

BASELINE ANTHROPOMETRIC INDICES PREDICT CHANGE IN VERTEBRAL SIZE IN EARLY ADULTHOOD – A 10-YEAR FOLLOW-UP MRI STUDY

Author list:

Petteri Oura^{1,2,3}

Juho-Antti Junno^{1,4,5,6}

Elsi Autio^{1,2,3}

Jaro Karppinen^{1,3,7}

Jaakko Niinimäki^{1,2,8}

Affiliations:

1 Medical Research Center Oulu, Oulu University Hospital and University of Oulu, Oulu, Finland

2 Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, Oulu, Finland

3 Center for Life Course Health Research, Faculty of Medicine, University of Oulu, Oulu, Finland

4 Cancer and Translational Medicine Research Unit, Faculty of Medicine, University of Oulu, Oulu, Finland

5 Department of Anatomy, Faculty of Medicine, University of Oulu, Oulu, Finland

6 Department of Archaeology, Faculty of Humanities, University of Oulu, Oulu, Finland

7 Finnish Institute of Occupational Health, Oulu, Finland

8 Department of Radiology, Oulu University Hospital, Oulu, Finland

Correspondence to:

Petteri Oura, MD, PhD

Email: petteri.oura@oulu.fi

Postal address: Center for Life Course Health Research, Faculty of Medicine, University of Oulu, PO Box 5000, FI-90014, University of Oulu, Oulu, Finland.

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ABSTRACT

The vertebral cross-sectional area (CSA) has an independent effect on vertebral strength. Recent evidence has shown that vertebral dimensions significantly increase in the third decade of life, and that lifestyle factors such as body size and composition are clearly associated with vertebral CSA. This study aimed to test the hypothesis that general anthropometric traits (stature, total body mass, lean body mass, fat mass, body mass index, waist circumference), each objectively measured at baseline, predict the change in vertebral CSA over the subsequent decade. A representative sample of young Northern Finnish adults was used ($n = 371$) with repeated magnetic resonance imaging (MRI) scans from ~ 20 and ~ 30 years (baseline and follow-up, respectively). Vertebral CSA was measured from the MRI scans with high reliability and low measurement error. The statistical analysis was performed using linear regression models adjusted for sex and exact length of MRI interval. According to the regression models, in descending order of effect size, lean body mass (standardized beta coefficient 0.243 [95% confidence interval 0.065—0.420]), total body mass (0.158 [0.043—0.273]), body mass index (0.125 [0.026—0.224]), waist circumference (0.119 [0.010—0.228]), and fat mass (0.104 [0.004—0.205]) were positively and significantly associated with CSA gain over the follow-up, whereas stature (0.079 [-0.066—0.224]) was not associated with CSA change. The results of this study suggest that anthropometric indices may be used for estimating subsequent change in vertebral size. In particular, greater lean body mass seems to be beneficial for vertebral size and thus potentially also for vertebral strength. Future studies should aim to replicate these associations in a dataset with longitudinal anthropometric trajectories and identify the potential common factors that influence both anthropometric traits and vertebral CSA gain.

KEYWORDS: vertebrae; epidemiology; anthropometry; magnetic resonance imaging; lumbar spine; osteoporosis

1. INTRODUCTION

Together with several material, microarchitectural and geometrical properties, vertebral cross-sectional area (CSA) has an independent effect on vertebral strength [1,2]. Recently, cross-sectional evidence has accumulated that lifestyle factors such as physical activity [3], nutrition [4], dieting [5], and body composition [6] are associated with vertebral CSA and can therefore potentially be further applied in the prevention of vertebral fractures.

Bone development and skeletal maturation appear to be site-specific [7,8]. Peak adult stature is reached in late adolescence or one's early 20s, lean body mass (i.e. fat-free mass) tends to accumulate until one's 30s, and fat mass increases until one's mid-50s [9-11]. Although total bone mass [7] and lumbar spine bone mass [8] reach their maxima during the third decade of life, the vertebrae seem to continue increasing in size thereafter [7,12]. However, it is largely unknown which factors contribute to this change in vertebral CSA, and whether modifications in these potential factors could accelerate CSA gain after peak bone mass.

