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DETERMINANTS OF AORTIC ROOT DILATATION AND REFERENCE VALUES AMONG YOUNG ADULTS OVER A 20-YEAR PERIOD: THE CORONARY ARTERY RISK DEVELOPMENT IN YOUNG ADULTS (CARDIA) STUDY

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Abstract

Aortic size increases with age, but factors related to such dilatation in healthy young adult population have not been studied. We aim to evaluate changes in aortic dimensions and its principal correlates among young adults over a 20-year time period. Reference values for aortic dimensions in young adults by echocardiography are also provided.

Healthy CARDIA study participants aged 23–35 years in 1990–91 (n=3051) were included after excluding 18 individuals with significant valvular dysfunction. Aortic root diameter by M-mode echocardiography at Year-5 (43.7% men; age 30.2±3.6y) and Year-25 CARDIA exams were obtained. Univariable and multivariable analyses were performed to assess associations of aortic root diameter with clinical data at Years-5 and -25. Aortic root diameter from Year-5 was used to establish reference values of aortic root diameter in healthy young adults.

Aortic root diameter at Year-25 was greater in men (33.3±3.7 vs 28.7±3.4mm, p<0.001) and in whites (30.9±4.3 vs 30.5±4.1, p=0.006). On multivariable analysis, aortic root diameter at Year-25

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Disclosures

None

was positively correlated with male gender, white ethnicity, age, height, weight, 20-year gain in weight, active smoking at baseline and 20-year increase in diastolic, systolic and mean arterial pressure. A figure showing the estimated 95th percentile of aortic root diameter by age and body surface area stratified by race and gender is provided.

This study demonstrates that smoking, blood pressure, and increase in body weight are the main modifiable correlates of aortic root dilation during young adulthood. Our study also provides reference values for aortic root diameter in young adults.

Keywords

Ascending Aorta; Aortic Diseases; Aortic Aneurysm; Echocardiography; Epidemiology

Introduction

Aortic dilatation in mid to advanced adulthood has been related to cardiovascular risk factors and cardiovascular events^{1–3} and it may begin early in young adulthood and be a marker for accelerated vascular aging. Furthermore, the study of aortic dilatation and its major determinants is crucial in the diagnosis and follow-up of several inherited aortic diseases (e.g. Marfan syndrome and bicuspid aortic valve). However the determinants of aortic root dilatation in young adults have not been previously described in a large generally healthy population.

Echocardiography is the most used technique in the clinical evaluation of aortic root dilatation because of its availability, low cost, and accuracy. Even though recent studies have defined equations and nomograms for aortic dimensions by 2-dimensional echocardiography in children⁴ and over broad ranges of age⁵, data focused on young adults is limited. Reference values for aortic dimensions are crucial in the follow-up of young patients with aortic conditions, and may become central to preventive cardiology efforts. Definition of aortic enlargement requires the use of nomograms, normalization by age and body size or the calculation of z-scores⁶. Those methods account for age and body size as these factors are direct determinants of aortic dimensions^{2,7}.

The Coronary Artery Risk Development in Young Adults (CARDIA) Study is a population based study involving four communities in the United States. CARDIA has followed 5115 black and white men and women age 18–30 recruited in 1985 for 25 years. Echocardiography was performed in 1990–91 (Year-5) and 2010–11 (Year-25) allowing for accurate measurements of aortic size which can be correlated with diverse risk factors and phenotypic observations. CARDIA is therefore ideal for the study of vascular structure and function in early adulthood and its alterations secondary to exposure to a large number of environmental risk factors. In the present study, we aim to investigate the main determinants of aortic dilatation through 20 years of follow-up and to establish reference values for aortic root diameters (ARD) by M-mode echocardiography in young adults.

Methods

Study Sample

The overall study design of Coronary Artery Risk Development in Young Adults (CARDIA) has been described in detail elsewhere⁸. In summary, CARDIA was initiated by the NHLBI as a large cohort of young adults to longitudinally investigate lifestyle and other variables that influence the evolution of coronary risk factors. The CARDIA cohort initially comprised 5115 participants who were aged 18 to 30 years at the time of enrollment (1985 through 1986), 5 years before the first echocardiography examination. CARDIA includes approximately equal numbers of participants from four geographically diverse urban field centers (Birmingham, AL; Chicago, IL; Minneapolis, MN; Oakland, CA) and similar proportions of black and white, men and women.

