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Two-dimensional transthoracic echocardiographic normal reference ranges for proximal aorta dimensions: results from the EACVI NORRE study

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Aims To report normal reference ranges for echocardiographic dimensions of the proximal aorta obtained in a large group of healthy volunteers recruited using state-of-the-art cardiac ultrasound equipment, considering different measurement conventions, and taking into account gender, age, and body size of individuals.

Methods and Results A total of 704 (mean age: 46.0 ± 13.5 years) healthy volunteers (310 men and 394 women) were prospectively recruited from the collaborating institutions of the Normal Reference Ranges for Echocardiography (NORRE) study. A comprehensive echocardiographic examination was obtained in all subjects following pre-defined protocols. Aortic dimensions were obtained in systole and diastole, following both the leading-edge to leading-edge and the inner-edge to inner-edge conventions. Diameters were measured at four levels: ventricular-arterial junction, sinuses of Valsalva, sino-tubular junction, and proximal tubular ascending aorta. Measures of aortic root in the short-axis view following the orientation of each of the three sinuses were also performed. Men had significantly larger body sizes when compared with women, and showed larger aortic dimensions independently of the measurement method used. Dimensions indexed by height and body surface area are provided, and stratification by age ranges is also displayed. In multivariable analysis, the independent predictors of aortic dimensions were age, gender, and height or body surface area.

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Conclusion The NORRE study provides normal values of proximal aorta dimensions as assessed by echocardiography. Reference ranges for different anatomical levels using different (i) measurement conventions and (ii) at different times of the cardiac cycle (i.e. mid-systole and end-diastole) are provided. Age, gender, and body size were significant determinants of aortic dimensions.

Keywords echocardiography • thoracic aorta • sinus of valsalva • reproducibility of results • reference values • NORRE study

Introduction

Transthoracic echocardiography is a wide spread imaging technique used for imaging of proximal aortic segments, and consequently frequently used for thoracic aortic aneurism screening and/or serial measurement of aortic root dimensions.[1,2] Normal reference ranges have been mainly established for two-dimensional (2D) echocardiography with fundamental imaging using the leading edge to leading edge (LL) measurement method.[3] Current recommendations advise measuring the aortic annulus in mid-systole using the inner-edge to inner-edge (II) convention, whereas the other dimensions of the aortic root complex should be measured at end-diastole using the LL convention.[4] However, this latter approach remains debatable, especially in the era of multimodality imaging of the aorta.[2,4]

Proximal thoracic aorta dimensions are known to be age and body size dependent.[5,6] Therefore, demographic and anthropometric factors are of paramount importance when interpreting aortic root measurements and its clinical implications.

The Normal Reference Ranges for Echocardiography study (NORRE study) is an international multi-centre study involving several accredited echocardiography laboratories of the European Association of Cardiovascular Imaging (EACVI).[7] The NORRE study aims to prospectively establish a set of normal echocardiographic values in a large cohort of healthy individuals over a wide range of ages. Recently, both the 2D chamber size and Doppler sub-studies of the NORRE study have been published.[8,9] In the present study, the normal ranges for echocardiography-derived dimensions of proximal aorta are provided, reporting the results for both the LL and II conventions measured in both systole and diastole while taking into account demographic and anthropometric factors.

Methods

Patient population

The NORRE study enrolled a total of 865 normal European subjects from 22 collaborating EACVI accredited echocardiography laboratories. Of these, 161 cases were excluded due to incompatible image format or inappropriate image quality for proximal aorta analysis. Thus 704 healthy adult volunteers with a mean age of 46.0 ± 13.5 years (range: 19–78 years) constituted the population of the Proximal Aorta Dimensions NORRE sub-study. All subjects underwent a comprehensive transthoracic echocardiographic examination. The study protocol obtained approval from every local ethic committee.

Echocardiographic examination

Transthoracic echocardiography examinations were performed using either a Vivid E9 (GE Vingmed Ultrasound, Horten, Norway) or iE33 (Philips Medical Systems, Andover, USA) ultrasound system, following the study protocol.[7] Echocardiographic images were recorded in native DICOM format and coded after anonymization for analysis at the EACVI Central Core Laboratory, at the University of Liège, Belgium. Transthoracic scans from the parasternal windows were acquired to obtain a long-axis view of the left ventricle (LV), which enabled aortic root and proximal ascending aorta visualization and subsequent measurements. From the same window, with convenient probe rotation, 2D short-axis views at the level of the aortic valve plane were taken. Image depth and sector width were adjusted to optimize proximal aorta visualization. Zoomed images of both left ventricle outflow tract (LVOT) in parasternal long-axis view, and of the aortic valve in parasternal short-axis view were obtained and recorded.

Measurements were performed both in end-diastole (QRS complex onset) and in mid-systole coinciding with the maximal diameter of the aorta. Aortic dimensions were measured at four different levels: (i) ventriculo-arterial junction (VAJ), at the hinge points of aortic valve in the distal LVOT; (ii) sinuses of Valsalva (SV); (iii) sinotubular junction (STJ); and (iv) tubular ascending aorta (TAA) at 1 cm above STJ. Measurements were performed in dedicated workstations using both the LL and II conventions as depicted in *Figure 1*.

Diastolic diameters of SV in a short-axis cross-sectional plane of the aortic root were also obtained using the II convention at the level of each commissural line and the corresponding opposite coronary sinus (according to which the diameter is named) as shown in *Figure 2*. In addition, the arithmetic mean of the last three measures was calculated, in order to act as the dependent variable later in regression analysis.

Statistical analysis

Normal distribution of continuous variables was assessed with the Kolmogorov–Smirnov test (Lilliefors correction). Variable magnitudes are described as means with standard deviation (SD), or median and interquartile range (IQR) as appropriate. Reliability was assessed by means of the intra-class correlation coefficient (ICC) using the two-way mixed model for average measurements. Differences between groups were analysed with the unpaired *t*-test; homogeneity of variances assumption was confirmed by Levene's test. For variables distributed otherwise than normally, differences were assessed by the nonparametric Mann–Whitney *U* test. Bivariate correlations between variables were performed with either Pearson or Spearman test as appropriate. Agreement between measurement conventions was tested with the Bland–Altman method. Passing–Bablok regression test was carried out to quantify constant and systematic deviations between measurement conventions. Univariable linear regression analysis was applied to test the association between demographic and anthropometric variables and aortic dimensions. Stepwise forward multivariable linear regression was later

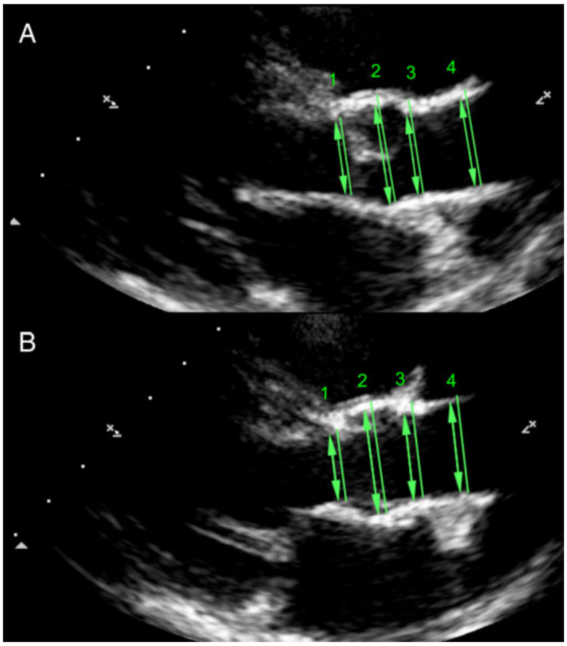

Figure 1 Echocardiographic parasternal long-axis views centered in the LVOT and proximal aorta, showing measurement methods. (*A*) End-diastolic image. (*B*) Mid-systolic image. (1) Ventriculo-arterial junction level; (2) sinuses of valsalva level; (3) STJ level; (4) TAA level. Lines ended in arrowheads show inner-edge to inner-edge convention. Lines without specific ending represent leading-edge to leading-edge measurement convention.