Stature is strongly associated with skeletal robustness, and body mass has an obvious association with bone size in weight-bearing skeletal sites [13]. Body mass index (i.e. body mass divided by the square of stature) and waist circumference are generally used as proxies for obesity [14]. In the axial skeleton, obesity has been associated with larger vertebral CSA relative to normal weight [15]. In a previous cross-sectional study that evaluated several anthropometric indices as correlates of vertebral CSA in a middle-aged sample [6], stature and lean body mass had the highest correlations with vertebral CSA (Pearson's $R = 0.4-0.5$). It remains unclear, however, whether anthropometric parameters possess information value as predictors of vertebral CSA gain among young adults.

In this study, we aimed to test our hypothesis that anthropometric traits, objectively measured at baseline, predict the change in vertebral CSA over the subsequent decade. We used a representative sample of young Northern Finnish adults with repeated magnetic resonance imaging (MRI) scans available from the ages of 20 and 30.

2. MATERIAL AND METHODS

2.1 Study protocol

The Northern Finland Birth Cohort 1986 (NFBC1986) database [16] provided the material for this study. The NFBC1986 is a population-based ongoing cohort study, which initially comprised infants who were born in the Northern Finnish provinces of Oulu and Lapland and had expected dates of birth between July 1, 1985 and June 30, 1986 (n = 9479). The initial coverage was up to 99% of applicable births in the area, and the NFBC1986 population is still followed up periodically.

The data collection procedure for the present study was as follows: In 2005—2008, all the NFBC1986 members who lived within 100 km of the Finnish city of Oulu and who had participated in the earlier data collection waves (n = 1987) were first invited to a clinical examination. The examination included objective measurements of stature, body mass and body composition. Then, those who had participated in the clinical examination (n = 874) were subsequently invited to undergo a lumbar MRI scan (i.e. baseline MRI, n = 558 attendees). Approximately ten years later, in 2015—2018, individuals who had undergone the baseline MRI were invited to a second lumbar MRI scan (i.e. follow-up MRI, n = 375 attendees). As four individuals had missing data, the final sample comprised 371 individuals.

To evaluate the potential selection bias associated with this data collection procedure, the baseline and follow-up MRI populations were studied for representativeness against the original cohort population. Importantly, it was concluded that both MRI populations were essentially representative of the original cohort [12,17]. The flowchart in **Figure 1** demonstrates the study protocol with exclusions.

2.2 Anthropometric measurements

The clinical examination comprised several anthropometric measurements which were systematically obtained by a trained study nurse after an overnight fasting period. Height (i.e. stature, in cm) and weight (i.e. total body mass, in kg) were measured using calibrated standard scales to an accuracy of 0.1 cm and 0.1 kg, respectively. Body mass index (in kg/m²) was calculated as weight (kg)/height² (m²). Waist circumference (in cm) was measured from the middle of the lowest rib margin and the iliac crest. Body composition was estimated using a bioelectrical impedance analyser (InBody, Biospace Co, Seoul, Korea). Fat mass (in kg) and lean body mass (i.e. difference between total body mass and fat mass, in kg) were calculated from the bioimpedance analysis output.

2.3 Vertebral measurements

Vertebral measurements were obtained from 1.5-Tesla lumbar MRI at baseline and follow-up. The Signa HDxt (General Electric, Milwaukee, Wisconsin, USA) and Optima MR450w (General Electric, Milwaukee, Wisconsin, USA) scanners were used at baseline and follow-up, respectively. At both time points, routine lumbar spine protocol was followed, including T2-weighted fast-recovery fast spin-echo images in sagittal and transverse planes (repetition time 3960 ms, echo time 116 ms, echo train length 29, number of excitations 4, acquisition matrix 448 × 224 px, field of view 280 × 280 mm, slice thickness 4 mm, interslice gap 1 mm). Tests for the geometric accuracy of the MRI equipment took place on a weekly basis.

One blinded researcher (P.O.) evaluated the scans and systematically performed the vertebral measurements using NeaView Radiology software version 2.31 (Neagen Oy, Oulu, Finland). Importantly,

the baseline and follow-up scans of each individual were evaluated independently. First, each scan was assessed for severe vertebral pathologies, which were not present. Then, L4 was located and its width (i.e. transverse dimension) and depth (i.e. anterior-posterior dimension) were measured at three levels: the most superior axial slice available (i.e. below the cranial endplate), the midaxial slice, and the most inferior axial slice available (i.e. above the caudal endplate). Each measurement was recorded to an accuracy of 0.1 mm. Finally, mean width and depth were calculated by averaging the respective measurements across levels. Mean values were used to account for the natural variety in vertebral shape among healthy individuals [18,19].