A total of 3069 subjects from the CARDIA study who underwent echocardiography both at the Year-5 examination (aged 23 to 35 years in 1990 through 1991) and at Year-25 constitute the study sample for this investigation. Subjects were excluded if they fulfilled any of the following criteria at any of the two studies, in hierarchical order: aortic regurgitation or stenosis more than mild (n=9), aortic bicuspid valve (n=8), or aortic valve prosthesis (n=1). Then, a total of 3051 subjects were included. Compared with the overall CARDIA population, subjects were older in the present subcohort (25.2 ± 3.6 yrs vs 24.9 ± 3.7 yrs, $p < 0.001$) but with a mean difference of only 0.3 yrs. Gender distribution was not different (56.3% vs 54.3% in the subcohort vs the overall cohort, respectively $p = 0.09$). However, the included subcohort showed a higher proportion of white (55.0% vs 48.5% in the overall cohort, $p < 0.001$).

Methods of Measurement and Definitions

A total of 3051 subjects with echocardiography at Year-5 and Year-25 were included. At Year-5, all studies were performed with an Acuson 128 cardiovascular system and Year-25 studies were performed with a Toshiba Artida ultrasound system. M-mode studies were obtained with 2-dimensional echocardiography guidance on the parasternal long-axis view. Aortic root size, both at baseline and at year-25, was measured from the M-mode tracings in accordance with the American Society of Echocardiography (ASE) guidelines using the leading edge-to-leading approach at end-diastole⁹ (Figure 1). Aortic root measurement variability in the CARDIA study has been previously published¹⁰. In summary, aortic root M-mode measurements had an Intraclass correlation coefficient of 0.81 and coefficients of variations (intra and inter-sonographer) below 6%.

Body height and weight measurements were obtained at the index examination and used to calculate BSA (body surface area) by the Du Bois formula¹¹ and BMI (body mass index). Blood pressure was measured at each examination; three blood pressure measurements were obtained and the second and third readings were averaged for analysis. Pulse pressure was calculated as systolic blood pressure minus diastolic pressure and mean arterial pressure as diastolic blood pressure plus one third of the pulse pressure.

Physical activity was assessed with the CARDIA Physical Activity History Questionnaire,¹² an interviewer-administered self-report of frequency of participation in each of 13 categories

of sports and exercise during the previous 12 months. Afterwards, the “exercise score” was computed taking into account the frequency and intensity of activity, and expressed in “exercise units” (EU).

Statistical Analysis

Demographic, anthropometric, and clinical characteristics at each examination were summarized with percentage or mean and standard deviation as appropriate.

Main determinants of aortic root diameter (ARD) at Year-25 were determined by analyzing univariate associations between demographic and clinical data at Years-5 and -25 and ARD at Year-25. Change in aortic root diameter (CAR) was calculated as ARD at Year-25 minus ARD at Year-5. Multivariable analyses were used to define the main determinants of ARD at Year -25 by introducing demographic and clinical covariates at Year-5 such as age, gender, race, weight, height, treatment for hypertension, diabetes, smoking status, physical activity, and total cholesterol levels and 20-year change of weight, cholesterol levels and physical activity. Each blood pressure measurement (systolic, diastolic, pulse pressure, and mean arterial pressure) and their 20-year change were separately introduced in a model with the rest of the covariates. Afterwards, in order to evaluate the steady and pulsatile components of blood pressure, pulse pressure (PP), mean arterial pressure (MAP), and 20-year change of both measurements were introduced simultaneously in the same model with ARD at year-25 as dependent variable. Multicollinearity was then evaluated by calculation of the variance inflation factor. Change in aortic root diameter (CAR) through the 20-year period of this study was evaluated by introducing Year-5 ARD as a covariate in the model.

Reference values for aortic root diameter in young adults were defined using data from Year-5. Number of cases for age intervals (5 years) and BSA intervals (0.1m^2) were analyzed in order to ensure proper representation of the entire spectrum. Mean unadjusted aortic root diameter (ARD) by M-mode was calculated for men and women, black and white separately. Since demographic and anthropometric variables have been previously described to account for most of the variation observed in aortic dimensions², only these variables were considered as covariates in order to obtain a simple model with more clinical applicability. Six multiple linear regression models were evaluated; one model included age, gender and race. Four models added each of the body size parameters separately (height, weight, BSA and BMI) and a sixth model included height and weight simultaneously. The most explanatory model (higher R^2 value) was selected. The B-coefficients for each covariate from the selected model were used to calculate the predicted mean aortic root diameter from a designated set of values for each of the covariates. This predicted mean and the standard error of the estimate (SEE) were then used to calculate the 95th percentile (predicted mean by the model $\pm 1.64\cdot\text{SEE}$).

