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Aortic root remodelling in competitive athletes.

Article

Title: ***Aortic root remodeling according to the classification of sport***

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ABSTRACT

Background: Controversy remains about the cutoff limits for detecting aortic dilatation in athletes, particularly in big sized individuals. The allometric scaling model has been used to obtain size-independent measurements in cardiovascular structures in general population. Aim: To validate the use of allometric scaling in the measurement of aortic root for competitive athletes and to offer reference values.

Methods: Cross-sectional study that analyzes the dimensions of aortic root found in the echocardiogram performed as part of the pre-participation sports screening in competitive athletes between 2012 and 2015. Beta exponents were calculated for height and body surface area (BSA) in the whole cohort. In order to establish whether a common exponent could be used in both genders the following model was assessed y=axb*exp (c*sex). If a common exponent could not be applied then sex specific beta exponents were calculated.

Results: 2083 athletes (64% men) were included, from a broad spectrum of 44 different sports disciplines, including basketball, volleyball and handball. The mean age was 18,2 ± 5,1 years (range 12-35 years) and all athletes were Caucasian, with a training load of 12,5 ± 5,4 hours per week. Indexed aortic root (AO) dimension showed a negative correlation with BSA (-0.419, $p<0.05$) and a very light positive correlation with height ($r=0.084$, $p<0.05$). The allometric scaling by BSA and height generated size independence values ($p>0.05$ for both BSA and height). The absolute value of aortic root was higher in men than in women ($p < 0.001$). These differences were maintained with allometric scaling (see Table 1).

Conclusion: Size-independent aortic root dimension values are provided using allometric scaling by BSA and height in a large cohort of competitive athletes. Aortic root values were larger in men than in women, both in absolute values and after allometric scaling. The use of these indexed aortic reference ranges can be useful for the early detection of aortic pathologies.

INTRODUCTION

Long-term exercise training generates a series of structural and functional adaptative changes in the heart, which are known as the “athlete’s heart”(1)(2). It is well known that the exercise-induced volume and pressure overload leads to global and harmonic dilatation of all cardiac chambers(3)(4). However, the impact of exercise training on aortic root size has only been recently evaluated. Dilatation of the aortic root at the level of the Valsalva sinuses is defined as a root diameter above the upper limit of the 95% confidence interval (or two standard deviation) in a general reference population(5)(6).

In the athlete`s population, recent studies have provided some evidence on how the aorta adapts to exercise. In a meta-analysis(7), athletes showed an aortic root diameter 3.2 mm larger than those observed in the general population but always within normal ranges set for the general population. In a recent study with 3281 Spanish athletes(8), the 95th percentile of the aortic root diameter was 36.1 mm for men and 32.1 mm for women. In the recent study by Cavarreta et al the impact of age on aortic root dimensions was evaluated in peri-pubertal athletes, providing reference values for aortic root dimension for the different age groups” (9).

On the other hand, as for other cardiac dimensions, aortic root size has demonstrated to be related to body size and thus, normalized aortic dimensions should be provided(10). Indeed, a non-linear relationship between aortic root size and BSA has been demonstrated in athletic and non-athletic populations(11). Scaling of vessel dimensions is important for comparison between individuals and for generating size-independent reference values(12)(13)(14). There is growing evidence recommend the use of allometric scaling, which produces size-independent indices. Allometric scaling refers to the relative size changes of the body parts (aortic root) correlated to the changes in body composition.

Accordingly, the aims of the study were: 1) to evaluate the impact of exercise training on aortic root size and 2) to offer aortic reference values in the athletes using an allometric scaling model.

METHODS

Subjects and Study Protocol.

A total of 2092 athletes, with ages between 12 and 35 years old, from three high sports performance centers in the Catalonia region (Centre d'Alt Rendiment de Catalunya, Joaquin Blume Residence and Futbol Club Barcelona) were included. As part of our pre-participation screening protocol, athletes underwent a study with familiar/personal anamnesis, physical examination, 12 lead electrocardiogram (ECG), a maximal exercise test and transthoracic Doppler echocardiography. Exclusion criteria were: known cardiovascular disease including bicuspid aortic valve and any kind of aortopathy.