Vertebral CSA was calculated using the previously validated ellipsoid formula [20,21] $CSA = \pi \times a/2 \times b/2$, where a = mean width and b = mean depth. CSA change over the follow-up was calculated as $CSA_{\text{follow-up}} - CSA_{\text{baseline}}$, with positive and negative values indicating increase and decrease in size, respectively. Vertebral CSA was selected as the outcome, as it has a substantial effect on the load-bearing capacity of the vertebra [22,23] and an independent association with vertebral fracture risk [1,2].

Our previous comparisons between MRI-derived measurements and direct measurements taken using osteometric calipers have shown that MRI is accurate in estimating vertebral dimensions [24]. Based on 180 repeated measurements, we have also shown that our vertebral measurements have high intra-rater reliability (intra-class correlation coefficient ≥ 0.93) and low measurement errors (technical error of measurement $\leq 3.7\%$) [12]. L4 was chosen as the vertebra of interest because it was located in the centre of the MRI scans and was therefore most likely to be accessible in the scans.

2.4 Statistical analysis

The data were administered and analysed using SPSS version 25 (IBM, Armonk, NY, USA). The threshold for statistical significance was set at $P = 0.05$.

First, descriptive statistics were calculated using means and standard deviations. All variables were visually confirmed to follow fairly normal distributions. Then, linear regression analysis was performed, with vertebral CSA change as the universal outcome in all models, anthropometric variables as primary predictors (each having their own model), and sex and follow-up length as universal covariates. The choice of constructing separate models for all anthropometric variables was based on two aspects: first, to avoid multicollinearity due to strong intercorrelations (Variance Inflation Factors 4.0—165.4 indicating at least doubled standard errors [25]; moreover, some variables were automatically excluded from multivariable models due to Minimum Tolerance < 0.001); and second, to enable *a posteriori* comparisons of the true predictive power of each anthropometric variable.

The following regression parameters were collected from the data output of each model: the unstandardized beta coefficient of the primary predictor (indicative of effect size; dependent on the unit and scale of the predictor; not comparable across variables with varying scales); the standardized beta coefficient of the primary predictor (indicative of effect size; normalized, unitless and independent of scale; enables *a posteriori* comparisons across variables); the 95% confidence intervals of the beta coefficients and the associated P value; and the adjusted R squared value of the model (R^2 ; indicative of the amount of variation in the outcome that is explained by the model). The regression parameters were tabulated, and the standardized beta coefficients were plotted for visual comparison. The standardized coefficients were further compared with each other by means of a one-tailed Z test.

2.5 Ethical approval

Approval was obtained from the Ethics Committee of the Northern Ostrobothnia Hospital District, and the Scientific Committee of the NFBC1986. The principles of the Declaration of Helsinki were followed at all stages of the study. Participation was voluntary, and informed consent was collected from the participants and, where applicable, also their guardians. The data were analysed in a pseudonymised format.

3. RESULTS

The study sample consisted of 371 individuals, of whom 145 were men (39.1%) and 226 women (60.1%). **Table 1** presents the characteristics of the sample. The mean follow-up length was 9.4 (SD 0.7) years, during which an average gain of 73.7 (SD 44.0) mm² in vertebral CSA occurred.

Table 2 presents the regression parameters for the association between the anthropometric variables recorded at baseline and the change in vertebral CSA over the follow-up. The standardized regression coefficients, which enable comparison of predictive power across the variables, are illustrated in **Figure 2**. In descending order of effect size, lean body mass, total body mass, body mass index, waist circumference and fat mass were identified as statistically significant predictors of vertebral CSA change, independently of sex and follow-up length (standardized beta = 0.104—0.243, $p = 0.007$ —0.042, adjusted $R^2 = 0.094$ —0.109). In contrast, stature was not associated with CSA change (standardized beta = 0.079, $p = 0.285$, adjusted $R^2 = 0.086$). The comparison of standardized betas revealed no statistically significant differences between the predictors ($Z \leq 1.408$, $p \geq 0.080$).

4. DISCUSSION

This study aimed to test whether general anthropometric traits, objectively measured at baseline, predict the change in vertebral CSA over the subsequent decade among young adults. To the authors' knowledge, this study is among the first to assess anthropometric traits as predictors of vertebral CSA change in the general population. According to our results, in descending order of effect size, lean body mass, total body mass, body mass index, waist circumference, and fat mass at baseline were positively and significantly associated with CSA gain over the follow-up, whereas stature was not associated with CSA change. The results of this study suggest that anthropometric measurements may provide tools for estimating change in vertebral size. In particular, greater lean body mass seems to be beneficial for vertebral size and thus potentially also for vertebral strength.

