ORIGINAL ARTICLE

Normal Values of Thoracic Aorta Dimensions by Echocardiography. The MATEAR (Measurement of Thoracic Aorta by Echocardiography in Argentina) Registry

Valores normales de aorta torácica por ecocardiografía. Registro MATEAR (Medición de Aorta Torácica por Ecocardiografía en Argentina)

MARÍA C. CARRERO[1], IVÁN CONSTANTIN[1], JUAN BENGER[1], FEDERICO M. ASCH[2], FEDERICO CINTORA[1], SILVIA MAKHOUL[1], SERGIO BARATTA[1], RODRIGO BAGNATI[1], IN REPRESENTATION OF THE MATEAR REGISTRY STUDY GROUP

ABSTRACT

Background: Differences in the thoracic aorta diameters have been found according to sex, age and body surface area. However, the results are very heterogeneous.
Objectives: The aim of this study was to establish the normal thoracic aortic diameters (AoD) by transthoracic echocardiography in our population and to analyze the influence of anthropometric, demographic and ethnic variables.
Methods: A national, prospective and multicenter registry was performed including 1,000 healthy adults (mean age: 38.3±12.7 years, 553 women, 56.7% of Caucasian origin and 38.3% Native Americans). Aortic measurements were made at 6 levels following current recommendations: aortic annulus, aortic sinuses, sinotubular junction, proximal ascending aorta, aortic arch and proximal descending aorta.
Results: The 95th percentile of all absolute AoD was below 3.80 cm; AoD indexed by height was 2.08 cm/m and 2.11 cm/m2 indexed by body surface area (BSA). The global analysis showed a positive and significant correlation of all AoD with BSA and height, as well as with age, except for the aortic annulus which did not change over time. In individuals with increased body mass index, BSA did not correlate with AoD. Women had lower AoD in all segments and in the aortic root, even after indexing it by height. Native American subjects had lower absolute and indexed AoD than Caucasian ones at all aortic levels ($p < 0.01$), except for the proximal descending aorta, which showed no significant differences.
Conclusions: Demographic, anthropometric and ethnic variables were significant determinants of aortic dimensions at all levels, so they must be taken into account for interpretation.

Key words: Aorta, Thoracic/Diagnostic Imaging - Echocardiography - Diagnostic Techniques, Cardiovascular - Argentina

RESUMEN

Introducción: Se han encontrado diferencias en los diámetros de la aorta torácica de acuerdo al sexo, la edad y la superficie corporal. Sin embargo, los resultados son muy heterogeneos.
Objetivos: Determinar los diámetros normales de la aorta (DAo) torácica por ecocardiograma transtorácico en nuestra población y analizar la influencia de las variables antropométricas, demográficas y étnicas en DAo.
Material y métodos: Se realizó un registro nacional, prospectivo y multicéntrico que incluyó 1000 adultos sanos (edad media: 38.3 ± 12.7 años, 553 mujeres, 56.7% de origen caucásico y 38.3% americanos nativos). Se realizaron mediciones aórticas siguiendo las recomendaciones actuales en 6 niveles: anillo, sinusal, unión sinotubular, ascendente proximal, cayado y descendente proximal.
Resultados: El percentilo 95 se encontró por debajo de los 3.80 cm para todos los DAo absolutos, 2.08 cm/m para los indexados por altura y 2.11 cm/m2 por superficie corporal (SC). El análisis global mostró correlación positiva y significativa entre todos los diáme-

Rev Argent Cardiol 2020;88:14-24. http://dx.doi.org/10.7775/rac.v88.i1.17194
SEE RELATED ARTICLE: Rev Argent Cardiol 2020:88:2-3. http://dx.doi.org/10.7775/rac.v88.i1.17275
SEE RELATED ARTICLE: Rev Argent Cardiol 2020:88:6-8. http://dx.doi.org/10.7775/rac.v88.i1.17053
Received: 10/12/2019 – *Accepted:* 22/01/2020

Address for reprints: María Celeste Carrero, registro.matear@gmail.com, Azcuénaga 980 - C1115AAD – Buenos Aires, Argentina. +54-11- 4961-6027.
This work received the 2019 Pedro Cossio Award

On behalf of the MATEAR Registry Study Group:
[1] Research Group of the "Oscar Orías" Echocardiography and Vascular Doppler Council of the Argentine Society of Cardiology, Buenos Aires, Argentina.
[2] Advisor to the Research Group of the"Oscar Orías" Echocardiography and Vascular Doppler Council of the Argentine Society of Cardiology. Staff at MedStar Health Research Institute and Georgetown University, Washington DC.
- Juan Celedonio Martinez , Emiliano Torres, Ivana Oliveri, Ma. Cecilia López, Emanuel González, Roger B.Ugarte, Jose F Cabral, Silvina Galetto, Lara Vozzi, Eugenia Beacon, Rosina Arbucci, Gabriel Scattini, Curcio Andrea, Jorge Klyver, Martin Ibarrola, Matías Forestier, Cristian M. Toldo, Gerardo C. Filippa, Ricardo S. Galdeano, Mauricio Priotti, Miguel Ayon, Matias Failo, Ma. Luz Fernandez Recalde, Graciela Rouss, Javier F Ventrici, Gerardo Masson, Cesar Alfredo Cadó, Antonio Provenzal, Susana B. Taboada, Federico Sosa, Julio Kramer, Silvia Barslund, Claudio Pereyra Sueldo, Alejandro Oria, Ezequiel Forte, Mariano Pipkin, Maldonado Pablo, Oscar A Vogelman, Guillermo López Soutric, Leonardo Schiavone, Carlos F. Manganiello, Damián E.Holownia, Karina Analía Ramos, María C. Carrero , Iván Constantin, Juan Benger , Federico M. Asch, Federico Cintora, Silvia Makhoul, Sergio Baratta y Rodrigo Bagnati.

tros aórticos, la SC y la altura, así como la edad con la excepción del anillo aórtico, que no presentó modificaciones con el paso del tiempo. En los individuos con índice de masa corporal aumentado, la SC no se correlacionó con los diámetros aórticos. Las mujeres presentaron menores DAo en todos los segmentos y en la raíz aórtica, aun luego de indexarla por altura. Los americanos nativos presentaron menores diámetros aórticos absolutos e indexados que los caucásicos en todos los niveles aórticos ($p<0.01$), exceptuando la aorta descendente proximal, que no mostró diferencias significativas.

Conclusiones: Las variables demográficas, antropométricas y étnicas resultaron determinantes significativos de las dimensiones aórticas en todos sus niveles, por lo que deben tenerse en cuenta para su interpretación.