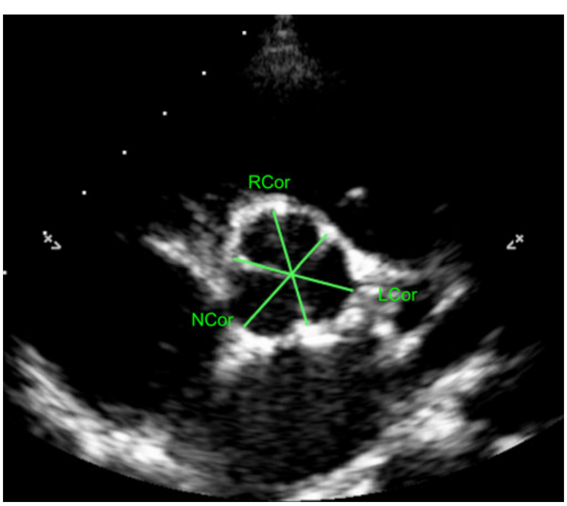

Figure 2 Diastolic still frame of echocardiographic parasternal zoomed short-axis view of aortic root, showing measurement of diameters corresponding to each aortic sinus and the facing commisural line. RCor, right coronary sinus; LCor, left coronary sinus; NCor, non-coronary sinus.

performed, including into the analysis all the variables with a *P*-value ≤0.1 in univariable analysis. Control for colinearity was warranted in the multiple linear regression analysis. Differences were considered as statistically significant at the two-tailed $P < 0.05$. All computations were carried out with the software SPSS version 19 (SPSS Inc., Chicago, IL, USA).

Results

Demographic data

A total of 310 men (44%) and 394 women (56%) were included. The mean age of the population was 46 years (range 19–78 years). *Table 1* shows the demographic and biological data of the entire study population, as well as by gender. Per protocol, subjects were healthy adults with normal anthropometric and clinical characteristics. As compared to men, women had significantly smaller body size. Minimal differences in blood pressure and glycaemia were detected, but age was similar in both gender groups.

Reliability of measurements

Reproducibility of the entire set of aortic measurements was good, with ICC ranging from 0.767 to 0.933 for intra-observer, and from 0.672 to 0.905 for inter-observer reproducibilities.

Normal dimensions of proximal aorta

Table 2 provides descriptive statistics of the dimensions of proximal aorta at the studied levels. Aortic-complex diameters were constantly significantly larger in men compared with women, irrespective of the site of assessment, cardiac cycle phase, or measurement convention applied. After indexing for height (*Table 3*), men showed statistically significant larger aortic dimension to height ratios at VAJ, SV, and STJ levels, but remained non-significant trend at the TAA level. In contrast, after indexing aortic diameters to BSA, dimensions of the proximal aorta tended to be larger in women. Description and statistical significance for each single measure is provided in *Table 3*. The values of aortic measurements according to gender and age are presented in *Table 4*. Both for men and women, non-indexed aortic dimensions tended to increase with age, with the exception of the VAJ diameter.

Predictors of proximal aorta dimensions

Both ascending aorta and aortic root measurements at the level of SV (expressed as the mean of the three short-axis dimensions shown in *Figure 2*) correlated significantly in the univariable analysis with gender, age, and body size variables. *Table 5* shows the results of the two approaches related to body size (height or BSA) and the subsequent multivariable linear regression analyses, with the coefficients (and their corresponding confidence intervals) for each linear equation.

Agreement between measuring conventions

Both Bland–Altman plots (*Figure 3*) consistently demonstrated an overestimation of measures of ∼2 mm of the LL method when compared with the II convention (except for a slightly smaller

Table 1 Characteristics of the population

Parameters	Total (n = 704)	Male (n = 310)	Female (n = 394)	P
Age (years)	45.0 (35.0–57.0)	48.0 (36.3–59.0)	46.0 (36.0–57.0)	0.597
Height (cm)	170.0 (162.0–177.0)	176.5 (171.0–180.5)	163.0 (158.0–168.0)	<0.001
Weight (kg)	68.5 (60.0–78.0)	78.0 (70.0–84.0)	63.0 (57.6–69.0)	<0.001
Body mass index (kg/m^2)	24.1 ± 3.1	24.9 ± 2.9	23.9 ± 3.1	<0.001
Body surface area (m^2)	1.8 ± 0.2	1.9 ± 0.2	1.7 ± 0.2	<0.001
Waist circumference (cm)	85.3 ± 10.7	88.2 ± 10.0	82.5 ± 10.6	<0.001
Systolic blood pressure (mmHg)	120.0 (110.0–130.0)	124.0 (118.0–130.0)	117.0 (110.0–128.0)	<0.001
Diastolic blood pressure (mmHg)	75.0 (70.0–80.0)	77.0 (70.0–80.0)	73.0 (70.0–80.0)	<0.001
Glycaemia (mg/dL)	92.0 (86.0–97.4)	93.0 (88.85–98.0)	91.0 (84.0–95.0)	0.001
Cholesterol level (mg/dL)	184.0 (167.0–199.5)	186.0 (170.0–203.0)	181.0 (165.0–196.0)	0.051

Table 2 Proximal aorta echocardiographic measurements

Parameters	Total (n = 704) mean ± SD	Total (n = 704) IQR	Total (n = 704) 95% CI of mean	Male (n = 310) mean ± SD	Female (n = 394) mean ± SD	P*
L–L end-diastole						
VAJ (mm)	20.4 ± 2.4	18.8–22.0	20.3–20.6	21.9 ± 2.2	19.3 ± 2.0	<0.001
SV (mm)	31.5 ± 4.1	28.6–34.0	31.2–31.8	33.6 ± 3.9	29.7 ± 3.3	<0.001
STJ (mm)	27.2 ± 3.3	25.0–29.5	26.9–27.4	28.7 ± 3.2	26.0 ± 2.9	<0.001
TAA (mm)	28.5 ± 3.8	26.0–30.9	28.2–28.8	29.9 ± 3.8	27.3 ± 3.4	<0.001
I–I end-diastole						
VAJ (mm)	19.2 ± 2.5	17.5–20.9	19.0–19.4	20.6 ± 2.2	18.2 ± 2.1	<0.001
SV (mm)	29.3 ± 3.9	26.4–31.8	29.0–29.6	31.4 ± 3.7	27.7 ± 3.1	<0.001
STJ (mm)	25.0 ± 3.2	22.9–27.0	24.8–25.3	26.4 ± 3.2	23.9 ± 2.8	<0.001
TAA (mm)	26.0 ± 3.6	24.0–28.7	26.2–26.8	27.8 ± 3.6	25.5 ± 3.3	<0.001
L–L mid-systole						
VAJ (mm)	21.5 ± 2.3	20.0–23.0	21.4–21.7	22.8 ± 2.1	20.6 ± 1.9	<0.001
SV (mm)	32.6 ± 3.9	30.0–35.0	32.3–32.9	34.6 ± 3.8	31.0 ± 3.1	<0.001
STJ (mm)	28.1 ± 3.3	25.9–20.3	27.9–28.4	29.6 ± 3.2	26.9 ± 2.8	<0.001
TAA (mm)	30.0 ± 3.6	27.6–32.0	29.7–30.3	31.4 ± 3.6	28.9 ± 3.2	<0.001
I–I mid-systole						
VAJ (mm)	20.1 ± 2.1	18.8–21.6	20.0–20.3	21.3 ± 2.0	19.2 ± 1.7	<0.001
SV (mm)	30.4 ± 3.8	28.0–32.8	30.1–30.7	32.4 ± 3.7	28.9 ± 3.1	<0.001
STJ (mm)	25.9 ± 3.1	23.8–28.0	25.6–26.1	27.2 ± 3.1	24.8 ± 2.7	<0.001
TAA (mm)	27.9 ± 3.5	25.6–30.0	27.7–28.2	29.2 ± 3.6	26.9 ± 3.1	<0.001
Short-axis end-diastole						
RCor (mm)	27.9 ± 3.5	25.5–30.0	27.7–28.2	29.7 ± 3.5	26.5 ± 2.8	<0.001
LCor (mm)	28.1 ± 3.6	25.6–30.4	27.8–28.4	29.6 ± 3.7	26.9 ± 3.0	<0.001
NCor (mm)	28.2 ± 3.7	25.9–30.6	27.9–28.5	29.7 ± 3.7	27.0 ± 3.2	<0.001

