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Scaling to produce size-independent indices of echocardiographic derived aortic root dimensions in elite Rugby Football League players

Abstract

Introduction: The assessment of aortic root dimensions is important in cardiac pre-participation screening. Scaling of cardiac dimensions removes the impact of body size allowing meaningful inter/intra group comparisons. Developing appropriate scaling approaches, scaling variables and extending the application to major vessels is warranted so underlying pathology can be detected and managed appropriately. The study aims to define relationships between Aortic Root dimensions and BSA/height.

Methods: 220 elite Rugby League athletes were recruited. All participants completed anthropometric assessments, a 12-lead ECG and echocardiogram. Aortic root was measured at the aortic annulus, sinus of valsalva, sinotubular junction and the proximal ascending aorta. Linear and allometric scaling were performed on the relationship between aortic measurements and BSA/height.

Results: Absolute aortic root measurements fell within normal population data (mean ± standard deviation [range]: aortic annulus: 22 ± 2 [17 – 28] mm, sinus of valsalva: 28 ± 3 [20-38] mm, sinotubular junction: 22 ± 3 [14 – 33] mm, proximal ascending aorta: 22 ± 3 [15-31] mm). Linear scaling to height produced size-independent indices at all aortic measurement sites ($P < 0.05$). Conversely, linear scaling using BSA did not produce size independent indices at any site ($P > 0.05$). Allometric scaling, using both BSA and height, produced size independent indices at all sites ($P < 0.05$).

Conclusions: We recommend linearly scaling aortic root dimensions to height in elite Rugby League athletes and discourage the use of BSA as a linear scaling quantity. Allometric scaling is also effective when using both BSA and height.

Introduction

The athlete's heart is a term used to describe the morphological, functional and electrical cardiac adaptations that occur in response to chronic exercise training [1,2]. Athletes exhibit increased left ventricular wall thickness and enlargement of all cardiac chambers [3] which occasionally overlap with mild phenotypes of cardiac disease. The differentiation between physiology and pathology is crucial to ensure that individuals at potential risk of sudden cardiac death are identified and managed appropriately [4]. Aortic dissection accounts for a small but significant (0.8%) proportion of sudden cardiac deaths in athletes [4] and accurate assessment of aortic root dimensions is important to aid the identification of at-risk individuals during cardiac pre-participation screening.

Unlike the cardiac chambers, it is not clear whether the major vessels adapt structurally to intense training. In a mixed cohort of athletes, the absolute and linearly scaled to body surface area (BSA) aortic root dimensions were found to be within published guidelines for the general population [5,6,7]. To simplify clinical assessment an absolute diameter of 40 mm has been proposed as the upper limit of an acceptable aortic dimension, irrespective of body habitus or athletic activity. Such practice may, however, falsely reassure smaller individuals with aortopathy or, conversely, cause unnecessary concerns and further investigation in larger individuals such as basketball players in whom up to 4.6% have aortic root dimensions > 40 mm [8,9].

It is understood that aortic root dimensions are related to body size [10]. Scaling (or indexing) of vessel dimensions is important for comparison between individual patients and for generating size-independent reference values [11]. The process of scaling and the choice of the scaling variable is vital to the validity of any indexing process [12]. Currently recommendations suggest that aortic root dimensions are indexed linearly by BSA [7]. This provides a simplistic approach, which has been adopted unchallenged in clinical practice. It is, however, potentially fallacious, as simply dividing aortic root dimensions (1-dimensional measure) by BSA (a 2-dimensional area) assumes linearity between the two variables and ignores dimensionality theory [12]. The retention of linear scaling with BSA in clinical evaluation is one of mathematical ease rather than scientific merit. Previous work has demonstrated the non-linear relationship of aortic root size to BSA in a non-athletic population but also highlighted a close to linear relationship to height [13]. There is a growing evidence base in clinical cardiology to recommend the use of allometric scaling [11,12,13], which produces size independent indices [11].