The study follows the guidelines for reporting observational studies in accordance with standards established by the Declaration of Helsinki and received the approval of our center's Ethics Committee for Clinical Research. Written consent was obtained from individuals older than 16 years of age and from a parent for younger athletes.

TRANSTHORACIC ECHOCARDIOGRAPHY

A standard echocardiogram following international guidelines was performed. Images were acquired from the parasternal (long- and short-axis) and apical (4-, 3- and 2-chamber) views. Echocardiographic images were acquired with commercial available ultrasound systems (Vingmed Vivid-7, General Electric Vingmed, Milwaukee, Wisconsin, USA, or Aplio 400, Canon Medical Systems Corporation, Otawara, Japan). Transverse anteroposterior aortic root dimension was measured from the parasternal long axis view in end-diastole, at the level of the sinuses of Valsalva on M-mode images, from the leading edge of the anterior aortic wall to the leading edge of the posterior wall (in accordance with the recommendations of the American Society of Echocardiography)(6).

STATISTICAL ANALYSES

Data were analyzed with SPSS software for Windows (19 version , SPSS Inc., Chicago, New York, USA). Gaussian distribution of all continuous variables was tested using a Kolmogorov–Smirnov test and values reported as mean + standard deviation (SD). Differences between female and male athletes were compared with T student test when normal distribution was confirmed and with U Mann Whitney otherwise. Aortic root size according to sports classifications were compared by one-way independent ANOVA with deviation contrasts to assess values that differed from the mean. If the ANOVA test showed an overall difference, post hoc comparisons were performed with Bonferroni test.

Aortic root values were indexed by two different scaling models: Ratiometric and allometric scaling. First, aortic measurement was assessed to establish whether it met Tanners special circumstance. Tanners special circumstance(15) is met when the coefficient of variation for the body size variable divided by the coefficient of variation of the aortic dimension is equal to the Pearson's correlation between the two variables, with the fit line passing through the origin. When met, it indicates that size-independence has been achieved and ratiometric scaling would generate size-independent values. We observed that Tanners special circumstances were not met. Therefore, it was necessary to use the allometric scaling to generate size independent values.

Another way to indicate if size-independence has been achieved is to correlate the scaled variable with the variable used to scale. For scaling, aortic root dimensions (Y) were linearly scaled to BSA and Height (X) such that the index produced was Y/X. These scaled values were then correlated to BSA and height. Later, aortic root dimension was allometrically scaled to BSA and Height. The allometric correction is thus given by X/Y^b where b is defined as the allometric scaling component. Beta exponents (b) were determined using allometric scaling of the order $y=aX^b$ via a non-linear iterative method to generate allometrically scaled values. In order to establish whether a common exponent could be used in both genders the following model was assessed y=axb*exp (c*sex). To assess the impact of age on aortic root size independent of body size, a covariate analysis was undertaken using the model y=axb*exp(c*age). Common exponent could be applied if C value is closed to 0. If a common exponent could not be applied then sex and age specific beta exponents were calculated. These allometric values were then correlated to BSA and Height. The main objective is to determine size independent values, and, in this way, to eliminate the effect of BSA and height.

RESULTS

Nine athletes who had bicuspid aortic valve were excluded. None of the athletes included in the study showed cardiac abnormalities. Therefore, the final study population included 2083 athletes, 1326 men (63.7%) and 757 women (36.3%).

Mean age was 18.2 ± 5.1 years (range 12-35 years). All athletes were Caucasian, with a weekly average training load of 12.5 ± 5.4 hours and were involved in different levels of competition (*see Table 1).* Athletes practiced a broad spectrum of 44 different sports disciplines and were grouped according to modified Mitchell's classification and, also, according to the Sports Disciplines classification. (*See Supplemental Figure 1 and Supplemental Figure 2*).