SD, standard deviation; IQR, interquartile range; CI, confidence interval; L–L, leading edge to leading edge convention; I–I, inner-edge to inner-edge convention; RCor, diameter of aortic root at the level of the right coronary sinus; LCor, diameter of aortic root at the level of the left coronary sinus; NCor, diameter of aortic root at the level of the non-coronary sinus.
*P differences between male vs. female.

deviation at the VAJ level). Passing–Bablok regression yielded both constant and proportional coefficients of the prediction model for the estimation of a diameter from a measuring convention to another (*Table 6*).

Nomograms

In order to provide a graphical approach to normalcy assessment when dealing with proximal aorta dimensions, dedicated nomograms have been constructed for aortic root and TAA

Table 3 Proximal aorta echocardiographic measurements indexed by body size

Parameters	Total (n = 704) Mean ± SD	Total (n = 704) IQR	Total (n = 704) 95% CI of mean	Male (n = 310) Mean ± SD	Female (n = 394) Mean ± SD	P*
Ratios to height						
L–L end-diastole						
VAJ/Ht (mm/m)	12.1 ± 1.2	11.2–12.8	12.0–12.1	12.40 ± 1.2	11.8 ± 1.2	<0.001
SV/Ht (mm/m)	18.5 ± 2.1	17.2–19.9	18.4–18.7	19.0 ± 2.1	18.1 ± 2.0	<0.001
STJ/Ht (mm/m)	16.0 ± 1.8	14.8–17.1	15.9–16.1	16.2 ± 1.8	15.8 ± 1.8	0.004
TAA/Ht (mm/m)	16.8 ± 2.2	15.2–18.2	16.6–17.0	17.0 ± 2.2	16.7 ± 2.2	0.079
I–I end-diastole						
VAJ/Ht (mm/m)	11.3 ± 1.3	10.5–12.1	11.2–11.4	11.7 ± 1.2	11.1 ± 1.3	<0.001
SV/Ht (mm/m)	17.3 ± 2.0	15.9–18.0	17.1–17.4	17.8 ± 2.0	16.9 ± 1.9	<0.001
STJ/Ht (mm/m)	14.7 ± 1.8	13.5–15.9	14.6–14.9	15.0 ± 1.8	14.4 ± 1.7	0.003
TAA/Ht (mm/m)	15.6 ± 2.1	14.2–16.8	15.5–15.8	15.7 ± 2.1	15.6 ± 2.1	0.283
L–L mid-systole						
VAJ/Ht (mm/m)	12.7 ± 1.1	12.6–12.8	12.0–13.4	12.9 ± 1.1	12.5 ± 1.1	<0.001
SV/Ht (mm/m)	19.2 ± 2.0	17.9–20.4	19.0–19.3	19.6 ± 2.1	18.9 ± 1.9	<0.001
STJ/Ht (mm/m)	16.7 ± 1.8	15.3–17.7	16.4–16.7	16.8 ± 1.8	16.4 ± 1.8	0.006
TAA/Ht (mm/m)	17.7 ± 2.1	16.3–20.0	17.5–17.9	17.8 ± 2.1	17.6 ± 2.1	0.297
I–I mid-systole						
VAJ/Ht (mm/m)	11.9 ± 1.0	11.2–12.5	11.8–11.9	12.1 ± 1.1	11.7 ± 1.0	<0.001
SV/Ht (mm/m)	17.9 ± 2.0	16.7–19.1	17.8–18.1	18.3 ± 2.0	17.6 ± 1.9	<0.001
STJ/Ht (mm/m)	15.3 ± 1.7	14.0–16.3	15.1–15.4	15.4 ± 1.8	15.1 ± 1.7	0.038
TAA/Ht (mm/m)	16.5 ± 2.0	15.1–17.6	16.3–16.6	16.5 ± 2.1	16.4 ± 2.0	0.525
Short-axis end-diastole						
RCor/Ht (mm/m)	16.5 ± 1.9	15.3–17.6	16.3–16.6	16.8 ± 2.0	16.1 ± 1.7	<0.001
LCor/Ht (mm/m)	16.6 ± 2.0	15.1–17.7	16.4–16.7	16.8 ± 2.0	16.4 ± 1.9	0.02
NCor/Ht (mm/m)	16.6 ± 2.0	15.5–17.9	16.5–16.8	16.8 ± 2.0	16.5 ± 1.9	0.011
Ratios to BSA						
L–L end-diastole						
VAJ/BSA (mm/m^2)	11.7 ± 1.8	10.6–12.4	11.6–11.9	11.6 ± 1.8	11.8 ± 1.8	0.34
SV/BSA (mm/m^2)	18.0 ± 2.6	16.2–19.1	17.8–18.2	17.9 ± 2.7	18.1 ± 2.6	0.293
STJ/BSA (mm/m^2)	15.5 ± 2.4	13.9–16.7	15.3–15.7	15.2 ± 2.5	15.8 ± 2.3	0.004
TAA/BSA (mm/m^2)	16.3 ± 2.8	14.4–17.6	16.1–16.5	15.9 ± 2.8	16.6 ± 2.8	0.001
I–I end-diastole						
VAJ/BSA (mm/m^2)	11.0 ± 1.8	9.9–11.7	10.8–11.2	10.9 ± 1.7	11.1 ± 1.8	0.363
SV/BSA (mm/m^2)	16.8 ± 2.5	15.2–17.9	16.6–16.9	16.7 ± 2.5	16.8 ± 2.4	0.375
STJ/BSA (mm/m^2)	14.3 ± 2.3	12.8–15.5	14.1–14.5	14.0 ± 2.3	14.4 ± 2.2	0.009
TAA/BSA (mm/m^2)	15.2 ± 2.7	13.3–16.5	15.0–15.4	14.7 ± 2.6	15.5 ± 2.7	<0.001
L–L mid-systole						
VAJ/BSA (mm/m^2)	12.4 ± 1.7	11.3–13.0	12.2–12.5	12.1 ± 1.7	12.5 ± 1.7	0.005
SV/BSA (mm/m^2)	18.6 ± 2.6	17.0–20.0	18.4–18.8	18.4 ± 2.7	18.8 ± 2.6	0.03
STJ/BSA (mm/m^2)	16.1 ± 2.4	14.4–17.2	15.9–16.3	15.8 ± 2.4	16.4 ± 2.4	0.002
TAA/BSA (mm/m^2)	17.2 ± 2.8	15.3–18.7	17.0–17.4	16.7 ± 2.8	17.6 ± 2.7	<0.001
I–I mid-systole						
VAJ/BSA (mm/m^2)	11.5 ± 1.6	10.5–12.2	11.4–11.7	11.3 ± 1.6	11.7 ± 1.6	0.002
SV/BSA (mm/m^2)	17.4 ± 2.5	15.8–18.7	17.2–17.6	17.2 ± 2.6	17.5 ± 2.4	0.07
STJ/BSA (mm/m^2)	14.8 ± 2.3	13.3–16.0	14.6–15.0	14.5 ± 2.3	15.1 ± 2.2	<0.001
TAA/BSA (mm/m^2)	16.0 ± 2.7	14.2–17.4	15.8–16.2	15.5 ± 2.6	16.4 ± 2.6	<0.001
Short-axis end-diastole						
RCor/BSA (mm/m^2)	16.0 ± 2.4	14.4–17.0	15.8–16.2	15.8 ± 2.5	16.1 ± 2.4	0.058
LCor/BSA (mm/m^2)	16.1 ± 2.5	14.4–17.4	15.9–16.3	15.7 ± 2.5	16.4 ± 2.5	<0.001
NCor/BSA (mm/m^2)	16.1 ± 2.5	14.5–17.4	15.9–16.3	15.8 ± 2.4	16.4 ± 2.6	0.001

Ht, height; BSA, body surface area; SD, standard deviation; IQR, interquartile range; CI, confidence interval; L–L, leading edge to leading edge convention; I–I, inner-edge to inner-edge convention; RCor, diameter of aortic root at the level of the right coronary sinus; LCor, diameter of aortic root at the level of the left coronary sinus; NCor, diameter of aortic root at the level of the non-coronary sinus.
*P differences between male vs. female.