Palabras clave: Aorta torácica/diagnóstico por imagen - Ecocardiografía - Técnicas de Diagnóstico Cardiovasculares - Argentina

Abbreviations

ACI	AoD Aortic diameters	**LV**	Left ventricle
BMI	Body mass index	**LVEF**	Left ventricular ejection fraction
BSA	Body surface area	**MBP**	Mean blood pressure
DBP	Diastolic blood pressure	**RWT**	Relative wall thickness
D	Diameters	**SBP**	Systolic blood pressure
LAVi	Left atrial volume indexed by body surface area	**TTE**	Transthoracic echocardiography

INTRODUCTION

Aortic dilatation is associated with the presence and severity of aortic regurgitation and the risk of acute aortic syndromes (1–3). Its early diagnosis allows patient monitoring to determine the optimal time of treatment and prevent its potential complications (4, 5) On the other hand, its overdiagnosis involves alterations in patients' quality of life, as well as increased health costs. Therefore, it is of great importance to know the normal values of each aortic segment and for each technique to accurately establish when it is dilated. (2, 6, 7)

Transthoracic echocardiography (TTE) is the main method for the initial evaluation of the thoracic aorta and, in most patients, allows measurement of all its segments. Several studies evaluated the normal values of the aortic root with TTE that served for the publication of nomograms. (6, 8, 9) However, the methodology used for the measurement of the aorta is controversial and many data considered as normal limits have been obtained with disused techniques, small number of patients and with little representation of teenagers and older adults. (6) Additionally, there is almost no data on the normal diameters of the aortic arch and the proximal descending aorta.

Age, height, BSA and gender differences of aortic root diameters have been published, indicating that anthropometric and demographic factors are of vital importance for their interpretation. (8–11) However, there is still no agreement on some issues, as whether the variations of aortic diameters in relation to gender are due to differences in BSA or to a different growth rate between men and women influenced by hormonal factors, or whether indexing by BSA underestimates the degree of aortic dilatation in obese subjects. In fact, most studies exclude overweight and obese patients or they are underrepresented in few studies, even when a large part of the current population suffers from this disease. (9, 10) More importantly, published data have included population with anthropometric, demographic and ethnic characteristics different from that of our country; hence, the influence of these variables is unknown. We might then question whether the values currently published as upper normal limits of aortic diameters (AoD) apply to the Argentine population.

The National Registry of Thoracic Aorta Measurement by Echocardiography in Argentina (MATEAR) was designed to prospectively assess, following current methodological recommendations, (12) the normal diameters (D) and the cut-off point of each thoracic AoD segment in a cohort of healthy Argentine patients, and to determine their correlation with age, gender, anthropometric variables and ethnicity.

METHODS

The MATEAR Registry was a prospective, observational, multicenter registry, originated from the Echocardiography and Vascular Doppler Council of the Argentine Society of Cardiology, developed from February 2018 to June 2019. This registry included consecutive healthy patients above 18 years of age undergoing a TTE by medical indication in 45 centers from 16 provinces of the Argentine Republic. Patients with pathologies that could affect AoD or hinder their correct measurement were excluded (exclusion criteria in Supplementary Material, Table 1). Demographic and anthropometric variables, blood pressure and cardiovascular history, both personal and of first-degree family members, as well as clinical variables of relevance were collected for each patient. The data was loaded through a web platform with a single password per researcher.

Aortic measurements

The operators were trained through an explanatory video to unify measurement techniques according to current international recommendations. Each patient underwent a conventional and complete TTE to rule out unknown cardiovascular diseases.

Measurements were made according to current recommendations. (7, 12) Measurements of the aortic annulus (at the insertion of the aortic leaflets), Valsalva sinuses, sinotubular junction, and proximal tubular (or ascending) portion (at 1 cm from the sinotubular junction or where the largest D of the tubular portion was established) were performed in left parasternal long axis view. The aortic annulus was measured from internal edge to internal edge in mid-systole and the rest of the measurements were performed from upper edge to upper edge at end diastole. The proximal aortic arch, between the origin of the brachiocephalic trunk and the common carotid artery, was measured from superior border to superior border, and the proximal descending aorta, immediately after the origin of the left subclavian artery, from the left border to the right border, including only the left border. Measurements of the last two segments were performed in suprasternal view at end diastole.

Statistical analysis

The values included in the 5th-95th percentile were considered as reference values. Discrete variables are expressed as proportions. Continuous variables with normal distribution are expressed as mean and standard deviation, while those with non-normal distribution are expressed as median and interquartile range. Student's t-test was used to compare continuous variables with parametric distribution.

A simple linear regression analysis was performed between dependent variables (aortic diameters at each level) and anthropometric variables such as age, BSA, height and body mass index (BMI), using Pearson's minimum square test to obtain coefficients of determination (R) and prediction intervals (95%). The analysis was repeated stratifying the population according to gender, age and ethnicity. A multiple regression analysis was performed to assess the relative influence of the predictor variables in AoD, using variables that showed significant association in the simple regression analysis. STATA 13 software package was used for statistical analysis. A two-tailed p-value <0.05 was considered significant.

Ethical considerations

The registry was approved by the bioethics committee of the Argentine Society of Cardiology and an informed consent was obtained from each participant.

RESULTS

The study included 1,000 apparently healthy individuals (mean age: 38.3±12.7 years and 553 (55.3%) women). Table 1 shows the anthropometric variables and the complete global and differentiated by gender echocardiographic values.

As expected, men showed significantly greater anthropometric dimensions, left ventricular dimension and thickness values. Moreover, men had higher systolic, diastolic and mean blood pressure values, but within the normal range. The observed differences between genders can be seen in Table 1. Body surface area was calculated by the Mosteller method and by the Dubois formula, without significant differences between the two methods (1.85 m2±0.24 by the Mosteller method vs. 1.84 m2±0.26 by the Dubois method, p=NS), so for subsequent calculations the Mosteller result was taken.

Men had increased BMI more frequently than women [310 (69.5%) men with BMI> 25, vs. 260 (47%) women, p<0.0001].

The reproducibility of aortic dimension measurements was good, with an intra-class correlation coefficient (ICC) of 0.77-0.95 for intraobserver variability and between 0.68-0.92 for interobserver variability.

Aortic diameters by echocardiography and body size

Table 2 provides the descriptive statistics of absolute aortic diameters at the six levels analyzed for both genders. Aortic diameters were significantly higher in men at the six levels analyzed. The 95th percentile of all absolute aortic diameters was below 3.80 cm. A

Table 1. Anthropometric and echocardiographic characteristics according to gender.