Rugby League is a team sport that utilises a mixed training load and is classified as a moderate static / moderate dynamic sport [14]. Due to the nature of the sport, the body size of individuals can vary significantly. In view of this, Rugby League athletes serve as an ideal model to assess the impact of body size on aortic root dimensions. The aim of this study was to establish the range of aortic root dimensions in a large cohort of elite Rugby League athletes and define the nature of the relationship between body size (BSA and height) and aortic root dimensions using both linear (ratiometric) and allometric models.

Methods

220 male Rugby League players (mean ± standard deviation [range]) age: 21 ± 5 [14 to 34] years) were prospectively recruited from three English Super League teams during their annual cardiac pre-participation screening. All players were non-smokers, free from cardiovascular disease and diabetes and not taking any prescribed medication. Players were asked to refrain from training and drinking caffeine or alcohol up to 24 hours prior to data collection. The pre-participation screening involved completion of a health questionnaire, the assessment of height and body mass, a measurement of brachial artery blood pressure, a resting 12 lead electrocardiogram and a transthoracic echocardiogram. Screening results were reported by a Sports Cardiologist (JS) with clinical referrals made for any participant requiring further cardiac evaluation. After screening and further evaluation, if necessary, all participants were included in the study and determined to be free of underlying cardiac disease. All players provided written informed consent.

2.1) Anthropometric Assessment

A routine standard anthropometric assessment included measurements of body mass (Seca supra 719, Hannover, Germany) and height (Seca 217, Hannover, Germany) with BSA calculated as previously described [15].

2.2) *12 lead Electrocardiogram*

A resting 12-lead electrocardiogram was undertaken in accordance with American Heart Association guidelines [16]. All electrocardiograms were acquired using commercially available equipment (Schiller, Cardiovit ms-2010, Doral, US).

2.3) Transthoracic echocardiogram

Echocardiograms were performed using a commercially available ultrasound system with multi-frequency-phased array transducer (2.5 - 4 MHz) (Vivid Q, GE Medical, Horton, Norway), by two experienced sonographers adhering to guidelines by the American Society of Echocardiography [7]. Standard or high parasternal long axis views were utilised to assess the aortic root and all measurements were made offline using dedicated analysis software (EchoPac Version 110.0.2 GE Medical, Horton, Norway). The aortic root was assessed at 4 levels; the aortic annulus, defined as the level of the hinge point of the aortic cusps; the sinus of Valsalva, at the level of the coronary ostia; the sinotubular junction, defined as the level where the sinus bulge terminates and the proximal ascending aorta, defined as 1 cm distal to the sinotubular junction. All sites were measured at end diastole as defined by the onset of the QRS complex using the inner edge to inner edge method [7,13]. Measurements were averaged over three cardiac cycles. A previous study from our laboratory demonstrated excellent inter and intra-observer variability data for all measurement sites with intraclass correlation coefficients ranging from 0.84 to 0.97 [13].

2.4) Statistical Analysis

Significance was set at ($P < 0.05$). All absolute and scaled aortic root dimensions are presented as mean ± standard deviation. Absolute values were compared to the American Society of Echocardiography guidelines [7]. Firstly, each aortic parameter was assessed to establish whether it met Tanners special circumstance [17]. Tanners special circumstance 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 [17]. When met it indicates size independence has been achieved. For scaling, initially all 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, via bivariate correlation analysis, to BSA and height to establish whether the linear scaling approach resulted in size-independent indices. Subsequently all aortic root dimensions were scaled allometrically to BSA and height. β exponents were determined using allometric scaling of the order $y = a.x^b$ via a non-linear iterative method to generate allometrically scaled values. The allometrically scaled values were then correlated against BSA or height to determine size-independence. To assess the impact of age on aortic root size independent of body size, a covariate analysis was undertake using the model y = a:xb*exp(c * age). The subsequent β was compared with that obtained using the general model $y = a .x^b$ and the c value was calculated.