Table 4 Aortic measures according to age and gender

Parameters	<40 years				40–59 years				≥60 years				P*			Male**		Female**	
	Total Mean ± SD	Total 95% CI	Male Mean ± SD	Female Mean ± SD	Total Mean ± SD	Total 95% CI	Male Mean ± SD	Female Mean ± SD	Total Mean ± SD	Total 95% CI	Male Mean ± SD	Female Mean ± SD	Total	Male	Female	r	P	r	P
L–L end-diastole																			
VAJ (mm)	20.4 ± 2.6	20.0–20.7	22.1 ± 2.1	19.0 ± 2.0	20.5 ± 2.3	20.3–20.8	21.8 ± 2.3	19.6 ± 1.8	20.8 ± 2.8	19.6–21.4	22.3 ± 2.1	18.7 ± 2.1	0.653	0.553	0.01	−0.09	0.105	0.06	0.232
SV (mm)	30.3 ± 4.0	29.8–30.8	32.5 ± 3.6	28.6 ± 3.5	31.7 ± 3.9	31.3–32.1	34.0 ± 3.9	30.0 ± 2.8	33.1 ± 3.6	31.9–34.3	35.2 ± 3.4	31.0 ± 2.5	<0.001	0.001	<0.001	0.21	<0.001	0.31	<0.001
STJ (mm)	25.8 ± 3.0	25.4–26.2	27.2 ± 2.6	24.7 ± 2.9	27.6 ± 3.3	27.2–28.0	29.3 ± 3.2	26.3 ± 2.6	29.2 ± 3.5	27.9–30.4	30.9 ± 3.2	27.3 ± 2.8	<0.001	<0.001	<0.001	0.33	<0.001	0.35	<0.001
TAA (mm)	26.7 ± 3.5	26.3–27.1	28.0 ± 3.1	25.6 ± 3.0	28.9 ± 3.6	28.5–29.3	30.5 ± 3.5	27.6 ± 3.0	31.5 ± 4.6	29.9–33.1	33.5 ± 3.8	29.4 ± 4.6	<0.001	<0.001	<0.001	0.42	<0.001	0.40	<0.001
I–I end-diastole																			
VAJ (mm)	19.1 ± 2.6	18.8–19.4	20.6 ± 2.1	17.9 ± 2.3	19.3 ± 2.2	19.1–19.5	20.5 ± 2.2	18.4 ± 1.8	19.4 ± 2.9	18.4–20.4	21.4 ± 2.2	17.3 ± 2.0	0.574	0.267	0.019	−0.03	0.554	0.04	0.401
SV (mm)	28.2 ± 3.9	27.7–28.8	30.2 ± 3.5	26.6 ± 3.4	29.6 ± 3.7	29.1–30.0	31.8 ± 3.7	27.9 ± 2.7	30.9 ± 3.4	29.7–32.0	32.9 ± 3.2	28.9 ± 2.3	<0.001	<0.001	<0.001	0.23	<0.001	0.31	<0.001
STJ (mm)	23.8 ± 3.0	23.4–24.2	27.2 ± 2.6	24.7 ± 2.9	25.4 ± 3.1	25.1–25.8	29.3 ± 3.2	26.3 ± 2.6	26.9 ± 3.4	25.7–28.1	30.9 ± 3.2	27.3 ± 2.8	<0.001	<0.001	<0.001	0.33	<0.001	0.35	<0.001
TAA (mm)	26.7 ± 3.3	26.3–27.1	28.0 ± 3.1	25.6 ± 3.0	28.9 ± 3.6	28.5–29.3	30.5 ± 3.5	27.6 ± 3.0	31.5 ± 4.6	29.9–33.1	33.8 ± 3.8	29.4 ± 4.6	<0.001	<0.001	<0.001	0.42	<0.001	0.40	<0.001
L–L mid-systole																			
VAJ (mm)	21.4 ± 2.5	21.1–21.7	22.9 ± 2.1	20.3 ± 2.2	21.7 ± 2.2	21.5–21.9	23.0 ± 2.0	20.7 ± 1.7	21.6 ± 2.1	20.9–22.4	23.0 ± 2.1	20.3 ± 1.2	0.374	0.918	0.086	0.10	0.093	0.06	0.274
SV (mm)	31.4 ± 3.8	31.1–32.0	33.4 ± 3.4	30.0 ± 3.4	32.7 ± 3.8	32.3–33.2	35.0 ± 3.8	31.1 ± 2.8	34.7 ± 3.2	33.6–35.7	36.6 ± 3.0	32.7 ± 2.1	<0.001	<0.001	<0.001	0.23	<0.001	0.27	<0.001
STJ (mm)	27.1 ± 3.2	26.7–27.5	28.5 ± 2.8	26.0 ± 3.0	28.5 ± 3.1	28.1–28.8	30.1 ± 3.1	27.2 ± 2.5	30.0 ± 3.4	28.8–31.3	31.8 ± 3.2	28.1 ± 2.6	<0.001	<0.001	<0.001	0.26	<0.001	0.25	<0.001
TAA (mm)	28.5 ± 3.1	28.1–28.9	29.8 ± 3.0	27.5 ± 2.8	30.4 ± 3.4	30.1–30.8	32.0 ± 3.4	29.3 ± 3.0	32.7 ± 4.5	31.1–34.3	34.6 ± 4.0	30.5 ± 4.1	<0.001	<0.001	<0.001	0.38	<0.001	0.32	<0.001
I–I mid-systole																			
VAJ (mm)	20.0 ± 2.4	19.7–20.3	21.4 ± 2.2	18.9 ± 1.9	20.2 ± 2.0	20.0–20.5	21.4 ± 2.0	19.4 ± 1.6	20.2 ± 2.2	19.5–20.9	21.5 ± 2.1	18.9 ± 1.0	0.516	0.958	0.043	−0.11	0.059	0.07	0.159
SV (mm)	29.4 ± 3.7	29.0–29.9	31.1 ± 3.4	28.0 ± 3.3	30.6 ± 3.7	30.2–31.0	32.8 ± 3.6	29.0 ± 2.8	32.4 ± 3.3	31.2–33.5	34.1 ± 3.3	30.6 ± 2.1	<0.001	<0.001	0.001	0.23	<0.001	0.26	<0.001
STJ (mm)	25.0 ± 3.1	24.6–25.4	26.2 ± 2.7	23.9 ± 2.9	26.2 ± 3.0	25.9–26.6	27.8 ± 3.2	25.1 ± 2.3	27.4 ± 3.3	26.2–28.6	28.9 ± 3.3	25.7 ± 2.6	<0.001	<0.001	<0.001	0.24	<0.001	0.24	<0.001
TAA (mm)	26.5 ± 3.0	26.1–26.9	27.6 ± 2.9	25.5 ± 2.7	28.4 ± 3.3	28.0–28.8	29.8 ± 3.4	27.3 ± 2.8	30.1 ± 4.3	28.6–31.7	31.8 ± 4.0	28.3 ± 3.9	<0.001	<0.001	<0.001	0.35	<0.001	0.34	<0.001
Short-axis end-diastole																			
RCor (mm)	27.2 ± 3.3	26.9–27.6	28.8 ± 3.0	25.9 ± 3.0	28.0 ± 3.7	27.6–28.5	30.1 ± 3.9	26.4 ± 2.6	29.7 ± 3.4	28.6–30.9	31.4 ± 3.5	28.1 ± 2.4	<0.001	0.002	0.005	0.17	0.004	0.24	<0.001
LCor (mm)	27.4 ± 3.4	26.9–27.8	28.6 ± 3.4	26.3 ± 3.1	28.1 ± 3.7	27.7–28.6	29.9 ± 3.9	26.8 ± 2.8	29.6 ± 3.5	28.4–30.8	31.4 ± 3.5	27.8 ± 2.5	0.001	0.002	0.121	0.19	0.001	0.23	<0.001
NCor (mm)	27.6 ± 3.7	27.1–28.0	28.9 ± 3.5	26.5 ± 3.5	28.2 ± 3.7	27.8–28.6	30.0 ± 3.9	26.9 ± 2.9	30.2 ± 3.2	29.1–31.2	31.7 ± 3.0	28.6 ± 2.7	<0.001	0.004	0.021	0.16	0.005	0.22	<0.001

