorter individuals, probably due to the fact that they have better sensitivity to insulin and insulin like growth factors. This sensitivity is probably the product of early life over nutrition, which causes higher activation levels of their signaling pathways and have as a result both a greater stature and a lower liver fat content in adult life [11]. Our analysis has shown that height had indeed an inverse association both with the incidences of hypercholesterolemia and diabetes mellitus. It is also known that taller individuals display a tendency for lower systolic blood pressure than shorter ones [9] probably due to larger vessels' diameter and their lower level of stenosis due to atheromatous plaques [10] however non association was revealed between height and the incidence of hypertension or systolic blood pressure (data not shown) among the elderly of Attica region and Greek islands.

Strengths and Limitations

To our knowledge this is one of the few studies that evaluates the association of height with cardiometabolic risk factors profile and one of the first to do so on a Greek population of older adults. However, some limitations also exist; ATTICA and MEDIS studies measurements suffer from the typical flaws of epidemiologic studies genre, like the reverse causality bias and the non-response bias [20]. Since this is also a self-report survey it may suffer from recall bias as well. On a technical matter, since the current standing height of the volunteers was measured, which for some might have been slightly decreased as an inevitable consequence of aging, the results of the analyses might not depict accurately the effect of adult height in cardiometabolic risk.

Conclusion

This work suggests that standing height may serve as a useful predictor of cardiovascular disease risk. These findings also provide useful insights into the potential mechanisms connecting height and good health and therefore, better course of life. Height is undoubtedly a biological characteristic which can define individuals in many aspects of their life and may have a potential role as a diagnostic tool in the future; however modifiable risk factors can always play the same important role on the course of life. ◻

Conflict of interest

There is no conflict of interest.

Περίληψη

Το ύψος ως δείκτης καρδιομεταβολικού κινδύνου; συνδυασμένη ανάλυση δύο κοορτών

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Στόχος: Η μελέτη της σχέσης του ύψους με τον καρδιομεταβολικό κίνδυνο.

Μεθοδολογία: Μελετήθηκε η σχέση του συνολικού ύψους σώματος ενηλίκου των συμμετεχόντων της μελέτης ΑΤΤΙCΑ (n=1,128) και των Ελλήνων συμμετεχόντων της μελέτης ΜΕDΙS (n=2,221), με τον συνδυασμένο καρδιομεταβολικό κίνδυνο (ιστορικό υπερχοληστερολεμίας, διαβήτη, υπέρταση και παχυσαρκία).

Αποτελέσματα: Η αύξηση του ύψους εμφάνισε αρνητική συσχέτιση με τον καρδιομεταβολικό κίνδυνο, το ιστορικό υπερχοληστερολεμίας (p<0.001) και τον διαβήτη (p<0.05), μετά από προσαρμογή για διάφορους συγχετιτικούς παράγοντες.

Συμπεράσματα: Το αυξημένο συνολικό ύψος σώματος ενηλίκου φαίνεται πώς παίζει καθοριστικό ρόλο στον καρδιομεταβολικό κίνδυνο των ηλικιωμένων.

Λέξεις ευρητηρίου: καρδιαγγειακά νοσήματα, συνολικό ύψος, ύψος, ηλικιωμένοι

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