Results

Clinical and demographic characteristics at Year-5 (1990–91) and Year-25 (2010–11) are shown in Table 1. Mean aortic root diameter at Year-25 was greater than at Year-5 ($30.7\pm 4.2\text{mm}$; $27.8\pm 3.8\text{mm}$, $p<0.001$). ARD at Year-25 was greater in men than in women (33.3 ± 3.7 vs $28.7\pm 3.4\text{mm}$; $p<0.001$) and greater in whites than in blacks (30.9 ± 4.3 vs

30.5±4.1mm; $p<0.01$). However, no statistically significant differences were observed between blacks and whites stratified by gender (black men 33.1±3.5 vs white men 33.4±3.8mm, $p=0.070$; black women 28.8±3.5 vs white women 28.7±3.3mm, $p=0.377$). Mean 20-year change in ARD was 3.0±3.6mm.

Aortic root diameter at Year-25 was significantly correlated with baseline (Year-5) age, weight, height, body surface area, body mass index, blood pressure, total cholesterol levels, and physical activity in univariate analyses (Table 2). Height and body surface area were the anthropometric variables most linearly correlated with aortic root dimension at Year-25. Importantly, current smokers at Year-5 had higher ARD at Year-25 (31.1±4.2 vs 30.6±4.2mm; $p<0.01$). However, individuals under treatment for hypertension at Year-5 ($n=44$) had no significant differences in ARD at Year -25 compared to patients without treatment at year-5 ($p=0.838$). Twenty year change in aortic root (CAR) was weakly correlated with age, weight, height, and BSA, and with 20-year change in weight, SBP, DBP, and MAP (Table 3).

In multivariable analyses, age, male gender, white ethnicity, height, weight, and baseline active smoking, as well as changes in weight were significantly associated with larger aortic diameter at year-25 (Table 4). Models including SBP, DBP, MAP and PP separately are shown in Table 4. SBP, DBP, and MAP were significantly associated with ARD at Year-25. Also importantly, PP was negatively associated with ARD at year-25.

When introducing baseline ARD at each model, it was, as expected, positively associated with ARD at Year-25, but age lost its association to ARD at year-25. Similar results were found for the rest of covariables (supplemental material, S1).

A multivariable model including simultaneously PP and MAP was used to evaluate the pulsatile and non-pulsatile components of blood pressure (supplemental material, S2). In this, ARD at Year-25 was positively correlated with MAP and 20-year change in MAP and negatively correlated with PP and 20-year change in PP.

Although treatment for hypertension at year-5 was not related to ARD at year 25, further analyses were done to confirm this result: using the same model as in Table 4, treatment for hypertension was introduced with 4 categories: individuals that never received treatment (no treatment at year 5 or at year 25, $n=2215$), treatment only at year 5 ($n=9$), treatment only at year 25 ($n=775$) or treatment at both year 5 and 25 ($n=35$). When analyzed, these categories were also not significantly related to ARD at year 25. Moreover, the rest of the model remained similar.

Reference values for ARD were originated from Year-5 measurements. Mean ARD at year-5 used to estimate reference values ($n=3051$, mean 27.8±3.8mm) was similar to the overall CARDIA year-5 cohort ($n=4210$, mean 27.9±3.9mm). Appropriate representation of all age groups (5 years) as well as of different BSA strata (0.1m^2) was confirmed: all groups had > 5% of all individuals except for the BSA 1.5m^2 that included a 3.5% of the total sample, but comprised 108 individuals. Mean unadjusted ARD by M-mode were 29.7±3.4mm (black men), 30.1±3.7mm (white men), 26.1±3.2mm (black women) and 26.1±3.0mm (white women).