**P* for differences between age categories (one-way ANOVA).
***P* and *r* values of the bivariate correlation test for dimensions and age (as a continuous variable) for men and women groups.

Table 5 Multiple linear regression analyses of aortic root and TAA dimensions (mm) with either BSA or height as independent variables, adjusted for age and gender

	SV II end-diastole				TAA II end-diastole			
	Adj. R^2	β	95% CI of β	P	Adj. R^2	β	95% CI of β	P
Height model	0.301				0.29			
Constant		−1.67	−7.06 to 3.72	<0.001		2.4	−3.44 to 8.25	0.42
Age (years)		0.08	0.06 to 0.09	<0.001		0.13	0.11 to 0.15	<0.001
Gender (male)		0.98	0.40 to 1.57	0.001		0.87	0.24 to 1.50	0.007
Height (cm)		0.15	0.12 to 0.18	<0.001		0.11	0.07 to 0.14	<0.001
BSA model	0.259				0.267			
Constant		17.33	15.15 to 19.51	<0.001		16.07	13.72 to 18.42	<0.001
Age (years)		0.06	0.04 to 0.07	<0.001		0.11	0.09 to 0.13	<0.001
Gender (male)		1.86	1.32 to 2.39	<0.001		1.56	0.99 to 2.13	<0.001
BSA (m^2)		4.15	2.99 to 5.32	<0.001		2.56	1.23 to 3.81	<0.001

SV, sinuses of Valsalva level; TAA, tubular ascending aorta; II, inner-edge to inner-edge convention; BSA, body surface area; Adj. R^2, adjusted coefficient of determination; β, unstandarized regression coefficient; CI, confidence interval; P=significance value of the unstandarized regression coefficient.

measurements. *Figure 4* shows aortic root dimensions by gender, age, and height. *Figure 5* displays aortic root dimensions by gender, age, and BSA. *Figures 6* and *7* show tubular aortic dimension by gender and age, as indexed by height and BSA, respectively.

Discussion

The NORRE aortic dimensions sub-study offers a set of data for normal diameter values of the proximal aorta as assessed by means of transthoracic echocardiography using harmonic imaging. The potential clinical use is either to confirm normalcy in particular patients or to assess the clinical characteristics of proximal aorta in a variety of defined clinical conditions.

Proximal aorta echocardiographic measurements

Dimensions of the explorable proximal aorta were taken from convenient transthoracic echocardiographic images at the recommended levels.[1,4] In order to provide a set of data useful for potential comparisons, diameters have been measured at both end-diastole and mid-systole. In addition to the customary LL echocardiographic convention, the II convention has been considered to be more comparable with the measurements obtained from computed tomography and magnetic resonance imaging luminograms in the current era of multimodality imaging. The EACVI recommendations hint a future shift to the II convention when dealing with aortic dimensions in order to converge with other cardiovascular imaging techniques, but the lack of sufficient normal data prevent endorsement of the II method.[4]

Diameters of the aortic root at the levels of SV from short-axis images were assessed as advised by recent recommendations.[4,10] Although such approach is planned for reconstructions from a three-dimensional data-set, convenient short-axis views of the aortic root are routinely obtainable in 2D echocardiographic studies, and were included in the NORRE study protocol.[7] Dimensions obtained from the short-axis view (*Figure 2*) relied considerably on lateral resolution and consequently only the II convention was taken into account. As the imaging plane was chosen according to visual symmetry by each echocardiographer, rather than off-line reformatted as usually done in three-dimensional techniques, potential slanting from the true aortic short-axis could not be prevented. However, if it is assumed that wrong obliquity of 2D images randomly occurs in space orientation, errors would be cancelled by regression to mean in such a large sample, that is well enough powered. In fact all three diameters were similar, and only the Non-coronary sinus diameter was slightly larger. Regarding this fact, two considerations could be made. First, this measurement mostly relies on the more accurate axial ultrasound resolution, thus yielding a good blood-endocardium definition. Second, since the non-coronary sinus is the farthest to the parasternal transthoracic probe position, this diameter is the most prone to overestimation due to off-axis imaging.

Demographic associations of aortic dimensions

Non-indexed aortic dimensions were consistently larger in men with clear statistical significance. When dimensions were indexed to height, men tended to show larger values of aortic diameters, but with less robust statistical significance. Notably, ascending tubular aorta diameters were not dissimilar from a statistical point of view in men and women when indexed to height. In contrast, when aortic dimensions were related to BSA, women showed slightly larger indexed diameters that reached statistical significance at the two more distal aortic measurement levels, i.e. STJ and TAA.

In both genders, dimensions of proximal aorta were progressively larger with aging at all levels with the exception of the aortic annulus (VAJ), which appeared to remain stable unchanged irrespective of age. Blood pressure, glycaemia, and cholesterolaemia did not correlate with aortic dimensions in this set of healthy individuals.