Table 2 shows the echocardiographic characteristics of elite athletes according to gender. As expected, all absolute values obtained from echocardiography were larger in men. After indexing for BSA, the size of the cavities was slightly larger in women while ventricular walls were slightly thicker in men. Aortic root was larger in men than in women (men: 29.6 ± 3.4mm, women: 26.1± 2.6mm; p<0.01). When indexed ratiometrically by BSA these differences disappear (men: 15.9 ± 1.8mm, women: 16.1±1.7mm, p=0.75); and when indexed ratiometrically by height or allometrically by

BSA or height, all the values were greater in men (p<0.01). Only 5 male athletes (0.33%) had values larger than 40 mm and 4 (0.5%) female athletes larger than 34 mm (0.52%). The 95th percentile of the aortic root was 36.6 mm for men and 30 mm for women. The 99th percentile was 39 mm for men and 34 mm for women.

Aortic root values indexed by ratiometric scaling showed a moderate negative correlation with BSA (r: -0.419, p<0.05) and a very light positive correlation with height (r=0.084 p<0.05). Thus, ratiometric scaling by BSA did not generate size-independent values.

For the allometric scaling, the exponents beta generated from the model for sex were B: 0.519 for BSA (with C value: 0.05) and B: 0.870 for height (with C value: 0.07). The exponent beta generated from the model for age were B: 0.578 for BSA (with C value: 0.03) and B: 1.025 for height (with C value 0.05). We performed allometric scaling using B exponents generated by the model of age. Aortic root values indexed by allometric scaling showed a very light correlation both for BSA and for height (r: 0.063 for BSA , p:0.04) and (r:0.070 for height, p:0.001). Although there was a correlation, it was very weak with a significant improvement to linear scaling by BSA, where the correlation was much higher.

When aortic dimensions were scaled ratiometrically by BSA, there were no differences in the aortic values between genders. However, when they were scaled ratiometrically by height or allometrically by BSA, the differences between genders were maintained *(see Table 2).*

AORTIC ROOT DIMENSION ACCORDING TO SPORT DISCIPLINE

Figure 1 shows aortic root size according to Mitchell sports classification. Aortic root absolute values were larger in athletes practising sports with high dynamic component (p<0.001). For ratiometrically corrected values by BSA, athletes in the high dynamic group showed the largest aortic root values, greater than moderate dynamic group (p<0.001) and with a trend towards greater values to low dynamic group, but with no significance differences. (p=0.69). Athletes in the moderate dynamic group had the lowest corrected values of aortic root (p<0.001). However, when indexed by height with ratiometric scaling or by both BSA and height with allometric scaling, the group with high dynamic component kept the differences with the other two groups (p<0.001 for difference for both low and moderate group). Regarding the impact of the static component, absolute aortic root values were slightly larger in athletes from the low static as compared with those in the high static group (p<0.001) but with no differences with those in the moderate static group (p=0.9). However, when aortic root dimensions were corrected with both ratiometric and allometric scaling, no significant differences were demonstrated among athletes from different groups (p=0.06 for ratiometric scaling by BSA, p=0.565 for ratiometric scaling by height, p:=0.06 for allometric scaling by BSA and p=0.271 for allometric scaling by height).

Figure 2 shows aortic root values according to the Sports Disciplines classification.

Aortic root absolute values were higher in athletes practicing sports with more dynamic component (mixed and endurance) (p<0.001 for difference vs skill and power and p=0.91 for differences between mixed and endurance). For both ratiometrically and allometrically corrected values by BSA, endurance athletes showed the largest aortic root values (p:0.001 for differences between mixed and endurance for ratiometric values and p<0.05 for allometric values). However, after ratiometric and allometric correction for height, there were no differences between mixed and endurance group (p=0.31), although this last group presented a trend towards larger values.