	Total (n=1,000)	Female (n=553)	Male (n=447)	P value
Age, years	38.3 ± 12.9	39.1 ± 13.4	37.2 ± 12.3	0.02
Weight (kg)	74.4 ± 16.8	67.3 ± 14.5	83.2 ± 15.3	<0.0001
Height (cm)	167.4± 9.5	161.5 ± 6.0	174.6 ± 7.7	<0.0001
BSA - Dubois (m^2)	1.85 ± 0.24	1.73 ± 0.19	2.00 ± 0.21	<0.0001
BMI (kg/m2)	26.4 ± 5.07	25.8 ± 5.4	27.2 ± 7.4	<0.0001
SBP (mmHg)	113.3 ± 7.1	110.6 ± 9.1	114.6 ± 7.4	<0.0001
DBP (mmHg)	71.7 ± 7.8	70.2 ± 8.1	73.7 ± 7.1	<0.0001
MBP (mmHg)	85.5 ± 7.3	83.5 ± 7.4	88.8 ± 7.1	<0.0001
LVEF, %	64.8 ± 5.0	65.3 ± 4.9	64.1 ± 5.1	0.0003
LAVi (ml/m^2)	23.5 ± 6.8	23.4 ± 6.4	23.8 ± 7.2	NS
LV Mass indexed by BSA (g/m^2)	70.6 ± 13.2	67.1 ± 13.0	75.0 ± 13.1	<0.0001
RWT	0.36 ± 0.06	0.36 ± 0.06	0.36 ± 0.07	NS
E/A RATIO	1.47 ± 0.4	1.47 ± 0.48	1.45 ± 0.5	NS
LVEDV (cm)	4.6 ± 0.4	4.4 ± 0.38	4.8 ± 0.39	<0.0001
LVESV(cm)	2.81 ± 0.4	2.68 ± 0.36	2.97 ± 0.39	<0.0001
Septal thickness (cm)	0.89 ± 0.12	0.86 ± 0.12	0.94 ± 0.11	<0.0001
Posterior wall thickness (cm)	0.82 ± 0.12	0.79 ± 0.12	0.86 ± 0.12	<0.0001

BSA: Body surface area. BMI: Body mass index. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. MBP: Mean blood pressure. LVEF: Left ventricular ejection fraction. LAVi: Left atrial volume indexed by body surface area. RWT: Relative wall thickness. LVEDV: Left ventricular end-diastolic volume. LVESV: Left ventricular end-systolic volume. Results are expressed as mean ± SD.

positive correlation was observed between the six aortic diameters and anthropometric variables (height and BSA). Table 3 provides the aortic diameters at the six levels indexed by height for both genders. Women had lower aortic diameters indexed by height for the aortic annulus, Valsalva sinuses and sinotubular junction. No significant differences were observed between both genders in the ascending aorta, aortic arch and proximal descending aorta after indexing by height. The 95th percentile of all aortic diameters indexed by height was below 2.08 cm/m.

Regarding the increase in AoD with BSA, a linear and significant correlation was observed at the 6 aortic levels for patients with normal BMI. However, the strength of the correlation between AoD and BSA decreases with the increase in BMI, because BSA is no longer representative of the actual body size. Figure 1 shows the decrease in the correlation between sinus diameter and BSA as BMI increases. In patients with BMI >35 kg/m2 the correlation between diameters and BSA ceases to be significant at the level of Valsalva sinuses, sinotubular junction, proximal ascending aorta, aortic arch and descending aorta.

Therefore, for the calculation of AoD indexed by BSA, only the subgroup of patients with normal BMI was taken into account. The group of 430 patients with BMI under 25 kg/m2 [293 (68%) women] had BSA: 1.68±0.16m2, weight: 61.1±9.28 kg, height: 165.8±8.7 cm and BMI: 22.15±1.98 kg/m2. Table 4 shows the AoD at the six levels indexed by BSA for both genders in the group with normal BMI. Women had higher diameters indexed by BSA at the six levels analyzed. The 95th percentile of all AoD indexed by BSA was below 2.11 cm/m2.

Aortic dimensions and age

The AoD correlated significantly with age, except at the aortic annulus level. In both men and women there is a progressive and consistent increase in the absolute dimensions of the ascending aorta with increasing age, as a continuous variable. Moreover, an increase in the diameters of the aortic root, ascending aorta, aortic arch and descending aorta is observed for each gender and age group, as defined by Roman et al. (6) At each level, with the exception of the annulus, it was seen that age group 2 (26 to 40 years old) and 3 (over 40 years old) presented in both men and women aortic dimensions significantly larger than in younger subjects (Supplemental Figure 1).

The analysis by decades also shows a progressive increase in AoD every 10 years, except for the annulus that remains stable, as can be seen in Supplemental Figure 2. The normal ratio of the different aortic segments with respect to the aortic annulus is reported in Supplemental Figure 3.

Aortic dimensions and ethic origin

In relation to ethnic origin, the majority of patients included presented Iberian origin in 547 (55%) cases and Native American origin in 406 (41%).

Patients of American origin compared with those of Iberian origin present with different absolute diameters: significantly lower in the aortic annulus, Valsalva sinuses, sinotubular junction and proximal ascending aorta, similar in the aortic arch and greater in the proximal descending aorta (Table 5). On the other hand, when indexing by BSA, it was observed that the diameters in Iberian patients were greater at all levels, except for the descending aorta (aortic annulus 1.12 cm vs. 1.08 cm, aortic sinuses 1.66 cm vs. 1.48 cm, sinotubular junction 1.44 cm vs. 1.35 cm, proximal ascending aorta 1.54 cm vs. 1.43 cm, aortic arch 1.30 cm vs. 1.26 cm, and proximal descending aorta 1.04 cm vs. 1.12 cm, p<0.0001 in all cases). Regarding

Table 2. Absolute aortic diameters at the 6 levels measured, for both genders.

	TOTAL (N=1000) Absolute diameter (cm) Mean ±SD (P5-P95)	FEMALE (N=553) Absolute diameter (cm) Mean ±SD (P5-P95)	MALE (N=447) Absolute diameter (cm) Mean ±SD (P5-P95)	P value
Aortic annulus (cm)	2.02 ± 0.22 (1.70 - 2.40)	1.93 ± 0.18 (1.62 - 2.20)	2.13 ± 0.20 (1.80 - 2.50)	<0.0001
Valsalva sinuses (cm)	2.91 ± 0.40 (2.30 - 3.60)	2.76 ± 0.35 (2.20 – 3.40)	3.10 ± 0.39 (2.50 - 3.80)	<0.0001
Sinotubular junction(cm)	2.57 ± 0.37 (2.00 - 3.20)	2.44 ± 0.32 (1.96 - 3.00)	2.73 ± 0.38 (2.10 – 3.40)	<0.0001
Proximal ascending aorta (cm)	2.74 ± 0.38 (2.20 - 3.40)	2.64 ± 0.35 (2.10 - 3.30)	2.86 ± 0.37 (2.30 – 3.50)	<0.0001
Aortic arch (cm)	2.35 ± 0.35 (1.80 - 2.84)	2.27 ± 0.32 (1.80 - 2.80)	2.45 ± 0.36 (1.90 – 3.00)	<0.0001
Proximal descending aorta (cm)	1.97 ± 0.34 (1.50 – 2.60)	1.91 ± 0.32 (1.45 – 2.40)	2.05 ± 0.34 (1.60 – 2.70)	<0.0001

Women presented significantly smaller absolute aortic diameters at the 6 levels. All 95th percentiles were below 3.80 cm for the 6 levels in the total population. SD: Standard deviation.