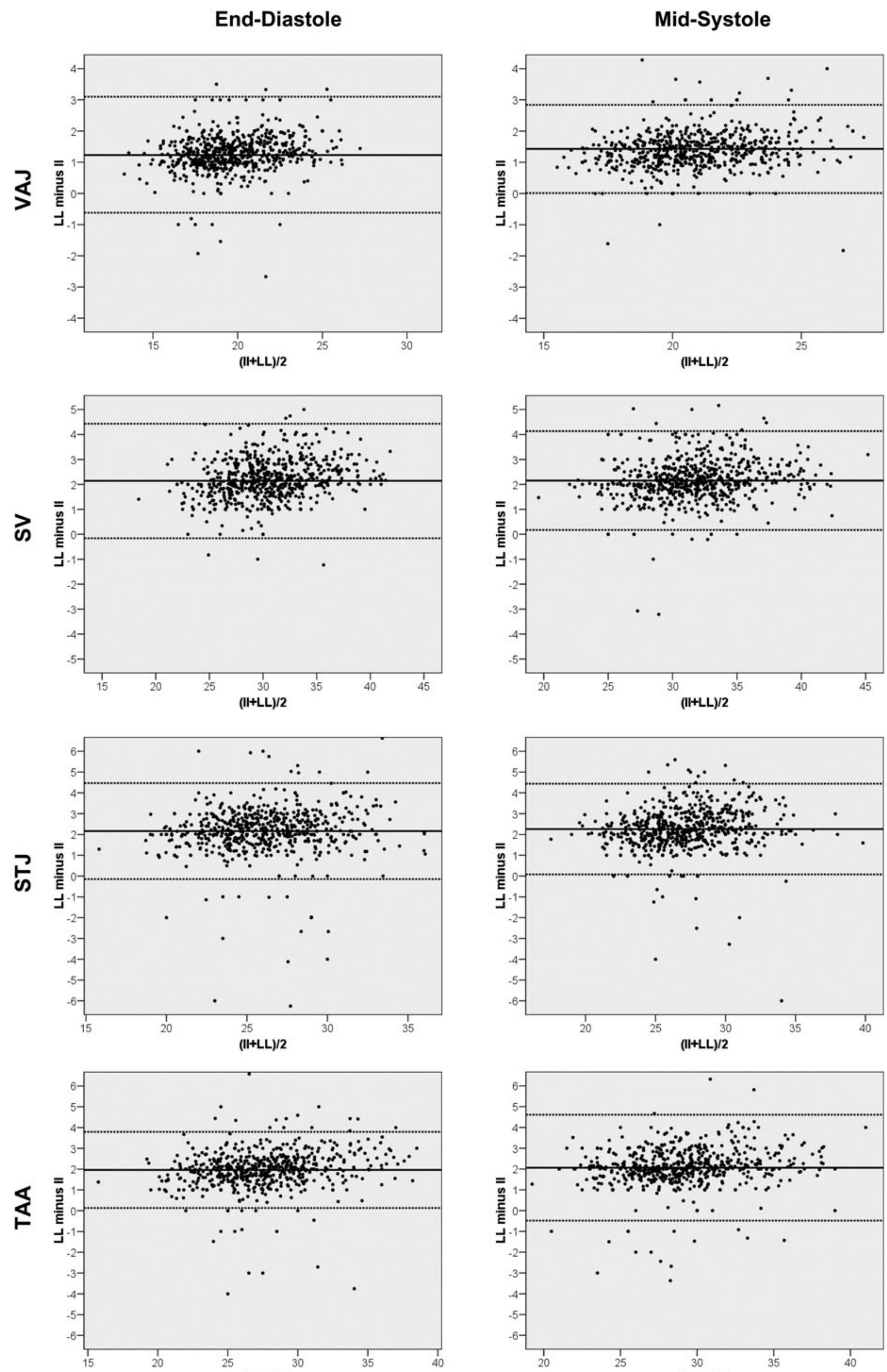

Figure 3 Bland–Altman plots of the agreement between the inner edge to inner edge (II) and the leading edge to leading edge (LL) conventions for proximal aorta measurements. The graphics are distributed in four rows representing measured levels: VAJ, SV, STJ, and TAA. End-diastolic measurements are represented in the left column. Mid-systolic dimensions are displayed on the column at the right. The solid line represents the mean difference. Dotted lines represent the 95% confidence limits of agreement.

Table 6 Differences between LL and II conventions for aortic measurements

Tested difference	BA mean difference LL − II ± SD	BA 95% IA of LL − II difference	PB constant coefficient (95% CI)	PB proportional coefficient (95% CI)
(LL) − (II) end-diastole				
VAJ (mm)	1.23 ± 0.95	−0.62 to 3.108	0.19 (−0.15 to 0.54)	1.04 (1.02 to 1.05)
SV (mm)	2.14 ± 1.17	−0.16 to 4.43	0.96 (0.57 to 1.35)	1.05 (1.04 to 1.07)
STJ (mm)	2.16 ± 1.18	−0.15 to 4.47	1.25 (0.72 to 1.76)	1.04 (1.02 to 1.06)
TAA (mm)	1.96 ± 0.93	0.13 to 3.79	0.89 (0.49 to 1.28)	1.05 (1.03 to 1.07)
(LL) − (II) mid-systole				
VAJ (mm)	1.43 ± 0.72	0.015 to 2.84	0.12 (−0.31 to 0.54)	1.05 (1.03 to 1.08)
SV (mm)	2.15 ± 1.01	0.17 to 4.13	0.60 (0.18 to 1.03)	1.03 (1.01 to 1.05)
STJ (mm)	2.26 ± 1.11	0.08 to 4.44	0.82 (0.30 to 1.33)	1.06 (1.03 to 1.08)
TAA (mm)	2.06 ± 1.30	−0.48 to 4.61	0.64 (0.20 to 1.06)	1.03 (1.02 to 1.05)

BA, Bland–Altman test; LL, leading edge to leading edge convention; II, inner edge to inner edge; SD, standard deviation; IA, interval of agreement; PB, Passing–Bablok regression test; CI, confidence interval.

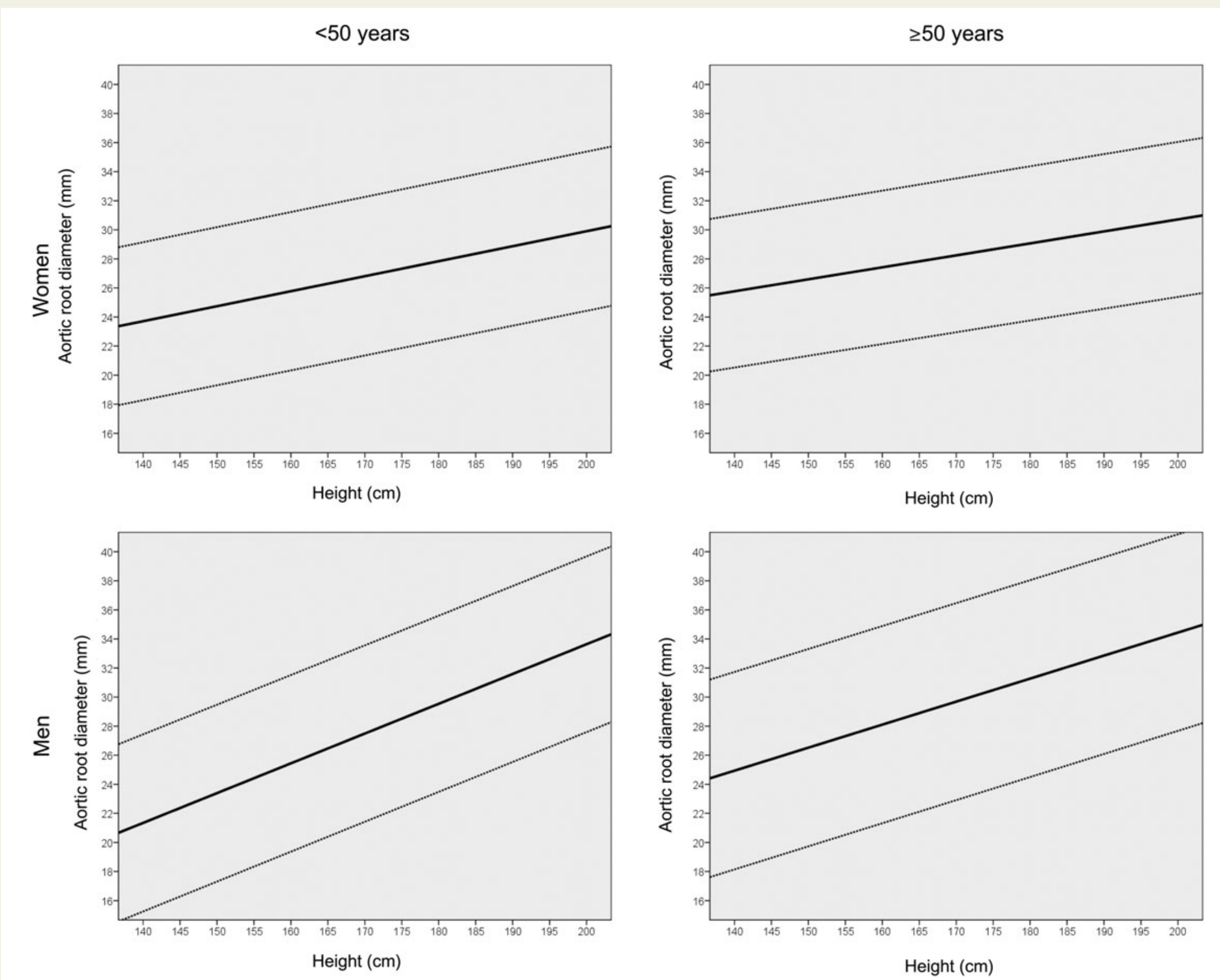

Figure 4 Nomograms of aortic root dimensions (SV level) according to different heights for both genders and two age groups (younger or older than 50 years). *X*-axis represents height in centimeters. *Y*-axis represents aortic root diameter in millimeters.