Body size, i.e. stature and body mass, have clear associations with bone dimensions in the weight-bearing skeleton [13], including the lumbar spine [6,26,27]. Here, we aimed to characterize the role of anthropometric traits as predictors of future change in vertebral size. Similarly to previous cross-sectional reports [6], total body mass and its main components (i.e. lean body mass and fat mass) were each associated with subsequent CSA gain. Of these three variables, lean body mass showed the strongest predictive potential relative to CSA change, fat mass the weakest, and total body mass remained in the middle. After the growth period, lean body mass is considered to remain relatively stable over the life course, whereas the amount and distribution of fat mass may undergo changes in a short period of time [28]. It is therefore plausible that high lean body mass at baseline is likely to remain relatively constant or increase over the subsequent decade, implying a natural load in the weight-bearing skeleton and thus an increase in vertebral CSA. Obesity measures, i.e. body mass index and waist circumference, showed intermediate effect sizes, supporting the conclusion that high lean body mass is superior to excess body fat as a predictor of future vertebral size.

Interestingly, baseline stature was not associated with subsequent change in vertebral CSA. This was contrary to earlier knowledge of the general relationship between stature and skeletal size [13], and previous cross-sectional results regarding the association between stature and vertebral CSA [6,26]. We believe this to be explained by the timing of skeletal maturation; at baseline, most individuals were at the very end of their pubertal growth spurt and close to reaching adult stature. We argue that although adult stature is an accurate proxy for skeletal size and therefore has a clear association with vertebral CSA in general, it is a poor predictor of CSA gain specific to the third decade of life. By the end of the pubertal growth spurt, most vertebral CSA gain is likely to have already occurred, and the other anthropometric indices seem to play a more prominent role as predictors of the remaining CSA gain, regardless of stature. For example, lean body mass and fat mass have greater potential to undergo changes from a person's 20s onwards and may thus be associated with the mechanisms behind the observed change in vertebral CSA over the follow-up. As such, our findings underline the possibility that an individual can affect their vertebral CSA change by lifestyle choices related to, e.g., gaining high lean body mass.

The main strengths of this study stem from its longitudinal MRI data with a follow-up of 10 years, its objective anthropometric measurements including body composition analysis, and its prospective birth cohort population. Given the long follow-up with repeated MRI scans, the sample size was considered relatively large. Importantly, the sample has shown to represent the Northern Finnish population well. This study is among the few to analyse the axial skeleton in a longitudinal manner with three-dimensional imaging using a general population approach.

This study also had limitations. First, despite the relatively large dataset, we lacked information on the subjects' anthropometry from the follow-up period. While we acknowledge that the associations observed here are likely to be mediated by an individual's anthropometric trajectory in the follow-up, we believe that

our study reveals valuable data on the predictive role of baseline anthropometry in estimating CSA gain over the subsequent decade. Second, we acknowledge that the aetiological basis of vertebral health and osteoporotic vertebral fracture is multifactorial, involving several material, microarchitectural and geometrical properties. Although our study was limited to only one of these, namely vertebral CSA, we underline that the independent role of vertebral CSA in vertebral strength is widely acknowledged [1,2]. Third, as our study concerned only L4, the analysis should be replicated using other vertebrae for a comprehensive view of the association. Fourth, although our results suggest that several parameters which are conventionally used to define obesity (i.e. higher fat mass, body mass index and waist circumference) seem to predict beneficial CSA gain, we emphasize the diverse unfavourable effects of obesity [14]. Importantly, lean body mass seemed to be the strongest predictor of vertebral CSA gain.

In summary, this MRI study of 371 young adults from Northern Finland revealed that baseline lean body mass, total body mass, body mass index, waist circumference, and fat mass were positively and significantly associated with vertebral CSA gain over the subsequent decade. The results of this study suggest that anthropometric indices may be used for estimating change in vertebral size. In particular, greater lean body mass seems to be beneficial for vertebral size and thus potentially also for vertebral strength. Future studies should aim to replicate these associations in a dataset with longitudinal anthropometric trajectories and identify the potential common factors that influence both anthropometric traits and vertebral CSA gain.

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7. TABLES

Table 1. General characteristics of the sample. Values are means with standard deviations.