Table 3. Aortic diameters indexed by height at the 6 levels, for both genders.

	TOTAL (N=1000) Diameter indexed by height (cm/m) Mean ±SD (P5-P95)	FEMALE (N=553) Diameter indexed by height (cm/m) Mean ±SD (P5-P95)	MALE (N=447) Diameter indexed by height (cm/m) Mean ±SD (P5-P95)	P value
Aortic annulus (cm/m)	1.21 ± 0.11 (1.04- 1.39)	1.19 ± 0.11 (1.01- 1.39)	1.22 ± 0.11 (1.05- 1.38)	0.001
Valsalva sinuses(cm/m)	1.74 ± 0.22 (1.39 – 2.11)	1.71 ± 0.21 (1.37 – 2.08)	1.77 ± 0.21 (1.41 – 2.11)	<0.0001
Sinotubular junction (cm/m)	1.54 ± 0.20 (1.21 – 1.89)	1.51 ± 0.20 (1.19 – 1.85)	1.56 ± 0.21 (1.26 – 1.94)	0.0002
Proximal ascending aorta (cm/m)	1.64 ± 0.21 (1.32- 2.01)	1.63 ± 0.22 (1.32- 2.00)	1.64 ± 0.21 (1.33- 2.02)	NS
Aortic arch (cm/m)	1.39 ± 0.25 (1.08 – 1.75)	1.39 ± 0.25 (1.08 – 1.73)	1.39 ± 0.25 (1.07 – 1.77)	NS
Proximal descending aorta (cm/m)	1.17 ± 0.24 (0.86 – 1.52)	1.17 ± 0.23 (0.87 – 1.52)	1.16 ± 0.24 (0.86 – 1.53)	NS

SD Standard deviation

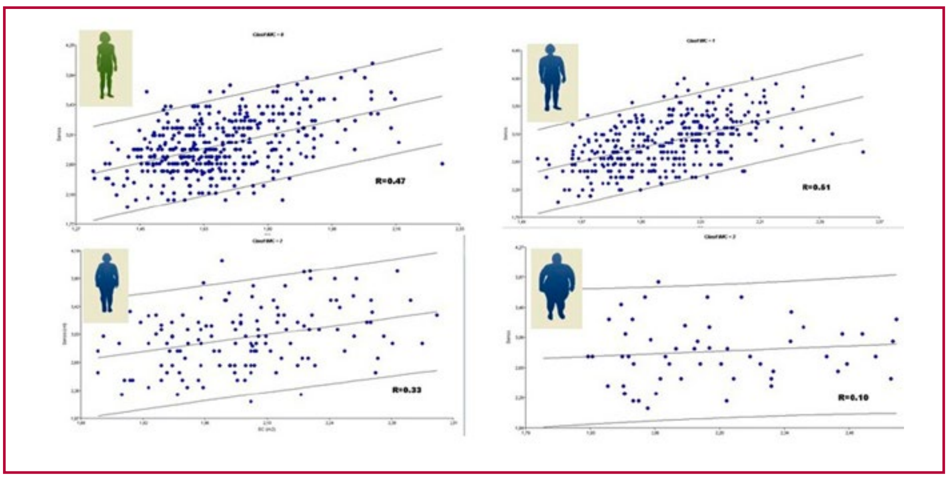


Fig. 1. Linear correlation between the Valsalva sinus diameters and body surface area, according to body mass index. From left to right and from top to bottom the correlation is shown in patients with normal body mass index (BMI), with overweight, obesity and grade II obesity or higher. It is observed how, as the BMI increases, the correlation between the sinus diameter and the body surface area decreases.

the indexation by height, it was observed that patients of American origin presented with smaller diameters in Valsalva sinuses, sinotubular junction and proximal ascending aorta, similar in aortic arch and larger in the proximal descending aorta than those of Iberian origin (Table 2 of Supplementary Material)

Predictors of aortic dimensions

In the univariate analysis, AoD correlated significantly with age, height and BSA. Two models were made for multivariate analysis, one using BSA as anthropometric variable and another using height for each aortic dimension.

Table 5 reports the results of both multiple linear regression models, the subsequent analyses and the coefficients for each linear equation at the level of the Valsalva sinuses. The analysis of both multiple linear regression models was performed for all patients and for the group with BMI <25 kg/m2. It was seen that in patients with increased BMI, BSA loses predictive value of aortic dimensions in the Valsalva sinuses, while height is not affected by BMI (adjusted R2 of the model with BSA in total patients: 0.07 vs. adjusted R2 of the model with BSA in patients with BMI <25 kg/m2: 0.27). On the other hand, in patients of Iberian origin, the multiple linear regression coefficient of the height model is greater than in patients of Native American origin.

DISCUSSION

The MATEAR registry provides the first national scientific evidence of normal thoracic AoD measured by echocardiography. These findings are of the utmost relevance, since they allow to determine, based on

Table 4. BSA indexed aortic diameters at the 6 levels for female and male patients.

	TOTAL (N=430) Diameter indexed by BS (cm/m^2) Mean ±SD (P5-P95))	FEMALE (N=293) Diameter indexed by BSA (cm/m^2) Mean ±SD (P5-P95)	MALE (N=137) Diameter indexed by BSA (cm/m^2) Mean ±SD (P5-P95)	P value
Aortic annulus (cm/m^2)	1.16 ± 0.12 (0.98 – 1.35)	1.18 ± 0.11 (0.99 – 1.36)	1.13 ± 0.12 (0.95 – 1.34)	<0.0001
Valsalva sinuses (cm/m^2)	1.71± 0.21 (1.36 – 2.04)	1.72± 0.21 (1.38 – 2.08)	1.67± 0.20 (1.31 – 1.98)	0.008
Sinotubular junction (cm/m^2)	1.50 ± 0.20 (1.17 – 1.83)	1.51 ± 0.20 (1.18 – 1.83)	1.46 ± 0.19 (1.16 – 1.83)	0.01
Proximal ascending aorta (cm/m^2)	1.58± 0.21 (1.26 – 1.95)	1.61± 0.20 (1.27 – 1.96)	1.53 ± 0.20 (1.21 – 1.88)	0.0002
Aortic arch (cm/m^2)	1.35 ± 0.21 (1.03 – 1.72)	1.38± 0.20 (1.07 – 1.72)	1.27 ± 0.20 (0.98 – 1.64)	<0.0001
Proximal descending aorta (cm/m^2)	1.11± 0.20 (0.83 – 1.47)	1.13± 0.18 (0.85 – 1.44)	1.07± 0.21 (0.79 – 1.54)	0.002

Women presented lower aortic diameters indexed by height in the aortic annulus, Valsalva sinuses and sinotubular junction. No significant differences were observed after indexing by height in the proximal ascending aorta, aortic arch, or proximal descending aorta. Women had greater aortic diameters indexed by body surface at the 6 levels. SD: Standard deviation.