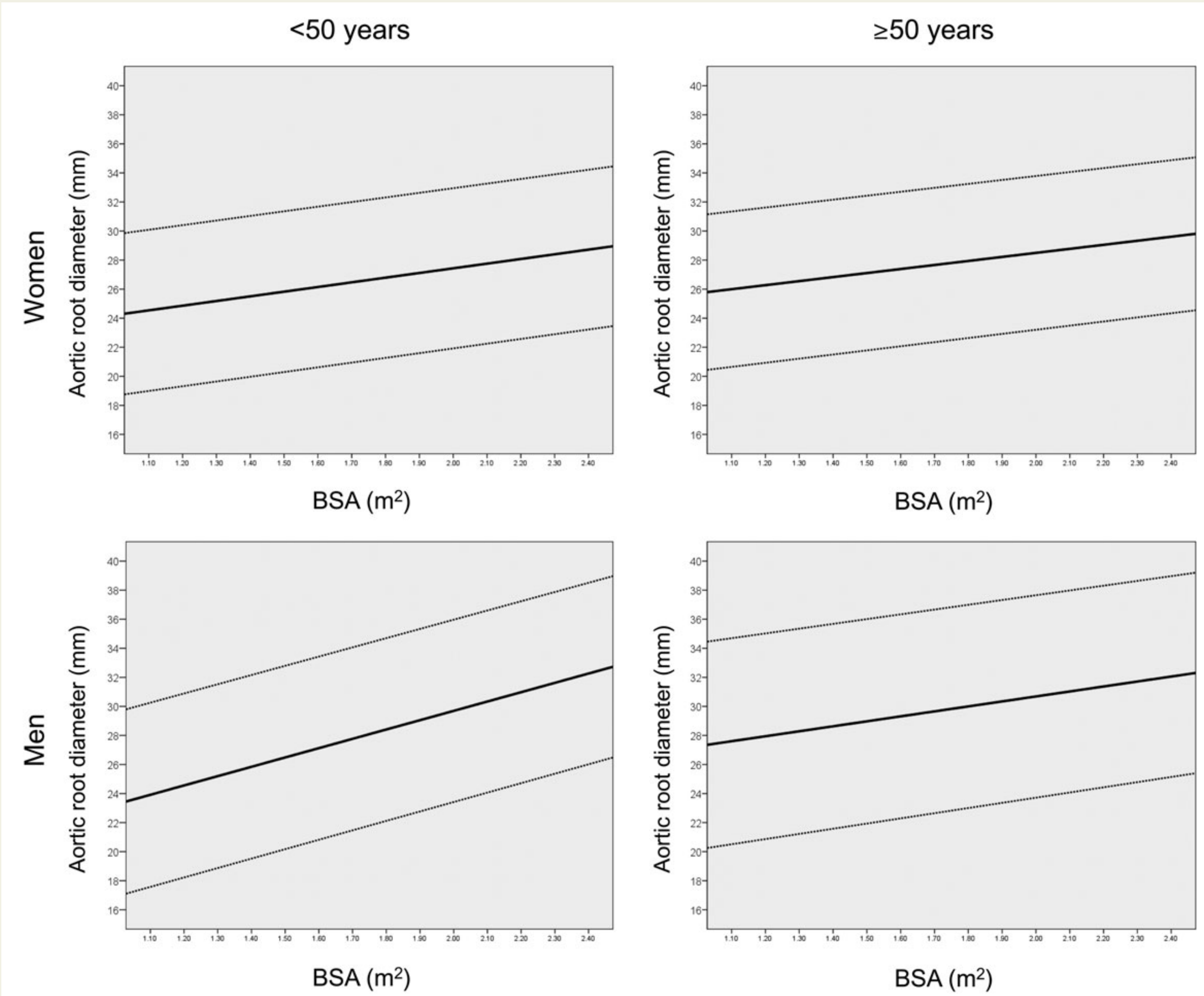

Figure 5 Nomograms of aortic root dimensions (SV level) according to different calculated body surface areas (BSA), for both genders and two age groups (younger or older than 50 years). *X*-axis represents BSA in square meters. *Y*-axis represents aortic root diameter in millimeters.

In contrast, each single measure of body size related to aortic diameters. Height, weight and waist circumference (and calculated indexes) were strongly correlated to each other. Hence, such predictors were exclusively considered one at a time when performing multivariable analysis to avoid multicollinearity.

Multiple linear regression analysis allowed building models for aortic size predictions taking into account age, gender, and either height or BSA. Notably, linear models considering age, gender, and body size barely explained around one-quarter of the total variance, as revealed by the adjusted coefficients of determination (between 0.259 and 0.301). Therefore, there may be wide biological variability in aortic dimensions not entirely explained by simple demographic and anthropometric variables. This is why, regression equations for prediction of aortic size (and derived nomograms) based only on these parameters should be interpreted with caution taking into account this limitation.

Differences between measuring conventions

As expected, the LL technique yielded greater mean diameters of the proximal aorta at all four measurement levels, confirmed by the convenient Bland–Altman tests of agreement and Passing–Bablok regression analysis. Differences between LL and II are due not only to spatial echo resolution but also due to the structures included in measurement, as the anterior aortic wall itself. The provided quantification of such deviation could be clinically valuable as both the LL and IL measurement conventions are used in clinical echocardiography, either for single measurements as for entire population studies. In addition, measurements were carried out in diastole following current chamber quantification guidelines,[4] as well as in systole when aortic wall stress is largest, following recommendations for paediatric and congenital heart disease echocardiography.[11]