Multivariable linear models for aortic root diameter including demographic and anthropometric covariates were evaluated to define reference values using ARD at Year-5. The model with highest R^2 was the one including BSA ($R^2=0.320$, $p<0.001$); this was similar to the one including both height and weight ($R^2=0.319$, $p<0.001$). The model with BSA was selected because of simplicity and also included age, gender, and race: aortic root diameter (mm) = $15.042 + 0.079 \times \text{years} + 2.612$ [if male gender] $- 0.407$ [if black] $+ 5.035 \times \text{BSA (m}^2\text{)}$, $\text{SEE}=3.14$. Interaction between gender and race was not significant ($p=0.618$). To calculate the predicted 95th percentile for ARD, a designated set of values was introduced in the model to obtain the predicted mean subsequently used to calculate the 95th percentile. Age was introduced by 5 year intervals and BSA by 0.1m^2 intervals. These values are graphically presented in Figure 2.

Discussion

Our study provides longitudinal data on clinical correlates of aortic root size and dilatation through a 20-year period of early adulthood, being age, gender, ethnicity, and body size the main determinants of aortic root dimensions and dilatation. Importantly, active smoking at early adulthood was positively correlated with aortic size and dilatation 20 years later. Furthermore, components of blood pressure had different roles in relation to aortic dimensions: studied separately, diastolic blood pressure, mean arterial pressure and 20-year change in systolic blood pressure were positively related to aortic dimensions while baseline pulse pressure was negatively correlated with aortic dimensions and dilatation 20 years later.

Alterations of aortic material properties, in parallel with alterations of the vasculature in general, have been conclusively related to adverse cardiac remodeling and cardiovascular outcomes^{13–15}. Aortic structural and functional alterations that occur in mid and late adulthood and their clinical correlates have been the object of extensive investigation^{2,7,16}. However, data focused in early adulthood is scarce. In this period of adulthood, vascular changes are incipient but may be more informative toward the overall understanding of vascular aging and also more malleable to intervention.

In this regard, prior investigation has clearly demonstrated that elastin, the constitutional element that affords distensibility to the aortic structure, has a half-life of 40 years, and, most importantly is not synthesized during mid to late adulthood^{17,18}. Fatigue and fracture of elastin due to repeated cycles of deformation is thought to be the mechanism of elastin degradation¹⁹. In this regard, recent magnetic resonance imaging studies showing marked decrease in aortic deformation before the 5th decade have provided important understanding on the time course of changes in aortic structure and function in early adulthood²⁰.

Our results are in line with a previous cross-sectional study from Palmieri et al,²¹ which showed that hypertensives with suboptimal blood pressure control have larger aortic root dimensions than normotensives or hypertensives with optimal blood pressure. However, the longitudinal design of our study emphasize the importance of progressive increase in BP with age on aortic root enlargement.

The simultaneous analysis of MAP and PP is meaningful as it provides information on the steady-flow versus pulsatile components of arterial pressure and circulatory function related to small-artery (steady-flow) and large-artery (pulsatile) contribution. In our study, MAP was positively correlated with aortic root size and dilatation. Conversely, PP was negatively associated with aortic root size and dilatation. This last finding appears counterintuitive at first, but may be explained by the decline in PP seen in several previous observational studies between ages 20 and 40²², the age-period during which baseline ARD measurements were obtained in our study. Moreover, studies of populations in mid to late adulthood have found similar results with SBP and PP being negatively associated with aortic dimensions^{2,14,16,23,24}.

Similar to previous studies², in our study, male gender was associated to greater aortic dimensions and dilatation, and white ethnicity related with greater aortic dimensions than black. Although no differences were observed between blacks and whites stratified by gender, this might be explained by the differences in weight between gender-race groups (data not shown) which is confirmed in the multivariable analysis where white ethnicity is associated with higher ARD adjusted by body size. Interestingly, our data suggest a positive correlation of active smoking at baseline with aortic root dimensions and dilatation through this 20-year period of follow-up. To the best of our knowledge, this last finding has not been previously described in a longitudinal study and it is notably important in the follow-up of aortic conditions.

Reference values of aortic root dimensions by M-mode echocardiography depending on age and body surface area in young adulthood stratified by gender and race are provided in the present study with the aim to guide physicians and other health care providers on what can be expected to be the normal aortic root dimensions in early adulthood.

Our study has some limitations. First, M-mode echocardiography was used for both Years-5 and -25 studies. Although currently bi-dimensional echocardiography is recommended to determine aortic dimensions⁹, this approach was not used 20 years ago. However, M-mode and bi-dimensional echocardiography are well correlated with a systematic underestimation of 2mm by M-mode in comparison with bi-dimensional measurements⁶. Second, although a higher proportion of white subjects was observed in the included subcohort respect to the overall CARDIA participants (55.0% vs 48.5% in the overall cohort, $p<0.001$), black and white ethnicities are well represented in our study and ethnicity has been introduced as a covariable in the analysis. Third, despite that the multivariable models used in our analysis only explain around a 40% of the variation of ARD at year-25, the significant predictors analyzed still represent the mean change in the response for one unit of change. Last, despite the associations found between smoking, blood pressure, and body weight gain and aortic root diameter, the real effect of the intervention on these factors to avoid aortic root dilatation cannot be elucidated from the present study.