DISCUSSION

Our study has three key findings: 1) the aortic root size in healthy trained athletes is within normal ranges established for the general population 2) sports with high dynamic component are related to significantly larger aortic root size and 3) allometric and ratiometric scaling to height provides almost perfect size independent models as shown by the lowest existing relationship with BSA and height using these scaling methods.

The aorta experiences a significant hemodynamic load during exercise that results in variable aortic remodeling in athletic individuals(2).The body surface area has an important influence on the dimensions of the heart. Therefore, in order to assess the extent of cardiac remodeling it is necessary to correct values for BSA(16) or height, to remove the impact of body size. Gender(17) and race(18) are other important determinants of cardiac remodeling in athletes. Several observational studies performed in the general non-athletic population have reported that height and body size are the most relevant determinants of aortic root size(19). However, there is limited information regarding their impact on aortic root size in athlete population.

Our results are in accordance with previous studies. In an study by Pelliccia et al.(20) including 2317 italian Olympic athletes and in a recent study by Gati et al.(21), including 3781 young competitive athletes, aortic root dilatation was established for values above 99th percentile of the sample. In the Italian study this value was 40 mm for male athletes and 34 mm for female athletes, while for the study by Gati, this value was 40 mm for male athletes and 38 mm for female athletes, significantly higher in female, which could be in relation with the fact that there were more women in sports of endurance than in the other study. In our study, these values were 39 mm for male athletes, very concordant with previous two studies, and 34 mm for female athletes; this was the same cut of value than in Italian study and slightly lower than the study by Gati.

In the study by Boraita et al.(8), aortic root dilatation was established as values above the 95th percentile of the sample. The established cut of values was 36,1 mm for male athletes and in 30,3 mm for female athletes. In keeping with these previous findings, in our study this cut off values were 36,6 mm for male athletes and 30 mm for female athletes.

In a meta-analysis(7) including 23 studies with a a sample of 5580 elite athletes, mean aortic root values were 31.6 mm in men and 25.1 mm in women. Our values are slightly lower in men and slightly larger in women, although within the range previously described (22.9-27.3mm).

Therefore, considering all these studies, we can confirm that the aortic root in athletes does not exceed the values established as normal for the general population and thus the cut-off for differentiating between physiology and pathology should be equivalent in athletes and in the general population. The reason why the increase in aortic size induced by exercise is not proportional to the one demonstrated in the four heart cavities could be related to the fact that aortic root is inside the fibrous pericardium along with the pulmonary artery, therefore there is a much reduced capacity for stretching(22).

There are very few studies that offer reference values for the aortic root using allometric scaling in a population of elite athletes. The study(11) by Oates et al., analyzed the aortic root in 220 elite rugby football players; they found size independent values for allometric scaling and for ratiometric scaling to height and offered reference values for a rugby players with high BSA.

To the best of our knowledge, our study is the first performed in a large cohort of elite athletes from different sports disciplines which provides reference values for aortic root using allometric scaling for elite athletes; since the correlation between allometric aortic values and BSA and height is practically nonexistent (r values: 0,063 for BSA and 0,070 for height), we conclude that it provides almost completely size independence when used, certainly showing a significant improvement from that obtained with linear scaling by BSA, where the correlation between linear scaling aortic root and BSA is much more higher (r value: 0,419). Linear scaling to height also provides size independent values which is, indeed, not surprising in that height as well as aortic root dimensions are both one-dimensional measures and thus likely to be linearly related

We have also analyzed how aortic root adapts to different sports disciplines practice. Mitchell's classification is based on a dynamic and static component during the competition. In accordance with Boraita and Gati's study(8)(21) the high dynamic component was associated with the larger aortic root values for both allometric and ratiometric scaling to height models. However, when using ratiometric scaling to BSA the largest values of aortic root were shown in low and high dynamic components. The BSA in the group with high dynamic component was superior to that in the group with low dynamic component. This generates larger relative values in the latter group. When using allometric scaling, the effect of BSA disappears and this generates size independent values and therefore, the differences between both groups remain. In both ratiometric and allometric scalling models the static component demonstrated no impact on aortic size. Therefore, sports disciplines with higher cardiovascular demand promote a more pronounced remodelling in both the heart and the aorta.