Results

All demographics are presented in Table 1. Four of the 220 players were referred for further evaluation due to meeting specific non-training related electrocardiography criteria [18] or inconclusive echocardiography but were subsequently deemed to have a normal heart.

Absolute and scaled aortic root dimensions are presented in Table 2. None of the participants presented with absolute aortic root dimensions > 40 mm. None of the aortic dimensions met Tanners special circumstance with linear scaling to BSA, however, this condition was met for all aortic root dimensions when assessed relative to height. Linear scaling of aortic root dimensions to BSA did not produce size independence for any of the aortic root dimensions (see Figure 1). Linear scaling to height produced size independent indices for all aortic root dimensions (see Figure 2).

Allometric scaling of aortic root dimensions to BSA produced size independence for all aortic root dimensions with β exponent values of 0.574, 0.571, 0.742 and 0.543 for aortic annulus, sinus of valsalva, sinotubular junction and proximal ascending aorta, respectively. Allometric scaling of aortic root dimensions to height also produced size independent indices with all β exponents close to 1. Following assessment for the impact of age, the β exponents were similar to those obtained from the single variant assessment with c values close to 0 suggesting the derived exponent can be used across the age range of this population.

Discussion

The key findings of this study were 1) linearly scaling aortic root dimensions to height produced size independent indices in elite Rugby League players. 2) allometric scaling using both height and BSA also produces size independent aortic root dimensions. 3) BSA was found not to produce size independent aortic root dimensions when using linear scaling methods and 4) absolute and linearly scaled aortic root dimensions were found to be within normal population limits.

The current study demonstrates a linear relationship of aortic dimensions to the athlete's height. This finding has also been seen in a non-athletic population [14]. The reason for this consistency likely reflects dimensionality theory in that height as well as all aortic root dimensions are 1-dimensional measures and are thus likely linearly related. In view of this we can suggest that adopting this approach will likely produce size-independent indices and support more accurate clinical decision making. The technique is simple, quicker and more intuitive to clinicians than allometric scaling, so is applicable to busy clinical environments with time pressures. Linear scaling of aortic root dimensions to height would potentially reduce the number of unnecessary further investigations in sports with athletes of large body size such as basketball, where up to 4.6% of players may demonstrate an SOV measurement above the cut off value of 40 mm [6,8]. Based on the results of our study we would recommend that linear scaling to height is applied in the clinical setting. Values of up to 14mm/m for the aortic annulus, 20mm/m for the sinus of valsalva, 16mm/m for the sinotubular junction and 16mm/m for the proximal ascending aorta should be accepted as the upper limits of normal in elite male Rugby League players.

In a large cohort of elite Rugby League athletes aortic root dimensions were all < 40 mm thus falling within the accepted normal range [7]. Similar to existing data, allometric scaling of aortic root dimensions to BSA and height produced size independent indices [14]. This method does not rely on a linear relationship between the two variables. This approach has not been widely adopted in the context of daily clinical practice [10]. This is likely due to the perceived mathematical complexities and hence linear scaling remains the primary scaling method for most measures of cardiac and vessel size [11]. The impact of age was also assessed in our non-linear model and supports the use of this exponent when scaling for BSA across this age range (14-34) of elite Rugby League players.

Linear scaling using BSA, the process suggested in current clinical guidelines [7], did not result in size independent aortic root dimensions. Similar to our study, current literature has consistently shown that linear scaling to BSA does not produce size independent indices for a range of cardiac variables [11]. Linear scaling assumes a linear relationship between the cardiac dimension and the body size parameter which is often not the case in biological relationships [12]. In addition, BSA is open to measurement estimation error and cannot differentiate the impact of excess fat or lean tissue [12].