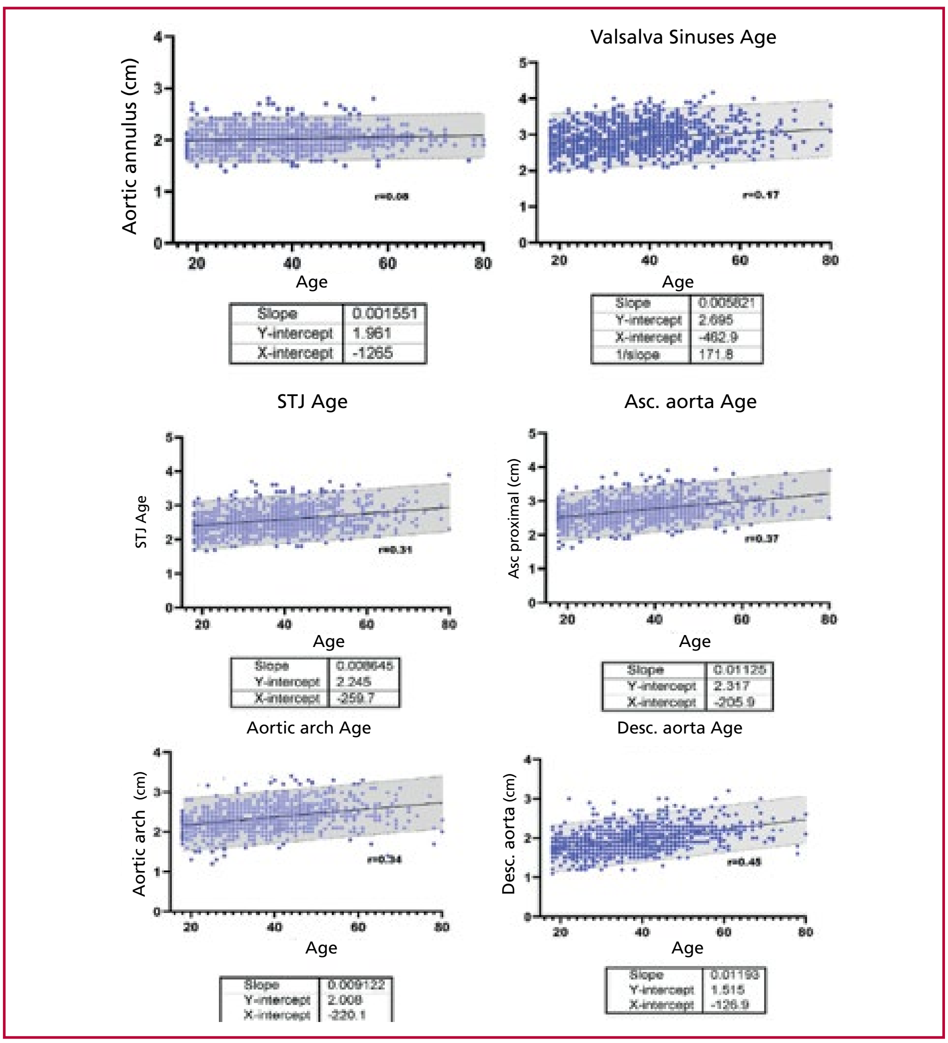


Fig. 2. Correlations between aortic diameters and age. Aortic diameters significantly increase with age, except at the level of the aortic annulus, which remains stable. STJ: Sinus tubular junction. Asc: Ascending. Desc: Descending.

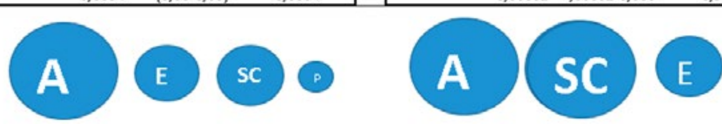
Table 5. Absolute aortic diameters at the 6 levels for patients of American and Iberian origin.

	Americans (N=406) Absolute diameter (cm) Mean ±SD (P5-P95)	Iberian (N=547) Absolute diameter (cm) Mean ±SD (P5-P95)	P value
Aortic annulus (cm)	2.00 ± 0.20	2.03 ± 0.23	<0.008
	(1.70 - 2.30)	(1.70 - 2.40)	
Valsalva sinuses(cm)	2.74 ± 0.37	3.02 ± 0.38	<0.0001
	(2.20 – 3.40)	(2.40 - 3.70)	
Sinotubular junction (cm)	2.50 ± 0.38	2.62 ± 0.37	<0.0001
	(2.00 - 3.20)	(2.00 - 3.20)	
Proximal ascending aorta (cm)	2.65 ± 0.35	2.81 ± 0.39	<0.0001
	(2.11 - 3.30)	(2.20 - 3.40)	
Aortic arch (cm)	2.33 ± 0.33	2.37 ± 0.36	NS
	(1.80 - 2.80)	(1.86 – 3.00)	
Proximal descending aorta (cm)	2.08 ± 0.33	1.90 ± 0.32	<0.0001
	(1.60 – 2.70)	(1.41 – 2.50)	

Patients of American origin have absolute diameters different from those of Iberian origin: lower in the aortic annulus, Valsalva sinuses, sinotubular junction and proximal ascending aorta, similar in the aortic arch and greater in the proximal descending aorta.

Table 6. Multiple linear regression models to determine predictors of aortic dimensions at the Valsalva sinus level. Models of both origins; on the left, in the general population and on the right, in the population with body mass index (BMI) <25. It is observed that in patients with increased BMI, body surface area loses predictive value of aortic dimensions, while height is not affected by BMI. In patients of Iberian origin, the height model has a higher R2 regression coefficient than in the Native American population. R2 represents the proportion of the total variability of the evaluated aortic diameter that is explained by the variables included in the model.

	Valsalva sinuses (cm) in the total population				Valsalva sinuses in BMI<25			
	Adjusted R2	Est.	95% CI B	p	Adjusted R2	Est.	95% CI B	p
HEIGHT MODEL	**0,26**				**0,27**			
Constant		-0,88	(-1,29 - -0,47)	<0,001		-0,76	(-1,38 - -0,15)	0,0154
Age (years)		0,01	(0,01-6,54)	<0,0001		0,01	(0,0004-0,01)	<0,0001
Height (cm)		0,02	(0,02-0,02)	<0,0001		0,02	(0,02-0,02)	<0,0001
MAP (mmHg)		0,0004	(0,0002-0,01)	0,0008		0,00007	),00003-0,004	0,71
BSA MODEL	**0,17**				**0,27**			
Constant		1,33	(1,90 - 2,42)	<0,0001		0,85	(0,46 - 1,24)	<0,0001
Age (years)		0,0003	(0,0002- 0,01)	<0,0001		0,01	(0,004- 0,01)	<0,0001
BSA (m^2)		0,56	(0,46- 0,67)	<0,0001		1,06	(0,86-1,25)	<0,0001
MAP (mmHg)		0,0004	(0,06-0,36)	0,0034		0,00001	,00001-0,000	0,94