Characteristic	All (n = 371)	Men (n = 145)	Women (n = 226)
Age			
At baseline examination (years)	19.1 (0.3)	19.1 (0.3)	19.1 (0.3)
At baseline MRI (years)	21.3 (0.6)	21.2 (0.6)	21.3 (0.6)
At follow-up MRI (years)	30.7 (0.6)	30.5 (0.6)	30.8 (0.5)
MRI interval length (years)	9.4 (0.7)	9.3 (0.8)	9.4 (0.7)
Anthropometry at baseline examination			
Stature (cm)	169.5 (9.4)	178.1 (6.8)	164.0 (6.0)
Total body mass (kg)	66.1 (14.3)	75.7 (13.2)	60.0 (11.3)
Lean body mass (kg)	51.0 (11.4)	62.9 (7.8)	43.4 (5.0)
Fat mass (kg)	15.1 (7.9)	12.7 (7.7)	16.6 (7.7)
Body mass index (kg/m ²)	22.9 (3.9)	23.8 (3.9)	22.3 (3.8)
Waist circumference (cm)	76.1 (10.3)	81.9 (9.8)	72.4 (8.9)
Vertebral cross-sectional area			
At baseline MRI (mm ²)	1053.1 (175.9)	1204.5 (152.2)	955.9 (108.6)
At follow-up MRI (mm ²)	1126.8 (186.5)	1291.4 (158.4)	1021.1 (111.6)
Change over follow-up (mm ²)	+73.7 (44.0)	+86.9 (46.0)	+65.2 (40.6)

MRI = Magnetic resonance imaging

Table 2. The association between anthropometric variables at baseline and change in vertebral cross-sectional area over the follow-up (n = 371). Results from linear regression models adjusted for sex and follow-up length. Bold denotes statistical significance.

Predictor	Regression parameters			
	Unstandardized beta coefficient (95% CI)	Standardized beta coefficient (95% CI)	P value	Adjusted R ²
Stature (cm)	0.371 (-0.310; 1.053)	0.079 (-0.066; 0.224)	0.285	0.086
Total body mass (kg)	0.486 (0.132; 0.840)	0.158 (0.043; 0.273)	0.007	0.101
Lean body mass (kg)	0.936 (0.252; 1.621)	0.243 (0.065; 0.420)	0.007	0.109
Fat mass (kg)	0.581 (0.022; 1.140)	0.104 (0.004; 0.205)	0.042	0.094
Body mass index (kg/m²)	1.397 (0.287; 2.507)	0.125 (0.026; 0.224)	0.014	0.099
Waist circumference (cm)	0.505 (0.042; 0.969)	0.119 (0.010; 0.228)	0.033	0.095