Perspectives

In summary, this study based on the 20-year longitudinal follow-up of CARDIA participants demonstrates that smoking, blood pressure, and body weight gain are the main modifiable

determinants of aortic root dilation through young adulthood. Our study also provides reference values for aortic root diameters in this age group.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ARD	aortic root diameter
BMI	body mass index
BSA	body surface area
CAR	change in aortic root diameter
CARDIA	Coronary Artery Risk Development in Young Adults
DBP	diastolic blood pressure
PP	pulse pressure
SBP	systolic blood pressure

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Novelty and Significance

What Is New?

This population-based study is the first to provide 20-year longitudinal data on clinical correlates of aortic root size and dilatation through early adulthood. Age, male gender, white ethnicity, body size, weight gain, blood pressure and smoking were the main determinants of aortic root dimensions and dilatation.

What Is Relevant?

Components of blood pressure had different roles in relation to aortic dimensions: diastolic blood pressure, mean arterial pressure and 20-year change in systolic blood pressure were positively related to aortic dimensions while baseline pulse pressure was negatively correlated with aortic dimensions and dilatation 20 years later.

Summary

This study based on the 20-year longitudinal follow-up of CARDIA participants demonstrates that smoking, blood pressure, and body weight gain are the main modifiable determinants of aortic root dilation through young adulthood. Our study also provides reference values for aortic root diameters in this age group.

Figure 1.
Echocardiographic aortic root measurements using the leading edge-to-leading edge approach at end-diastole.

Figure 2.

95th percentiles of predicted aortic root diameter by age, stratified by race and gender. This chart is designed for practical use: to evaluate ARD for a particular patient, use BSA to choose the line that defines the upper limit of normal from the appropriate race-gender group. ARD: aortic root diameter; BSA: body surface area

A: white females; B: black females; C: white males; D: black males.

Table 1

Clinical characteristics

Clinical or demographic variables	Year-5 3051	Year-25 3051	p-value (paired test)
Age, years	30.2±3.6	50.2±3.6	N/A
Gender, % male	1334 (43.7%)		N/A
Race, % black	1373 (45.0%)		N/A
Weight, Kg	75.7±17.9	87.4±21.9	<0.001
Height, cm	170.3±9.5	170.4±9.5	0.329
Body surface area, m ²	1.86±0.23	1.98±0.25	<0.001
Body mass index, kg/m ²	26.1±5.7	30.1±7.2	<0.001
Systolic blood pressure, mmHg	107.2±11.2	119.5±16.0	<0.001
Diastolic blood pressure, mmHg	68.8±9.8	74.7±11.1	<0.001
Pulse pressure, mmHg	38.4±8.2	44.8±9.0	<0.001
Mean arterial pressure, mmHg	81.6±9.5	89.6±12.2	<0.001
Hypertension (%)	241 (7.9%)	986 (32.3%)	<0.001
Treatment for hypertension (%)	44 (1.4%)	810 (26.5%)	<0.001
Total cholesterol, mg/dL	178.6±33.3	192.7±36.9	<0.001
Diabetes mellitus (%)	51 (1.7%)	317 (10.4%)	<0.001
Current cigarette smoker (%)	778 (25.5%)	483 (15.8%)	<0.001
Physical activity, exercise units *	378.6±291.9	337.7±274.2	<0.001
M-mode aortic root, mm	27.8±3.8	30.7±4.2	<0.001

N/A: not applicable

* Exercise score expressed in exercise units (EU) representing the frequency and intensity of exercise over the past year. For reference, 300 exercise units roughly approximates 5 sessions of 1260 kJ (300 kcal) of energy expenditure weekly.