	Valsalva sinuses (cm) in Iberian origin				Valsalva sinuses in American origin			
	Adjusted R2	Est.	95% CI B	p	Adjusted R2	Est.	95% CI B	p
HEIGHT MODEL	**0,36**				**0,22**			
Constant		-0,82	(-1,29 - -0,35)	0,0007		-0,46	(-1,58 - -0,66)	0,42
Age (years)		0,01	(0,01-0,01)	<0,0001		0,01	(0,0002-0,01)	0,0007
Height (cm)		0,02	(0,02-0,02)	<0,0001		0,02	(0,01-0,02)	<0,0001

local results, the normal upper limits of aortic annulus, Valsalva sinuses, sinotubular junction, proximal ascending aorta, aortic arch and descending aorta dimensions. Consequently, aortic dilatation can be detected early, allowing close monitoring of patients at risk of complications.

The population of the MATEAR registry is representative of the Argentine population in terms of age, BSA, height and weight for both genders. (13) We also believe that the inclusion in the registry of overweight and obese patients present in more than 60% of the population is a strength of the study, since it adds external validity (13). In this regard, the only work of normal AoD values that also included obese patients within its population was that of Campens et al. (9) with less than 10% of obese participants. However, in this work they did not report an analysis of the effect of obesity on the correlation between AoD and BSA. Given that our work group believed, according to previous studies, that the impact of the spurious increase in body size on BSA indexation should be analyzed, it was decided to include patients with BMI >25. To our knowledge, the MATEAR Registry is the first study that reports the relevance of taking into account BMI to avoid underdiagnosis of aortic dilatation in patients who are overweight/obese. In this population we recommend the use of indexation by height, since BSA in obese patients increases disproportionately and its correlation with AoD is lower.

Recent echocardiography and computed tomography studies report AoD indexing by height. (10, 14) In the NORRE European multicenter study, no gender differences were found in the AoD of the ascending aorta, aortic arch and descending aorta indexed by height. However, the aortic root presented larger diameters indexed by height in men, which would seem to suggest a behavior different of the aortic root with respect to the rest of the aortic segments in relation to gender.

On the other hand, regarding ethnical origin and its influence on aortic dimensions, some works have commented on the influence of ethnicity in AoD. (15, 16) However, published studies did not include different ethnical origins as a predictor variable of AoD, even though there are anthropometric and phenotypic differences between them. Our study provides information about the relevance of considering ethnicity to determine the normal AoD in each patient.

It is important to highlight that although predictor variables of AoD were detected in our population, the regression model only explains 36% of the total variability observed. These findings are compatible with those of the main published studies. (8) Therefore, when analyzing biological variables, it should not be forgotten that there are unmeasured aspects that influence the analyzed results.

Limitations

A limitation of the study was the difficulty to include patients older than 65 years who did not have exclusion criteria, mainly arterial hypertension and/or cardiovascular risk factors. This limitation, which is also present in most studies similar to ours, should be contemplated, as the applicability of our results should be performed in patients with similar characteristics.

Future directions

Our group is currently carrying out the development of the automatic calculation of the Z score for each of the aortic segments studied, in order to facilitate the interpretation of the results. In this way, entering height, weight, age, gender and aortic dimension, the Z score may be known and aortic dilatation can be diagnosed when the result is greater than 2.

On the other hand, a national multicenter corporate registry is proposed for the measurement of normal thoracic aorta values by computed tomography and cardiac magnetic resonance imaging in the years 2020-2021.

CONCLUSIONS

The results of this study, pioneer at a national level, show that AoD correlate with anthropometric and demographic variables. The BMI should be taken into account, since in obese individuals the correlation between AoD and BSA is lost. In that subgroup, indexing by height is recommended.

In addition, women had lower AoD due to lower height and BSA. In the aortic root, women's AoD were lower, even after indexing by height.

On the other hand, AoD increased with age except for the annulus. According to our findings, patients' ethnicity should be considered, since patients with Native American origin had lower absolute and indexed by BSA AoD at the aortic annulus, aortic sinuses, sinotubular junction and proximal ascending aorta than those of Iberian origin.

These findings allow obtaining precise cut-off points and national nomograms in adult patients in order to diagnose aortic dilatation, taking into account body size, age, gender and ethnical origin.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material)

Acknowledgements

We thank the patients who agreed to participate in the study and the researchers of the MATEAR Registry, selflessly and voluntarily committed to the development of independent and quality scientific material in Argentina.

To our families for understanding that being an independent researcher in Argentina implies work and commitment without any remuneration other than the satisfaction of the work accomplished.

REFERENCES

1. Roman MJ, Devereux RB, Niles NW, Hochreiter C, Kligfield P, Sato N, et al. Aortic root dilatation as a cause of isolated, severe aortic regurgitation. Prevalence, clinical and echocardiographic patterns, and relation to left ventricular hypertrophy and function. Ann Intern Med 1987;106:800-7. 10.7326/0003-4819-106-6-800

2. Asch FM, Yuriditsky E, Prakash SK, Roman MJ, Weinsaft JW, Weissman G, et al. The Need for Standardized Methods for Measuring the Aorta: Multimodality Core Lab Experience From the GenTAC Registry. JACC Cardiovasc Imaging 2016;9:219-26. 10.1016/j.jcmg.2015.06.023

3. American College of C, American Heart Association Task Force on Practice G, Society of Cardiovascular A, Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Inter-