4.1) *Limitations*

The participants in this study were a homogenous group of athletes suggesting that the results of this study can only be used to guide cardiac pre-screening for aortic root dilation in this population. The study only included male participants aged 14-34 so the results cannot be generalised to very young/older athletes or females. Ethnic differences were not considered and it has been noted that differential cardiac adaptations have been observed in varied ethnicities [19]. The study employed a cross-sectional design so a cause and effect relationship between aortic root dimensions and body size cannot be fully established.

4.2) Conclusions

This paper adds to a growing evidence base that advocates the use of evidence-based scaling of cardiovascular variables. The paper also discourages the use of BSA as a linear scaling quantity as it does not produce size independent measures of the aortic root, despite it being the current accepted practice in the clinical setting. The paper provides absolute and scaled values of the aortic root in an elite Rugby League population. This will help to guide practitioners in pre-screening programmes within this sport and may help prevent cardiac events in this population. The findings of this paper contribute to a growing database on normative aortic root measurements. Further work should be carried out to define normal values within other diverse sporting populations. These comparisons are made possible through the use of scaling to remove the effect of body size. Linearly scaling to height or allometric scaling is receiving growing attention from the scientific community as an appropriate method. Further research should aim to advocate this further.

References

[1] Pluim B, Zwinderman A, Laarse VD , et al. The Athlete's Heart: A Meta-Analysis of Cardiac Structure and Function. Circulation. 2000; 101(3):336-344.

[2] Utomi V, Oxborough D, Whyte G, et al. Systematic review and meta-analysis of training mode, imaging modality and body size influences on the morphology and function of the male athlete's heart. Heart. 2013; 99(23):1727-1733.

[3] D'Andrea A, Riegler L, Golia E, et al. Range of right heart measurements in top-level athletes: The training impact. Int J Cardiol. 2013; 164(1):48-57.

[4] Finocchiaro G, Papadakis M and Robertus J. Etiology of Sudden Death in Sports. J Am Coll Cardiol. 2016; 67(18):2108-2115.

[5] Iskandar A and Thompson P. A Meta-Analysis of Aortic Root Size in Elite Athletes. Circulation 2013; (127):791-798.

[6] Boraita A, Heras M, Morales F, et al. Reference Values of Aortic Root in Male and Female White Elite Athletes According to Sport. CLINICAL PERSPECTIVE. Circulation. 2016; 9(10):e005292

[7] Lang R, Badano L, Mor-Avi V, 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):1-39.

[8] Engel D, Schwartz A and Homma S. Athletic Cardiac Remodeling in US Professional Basketball Players. J Am Coll Cardiol. 2016; 1(1):80-87.

[9] Pelliccia, A., Caselli, S. and Sharma, S. (2017). European Association of Preventive Cardiology (EAPC) and European Association of Cardiovascular Imaging (EACVI) joint position statement: recommendations for the indication and interpretation of cardiovascular imaging in the evaluation of the athlete's heart. Eur Heart J. 2017; 39(21):1949-1969.

[10] Roman M, Devereux R, Kramer-Fox R, et al. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. J Am Coll Cardiol. 1989; 64(8):507-512.

[11] Dewey F, Rosenthal D, Murphy D, et al. Does Size Matter?: Clinical Applications of Scaling Cardiac Size and Function for Body Size. Circulation. 2008; 117(17):2279-2287.

[12] Batterham A, George K, Whyte G, et al. Scaling Cardiac Structural Data by Body Dimensions: A Review of Theory, Practice, and Problems. Int J Sports Med. 1999; 20(8):495-502.

[13] Oxborough D, Ghani S, Harkness A, et al. Impact of methodology and the use of allometric scaling on the echocardiographic assessment of the aortic root and arch: a study by the Research and Audit Sub-Committee of the British Society of Echocardiography. Echo Res Pract 2014; 1(1):1-9.

[14] Levine B, Baggish A, Kovacs R, et al. Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Task Force 1: Classification of Sports: Dynamic, Static, and Impact. Circulation. 2015; 66(21):2350-2355.