Traditionally according to Morganroth's theory, sports were divided into two groups: strength and endurance, based on their predominantly isometric or isotonic component. So far it has been shown that the endurance group has more remodeling of the aortic root(8)(21)**.** However, most sports are characterized by a varying degree of both isometric and isotonic components. Consequently, the recently proposed classification of sports disciplines suggested four groups to be considered when assessing an athlete heart and its remodelling: skill, power, mixed and endurance. Our study, is to our knowledge the first one that provides reference aortic root values based on this classification

We want to emphasize that allometric scaling to BSA and Height produce almost perfect size independence because this method does not rely on a linear relationship between the two variables. Through this method of scaling the interindividual variability due to the different body surface is eliminated. As shown in *Figure 3,* absolute aortic root values are larger as BSA increases. However, there are no differences when allometric scaling is used and the effect of BSA disappear. This approach has not been adopted in the context of daily clinical practice. However, ratiometric scaling to height also produce almost perfect size independence. In any case it’s necessary to use some scaling method. If is possible, to use the allometric model using the equation X/Y^b, being b the exponents generated for our cohort. If is not possible to use allometric method, it would be preferable to use ratiometric scaling to height than ratiometric scaling to BSA.

In the study, we have provided reference aortic root values for each of the groups of Mitchell’s classification and for the newly proposed classification of sports disciplines, with absolute values, as well as, with indexed values using ratiometric or allometric scaling to height, *see supplemental figure 3 and 4*. In cases of doubt in the absolute value of aortic root, especially in athletes with large body size such as basketball players, or even in those athletes with low BSA, it would be necessary to index the values and to use this reference values. If the value is within the 95^{th} percentile of this large cohort of elite athletes it will be considered as normal and, this would potentially reduce the number of unnecessary further investigations.

STUDY LIMITATIONS

One of the limitations of the study is the absence of a non-athlete group. Despite this, the sample includes a large group of competitive athletes, so we believe that reference values can be trusted. Secondly, all these athletes are 100% caucasian, and we cannot evaluate the different cardiac adaptations in different ethnic groups. Third, long-term follow-up of these athletes is not available, and we do not know the long-term behavior of the aortic roots of those athletes that were beyond the value of the percentile 95. Fourth, the echocardiographic images were measured on M mode images. Current recommendations(6) suggest that, 2D echocardiography is preferred over M-mode measurements of the aortic root. Unfortunately, the acquisitions of our echo images were not specifically designed to assess the aortic root, but rather were retrospectively measured from routine echocardiograms as part of our screening algorhythm. Despite 2D echo measurements might be more accurate according to current recommendations, we believe that M-mode measurements are also acceptable particularly given the large size of the studied population.

CONCLUSIONS

The size of the aortic root in competitive athletes is within the limits considered normal for the general population. The aortic root adapts differently depending on the practiced sports discipline. Thus, the largest values are found in those sports with higher cardiovascular demand.

This study provides more evidence in the use of the allometric scaling when indexing cardiovascular structures and their application also in high competitive athletes. Despite linear scaling to height is another appropriate method, our data also discourage the use of ratiometric scaling to BSA since it does not remove the effect of BSA. Finally, we provide reference values for allometric scaling and for ratiometric scaling to height for the aortic root of elite athletes.

AUTHOR CONTRIBUTION

MA is the corresponding author. He had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. He performed the statistical analysis and drafted the manuscript. GG, MSG, SM, AD, BV, GS, MB, RP, DB and MS participated in data collection. MA, GG, MSG, DB and MS revised critically the manuscript. MS is last author. All authors read and approved the final version of the study.

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