ventions and the Society of Thoracic Surgeons. J Am Coll Cardiol 2006;48(3):e1-148.
4. Davies JE, Sundt TM. Surgery insight: the dilated ascending aorta--indications for surgical intervention. Nat Clin Pract Cardiovasc Med 2007;4:330-9. 10.1038/ncpcardio0885
5. Kim SY, Martin N, Hsia EC, Pyeritz RE, Albert DA. Management of aortic disease in Marfan Syndrome: a decision analysis. Arch Intern Med 2005;165:749-55. 10.1001/archinte.165.7.749
6. Roman MJ, Devereux RB, Kramer-Fox R, O'Loughlin J. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. Am J Cardiol 1989;64:507-12. 10.1016/0002-9149(89)90430-X
7. Goldstein SA, Evangelista A, Abbara S, Arai A, Asch FM, Badano LP, et al. Multimodality imaging of diseases of the thoracic aorta in adults: from the American Society of Echocardiography and the European association of cardiovascular imaging: endorsed by the society of cardiovascular computed tomography and society for cardiovascular magnetic resonance. J Am Soc Echocardiogr 2015;28:119-82. 10.1016/j.echo.2014.11.015
8. Devereux RB, de Simone G, Arnett DK, Best LG, Boerwinkle E, Howard BV, et al. Normal limits in relation to age, body size and gender of two-dimensional echocardiographic aortic root dimensions in persons >/=15 years of age. Am J Cardiol 2012;110:1189-94. 10.1016/j.amjcard.2012.05.063
9. Campens L, Demulier L, De Groote K, Vandekerckhove K, De Wolf D, Roman MJ, et al. Reference values for echocardiographic assessment of the diameter of the aortic root and ascending aorta spanning all age categories. Am J Cardiol 2014;114:914-20. 10.1016/j.amjcard.2014.06.024
10. Saura D, Dulgheru R, Caballero L, Bernard A, Kou S, Gonjilashvili N, et al. Two-dimensional transthoracic echocardiographic normal reference ranges for proximal aorta dimensions: results from the EACVI NORRE study. Eur Heart J Cardiovasc Imaging 2017;18:167-79. 10.1093/ehjci/jew053
11. Muraru D, Maffessanti F, Kocabay G, Peluso D, Dal Bianco L, Piasentini E et al. Ascending aorta diameters measured by echocardiography using both leading edge-to-leading edge and inner edge-to-inner edge conventions in healthy volunteers. Eur Heart J Cardiovasc Imaging 2014;15:415-22. 10.1093/ehjci/jet173
12. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1-39 e14. 10.1016/j.echo.2014.10.003
13. 4ta Encuesta Nacional de Factores de Riesgo 2018. Secretaría de Gobierno de Salud Argentina. Republica Argentina. 2018.
14. Pham MH, Ballegaard C, de Knegt MC, Sigvardsen PE, Sørgaard MH, Fuchs A, et al. Normal values of aortic dimensions assessed by multidetector computed tomography in the Copenhagen General Population Study. Eur Heart J Cardiovasc Imaging 2019;20:939-48. 10.1093/ehjci/jez012
15. Bella JN, MacCluer JW, Roman MJ, Almasy L, North KE, Welty TK, et al. Genetic influences on aortic root size in American Indians: the Strong Heart Study. Arterioscler Thromb Vasc Biol 2002;22:1008-11. 10.1161/01.ATV.0000017473.78775.F6
16. Wang Y-L, Wang Q-L, Wang L, Wu Y-B, Wang Z-B, Cameron J, et al. Body surface area as a key determinant of aortic root and arch dimensions in a population-based study. Exp Ther Med 2013;5:406-10. 10.3892/etm.2012.839

SUPPLEMENTARY MATERIAL

Table 1. Detailed exclusion criteria.

1.	Inability or refusal to sign informed consent
2.	Patient who is actively participating in a randomized clinical trial (RCT)
3.	Pregnant patients
4.	Patients with confirmed diagnosis or suspicion of bicuspid aortic valve
5.	Patients with personal or family history of first diagnosis or suspicion of Marfan, Ehler-Danlos or Loeys-Dietz syndrome, aneurysm of the ascending and/or abdominal aorta
6.	Patients who have practiced a competitive sport in the last 5 years. (professional and/or federated practice, amateurs with average training ≥2 hours a day).
7.	Patients with any degree of aortic regurgitation and/or stenosis
8.	Patients with history of cardiovascular surgery
9.	Known hypertensive patients, in anti-hypertensive treatment and/or with blood pressure values in the office greater than 140/90 mmHg
10.	Patients with frequent arrhythmia at the time of the study..
11.	Patients with major cardiovascular risk factors (diabetes, smoking, hypertension, acute heart failure). o
12.	Suboptimal ultrasound window.

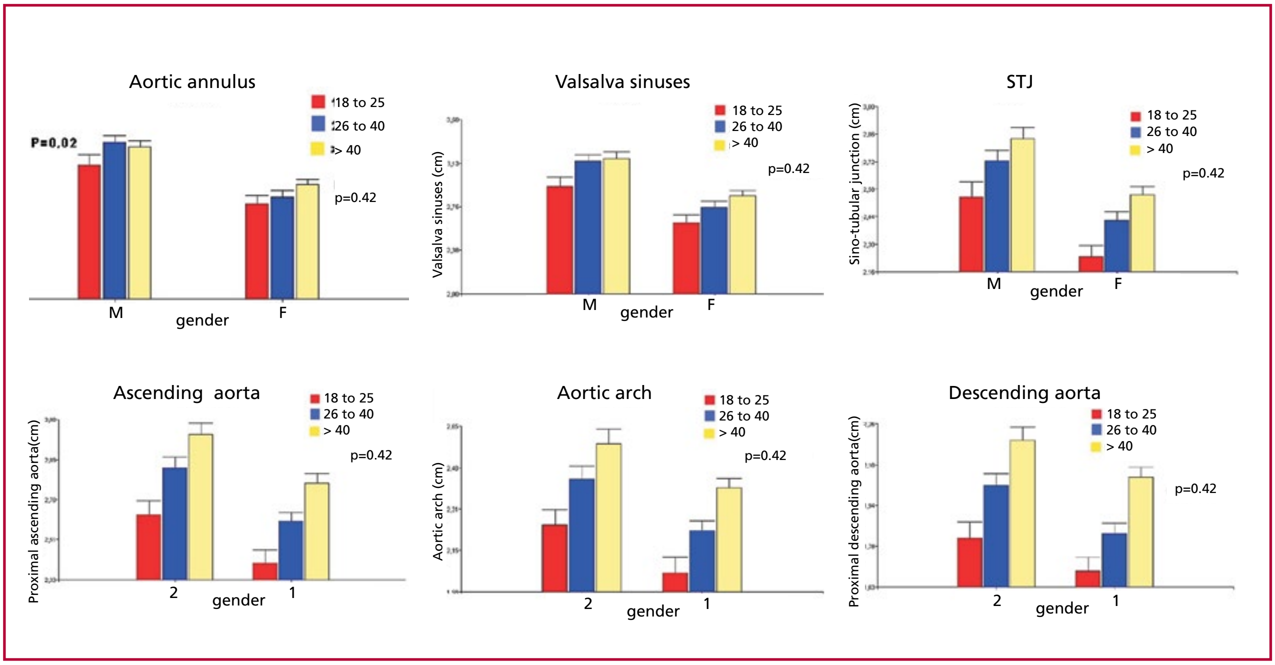


Fig. 1. Differences in the dimensions at the 6 aortic levels according to age and gender. A progressive and consistent increase in the absolute dimensions of the aorta is observed in both men and women as age increases at each level analyzed, except for the aortic annulus.