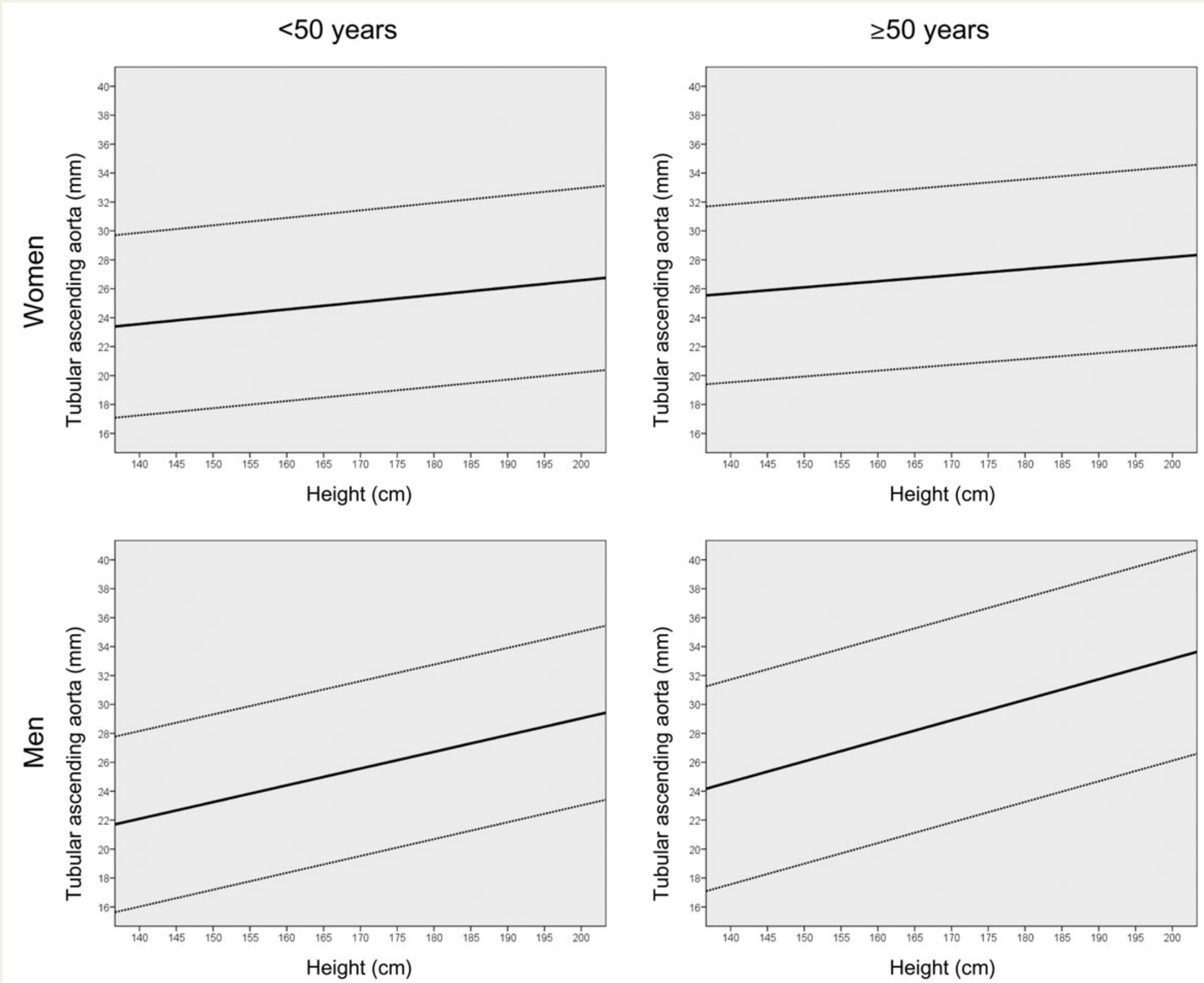

Figure 6 Nomograms of TAA diameters according to different heights for both genders and two age groups (younger or older than 50 years). *X*-axis represents height in centimeters. *Y*-axis represents TAA diameter in millimeters.

Comparison with previous studies

Our study confirmed and extended some previous studies on proximal aortic measurements.[6,12,13] However, previous studies were often limited by size, narrow age range of the participants, or obtained in patients with presumed normal findings. To date, the NORRE study comprises the largest prospective sample of normal volunteers not recruited from clinical practice. Candidates with doubtful clinical normalcy were excluded, having taken into account clinical history, cardiovascular examination, body size, and laboratory findings.[7]

Data for normal aortic measurements were collected from the beginning of 2D echocardiography, focused on aortic root diameters, which by then had been well characterized with M-mode technique.[3] The use of those relatively old 2D reference values of aortic root dimensions are customarily used in current recommendations.[2,4] An increase in the signal-to-noise ratio was recently achieved with the development of second harmonic imaging, resulting in better ultrasound visual assessment, but at the cost of a slight decrease in spatial resolution.[14] More recent studies have focused in the differences between LL and II conventions.[6,12,13] Our data compare favourably with those studies and confirm their findings in a prospective large healthy population, not only presenting normal ranges but also on aortic dimensions predictors.[6,12]

Normalization of aortic measurements and provision of *Z* scores requires refined statistical elaboration,[15] which is beyond the scope of this study. However, the data of this study could be useful in this regard.

Limitations

The NORRE study results come from a population of individuals of Caucasian ascend. Application to other populations might be flawed, as external validity is not fully warranted. Participants in the NORRE study were normal volunteers with pre-specified selection criteria, but the inclusion of patients with underlying subtle vascular disease (potentially affecting aortic dimensions) cannot be completely ruled out.

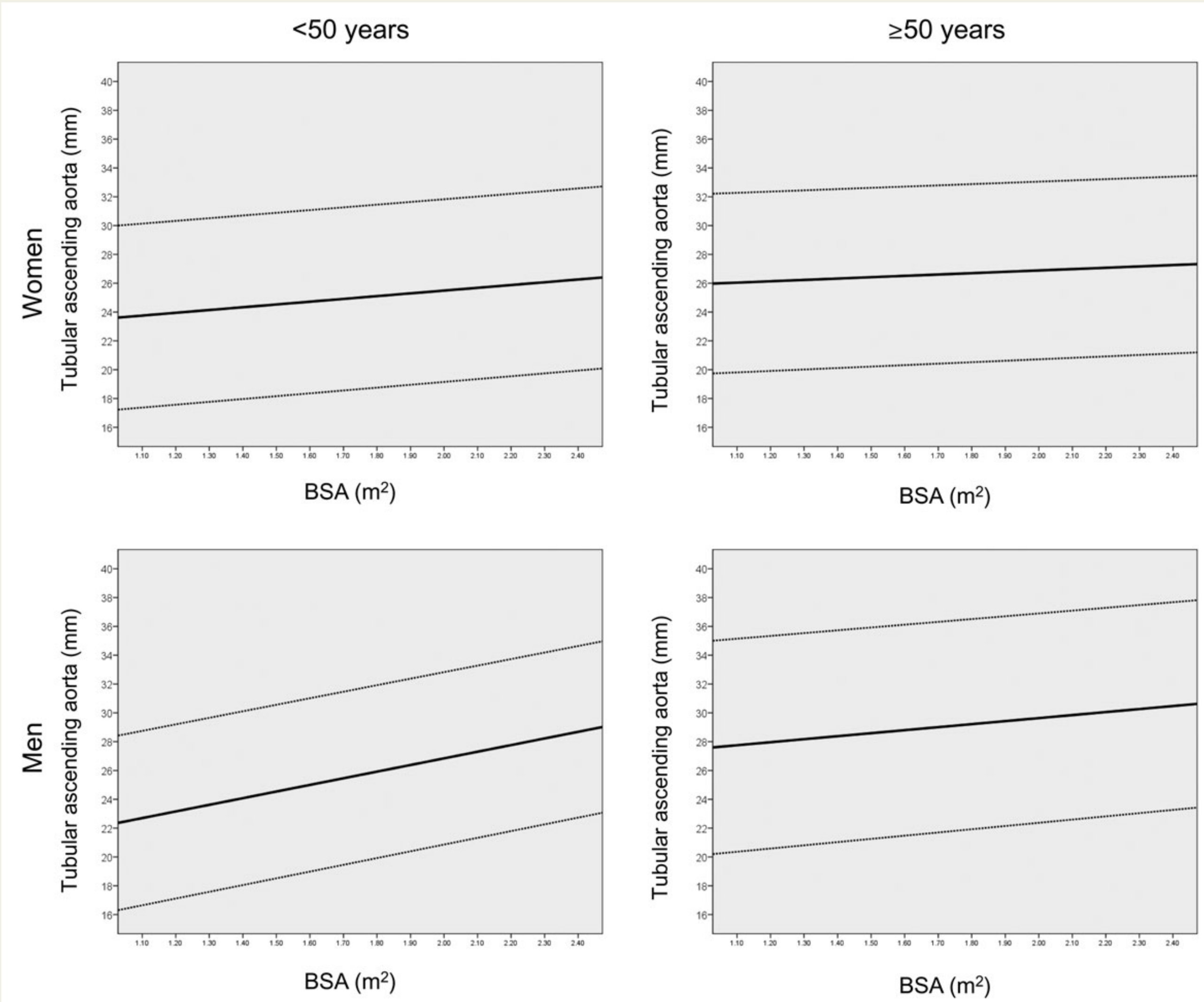

Figure 7 Nomograms of TAA diameters according to different calculated BSA for both genders and two age groups (younger or older than 50 years). *X*-axis represents BSA in square meters. *Y*-axis represents TAA diameter in millimeters.

Conclusion

The NORRE study yielded reference ranges for proximal aorta dimensions as assessed by transthoracic echocardiography, based on data of a large population of normal subjects of broad European origin. Normal reference values considering measurement method, time of heart cycle, and anatomical levels are provided. Gender, age, and body size need to be considered, as are major determinants of aortic dimensions.

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