Table 2

Unadjusted analyses for aortic root diameter at Year-25 and continuous variables at baseline (Year-5)

	Clinical variable	Pearson correlation coefficient with ARD at Year-25
Variable at baseline (Y5)	Age	0.051 [‡]
	Weight	0.383 [*]
	Height	0.492 [*]
	Body surface area	0.488 [*]
	Body mass index	0.166 [*]
	Systolic blood pressure	0.200 [*]
	Diastolic blood pressure	0.196 [*]
	Pulse pressure	0.037 [‡]
	Mean arterial pressure	0.213 [*]
	Total cholesterol	0.083 [*]
	Physical activity	0.145 [*]
	Aortic root diameter	0.592 [*]
20-year change [§]	Weight	0.023
	Systolic blood pressure	0.002
	Diastolic blood pressure	−0.014
	Pulse pressure	0.019
	Mean arterial pressure	−0.009
	Total cholesterol	−0.105 [*]
	Physical activity	−0.052 [‡]

* p<0.001;

[‡] p<0.01,[‡] p<0.05[§] Year-25 minus Year-5 value

ARD: aortic root diameter

Table 3

Unadjusted analyses for change in aortic root diameter (CAR) and continuous variables at baseline (Year-5)

	Clinical variable	Pearson correlation coefficient with CAR
Variable at baseline (Y5)	Age	-0.042 [‡]
	Weight	0.044 [‡]
	Height	0.095 [*]
	Body surface area	0.071 [*]
	Body mass index	0.002
	Systolic blood pressure	0.012
	Diastolic blood pressure	0.032
	Pulse pressure	-0.022
	Mean arterial pressure	0.027
	Total cholesterol	-0.005
	Physical activity	0.022
20-year change [§]	Weight	0.064 [*]
	Systolic blood pressure	0.077 [*]
	Diastolic blood pressure	0.075 [*]
	Pulse pressure	0.027
	Mean arterial pressure	0.081 [*]
	Total cholesterol	0.004
	Physical activity	-0.023

* p<0.001;

† p<0.01,

‡ p<0.05

§ Year-25 minus Year-5 value

Table 4

Multivariable analysis comparing contributions of blood pressure parameters to aortic root diameter at Year-25 (mm).

Clinical variable	Model 1 (SBP) R ² =0.361 p<0.001 B coefficient	Model 2 (DBP) R ² =0.365 p<0.001 B coefficient	Model 3 (PP) R ² =0.361 P<0.001 B coefficient	Model 4 (MAP) R ² =0.363 p<0.001 B coefficient
SBP at Y5, 10mmHg	0.023	-	-	-
Delta SBP, 10mmHg	0.197*	-	-	-
DBP at Y5, 10mmHg	-	0.419*	-	-
Delta DBP, 10mmHg	-	0.364*	-	-
PP at Y5, 10mmHg	-	-	-0.328 [†]	-
Delta PP, 10mmHg	-	-	0.019	-
MAP at Y5, 10mmHg	-	-	-	0.276 [†]
Delta MAP, 10mmHg	-	-	-	0.311*
Age, 10 years	0.412 [‡]	0.456 [‡]	0.408 [‡]	0.446 [‡]
Gender, being male	3.125*	3.000*	3.202*	3.028*
Race, being black	-0.510*	-0.602*	-0.398 [†]	-0.583*
Height at Y5, 10cm	0.590*	0.622*	0.561*	0.611*
Weight at Y5, 10kg	0.535*	0.479*	0.546*	0.498*
Delta weight, 10kg	0.137 [†]	0.105 [‡]	0.163 [†]	0.117 [‡]
Diabetes mellitus at Y5	0.119	0.197	0.107	0.166
Total cholesterol at Y5, 10mg/dL	-0.022	-0.003	-0.019	-0.028
Delta cholesterol, 10mg/dL	-0.015	-0.002	-0.001	-0.019
Current cigarette smoker at Y5	0.378 [†]	0.371 [†]	0.463 [†]	0.363 [‡]
Treatment for HBP at Y5	-0.333	-0.665	-0.329	-0.574
Physical activity at Y5, 100 EU [§]	0.014	0.018	0.025	0.015
Delta Physical activity, 100 EU [§]	0.002	0.005	0.003	0.003

Delta: Year-25 value minus Year-5 value

* p<0.001;

[†] p<0.01,

[‡] p<0.05

SBP: systolic blood pressure; DBP: diastolic blood pressure; PP: pulse pressure; MAP: mean arterial pressure.

[§] Exercise score expressed in exercise units (EU) representing the frequency and intensity of exercise over the past year. For reference, 300 exercise units roughly approximates 5 sessions of 1260 kJ (300 kcal) of energy expenditure weekly.