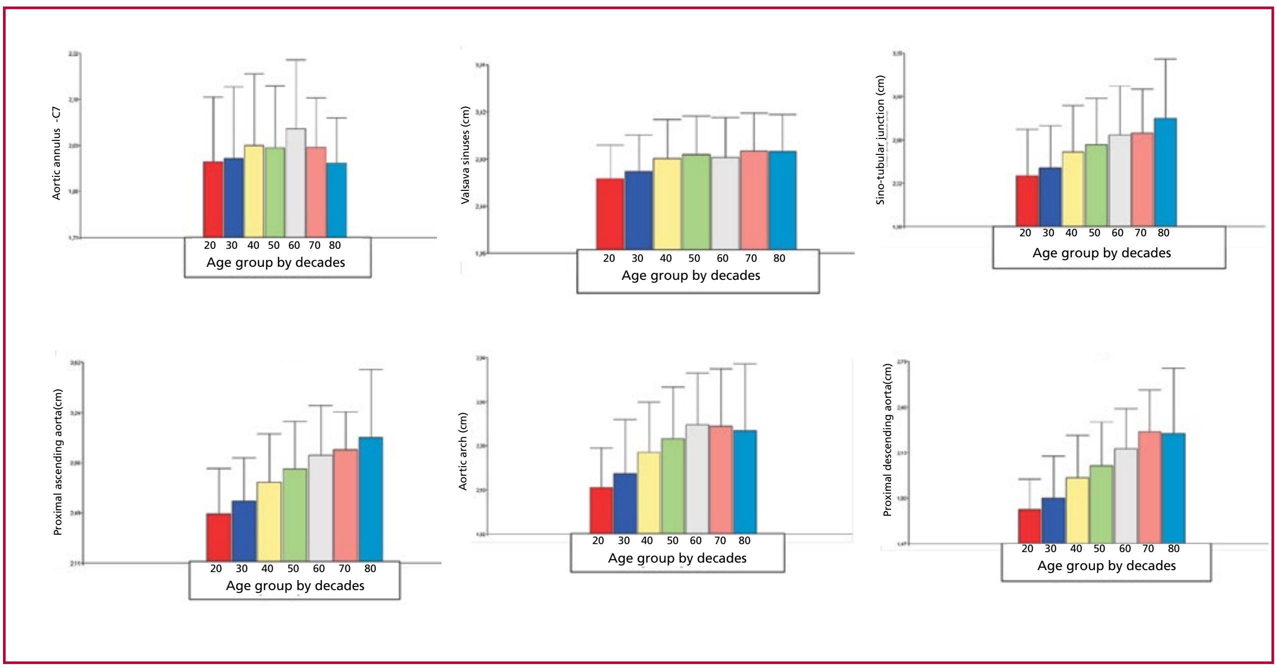


Fig. 2. Aortic diameters according to age, in categories every 10 years (red: up to 19 years, blue: up to 29 years; yellow: up to 39 years; green: up to 49 years; gray: up to 59 years; pink: up to 69 years; navy blue: up to 79 years). A progressive increase in average aortic diameters is seen with each decade, except for the aortic annulus, which remains stable.

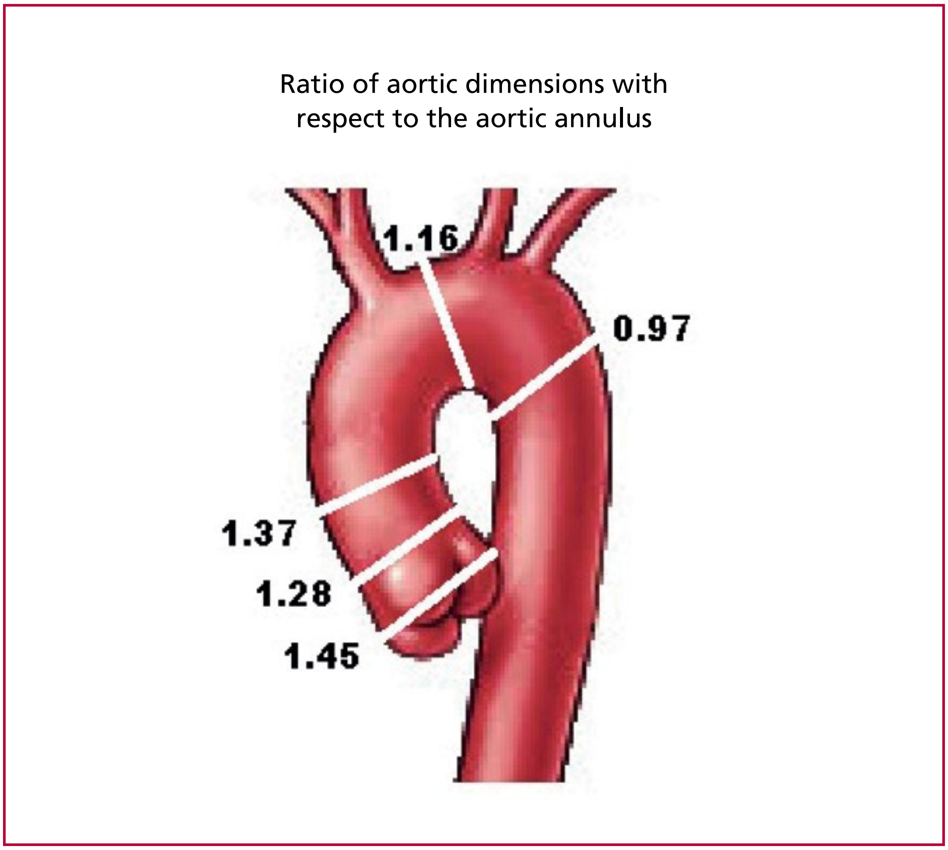


Fig. 3. Calculation of the ratio between each aortic dimension and the aortic annulus. It expresses the proportion between the different aortic segments with respect to the aortic annulus, which is the only segment which does not increase with age.

Table 2. Aortic diameters indexed by height at the 6 levels for patients of American and Iberian origin.

	Americans (N=406) Diameter indexed by height (cm/m) Mean ±SD (P5-P95)	Iberian (N=547) Diameter indexed by height (cm/m) Mean ±SD (P5-P95)	P value
Aortic annulus (cm/m)	1.20 ± 0.11 (1.02 – 1.38)	1.21 ± 0.12 (1.04 – 1.39)	0.15
Valsalva sinuses(cm/m)	1.65 ± 0.21 (1.34 – 2.01)	1.80 ± 0.20 (1.49 – 2.14)	<0.0001
Sinotubular junction (cm/m)	1.50 ± 0.21 (1.20 – 1.89)	1.56 ± 0.19 (1.25 – 1.89)	<0.0001
Proximal ascending aorta (cm/m)	1.59 ± 0.20 (1.30 – 1.98)	1.67 ± 0.21 (1.35 – 2.04)	<0.0001
Aortic arch (cm/m)	1.39 ± 0.19 (1.10 – 1.69)	1.39 ± 0.28 (1.07 – 1.79)	NS
Proximal descending aorta (cm/m)	1.25 ± 0.19 (0.96 – 1.59)	1.11 ± 0.24 (0.92 – 1.49)	<0.0001

Patients of American origin have lower height-indexed diameters in the aortic sinuses, sinotubular junction and proximal ascending aorta, similar in aortic arch and greater in proximal descending aorta.