CI = Confidence interval

8. FIGURE LEGENDS (FIGURE FILES SUBMITTED SEPARATELY)

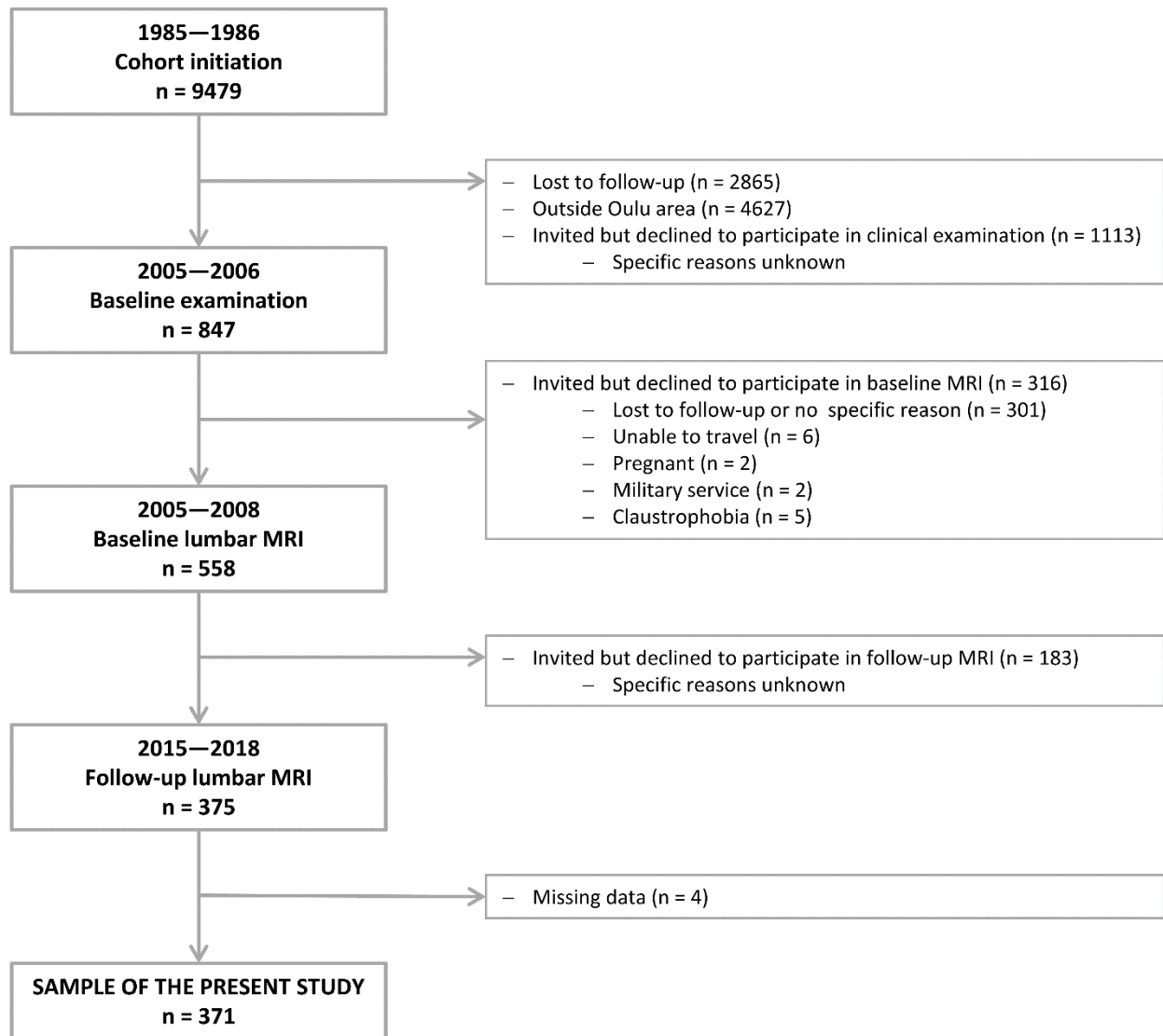


Figure 1. Flowchart of the study protocol with exclusions at each stage. MRI = Magnetic resonance imaging.

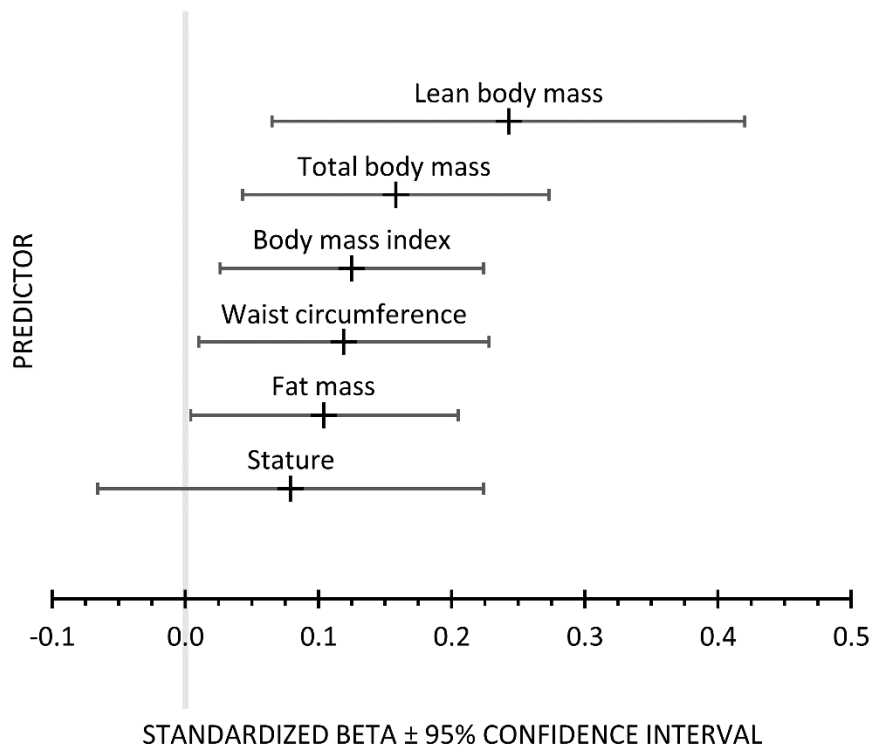


Figure 2. Plot illustrating the standardized beta coefficients of the anthropometric variables as predictors of change in vertebral cross-sectional area over the follow-up period.