[15] Mosteller, R. Simplified calculation of body surface area, N Engl J Med 1987; 317(17): 1098

[16] Kligfield P, Gettes L, Bailey J, et al. Recommendations for the Standardization and Interpretation of the Electrocardiogram. Part I: The Electrocardiogram and Its Technology. A Scientific Statement From the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. Circulation. 2007; 115(10):1306-1324.

[17] Tanner, J.M, Fallacy of per-weight and per-surface area Standards, and Their Relation to Spurious Correlation. J app physiol 1949; 2(1):1-15.

[18] Sharma S, Drezner J.A, Baggish A, et al. International recommendations for electrocardiographic interpretation in athletes. J Am Coll Cardiol 2017; 69(8):1057-1075.

[19] Chandra, N, Papadakis, M. and Sharma, S. Cardiac adaptation in athletes of black ethnicity: differentiating pathology from physiology. Heart 2012; 98(16):1194-1200.

Figure legends

Figure 1: Measurement sites of the Aortic Root using inner edge method at end diastole. A) Aortic Annulus, B) Sinus of Valsalva, C) Sinotubular Junction, D) Proximal Ascending Aorta.

Figure 2: Non-linear regression of the order y=ax^b for BSA to a) Aortic Annulus, b) Sinus of Valsalva, c) Sinotubular Junction, d) Proximal Ascending Aorta

Figure 3: Non-linear regression of the order y=ax^b for height to a) Aortic Annulus, b) Sinus of Valsalva, c) Sinotubular Junction, d) Proximal Ascending Aorta.

Table 1: Participant demographics

Demographic	Mean ± standard deviation [Range]
Age (Years)	21 ± 5 [14-34]
Height (cm)	181 ± 7 [161–198]
Weight (kg)	90 ± 13 [52-132]
BSA (m^2)	2.11 ± 0.17 [1.65–2.60]
Systolic blood pressure (mmHg)	131 ± 9 [98-152]
Diastolic blood pressure (mmHg)	68 ± 7 [53-91]
Training (years)	13 ± 4 [3-25]
Training (days per week)	5 ± 1 [4-7]
Training (hours per week)	17 ± 7 [6-40]

Table 2: Absolute and linearly/allometrically scaled aortic root measurements to BSA and height. Cut offs provided (+2 standard deviations) for linearly scaled to height measurements.

Measurement site	Absolute value ± standard deviation [Range] (mm)	Linearly scaled to body surface area [Range] (mm/m2)	Linearly scaled to height [Range] (mm/m)	Allometrically scaled to body surface area [Range] mm/(m2) $^{\beta}$	Allometrically scaled to height [Range] (mm/m $^{\beta}$)	Linearly scaled to height Cut offs (+2 standard deviations) (mm/m)
Aortic Annulus	22 ± 2 [17 – 28]	10 ± 1 [7 – 13]	12 ± 1 [9 – 16]	14 ± 2 mm/(m^{2})$^{0.574}$ [11 – 18]	13 ± 2 mm/m$^{0.843}$ [10 – 17]	14
Sinus of Valsalva	28 ± 3 [20 – 38]	13 ± 2 [9 – 19]	16 ± 2 [11 – 22]	18 ± 2 mm/(m2)$^{0.571}$ [14 – 26]	16 ± 2 mm/m$^{0.932}$ [12 – 23]	20
Sino Tubular Junction	22 ± 3 [14 – 33]	11 ± 1 [7 – 16]	12 ± 2 [8 – 19]	13 ± 2 mm/(m^{2})$^{0.742}$ [8 – 19]	11 ± 2 mm/m$^{1.214}$ [7 – 17]	16

Proximal Ascending Aorta	22 ± 3 [15 – 31]	10 ± 1 [7 – 15]	12 ± 2 [9 – 18]	15± 2 $mm/(m^2)^{0.513}$ [11 – 21]	14 ± 2 $mm/m^{0.768}$ [10 – 20]	16