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Left ventricular morphology and geometry in élite athletes characterized by extreme anthropometry

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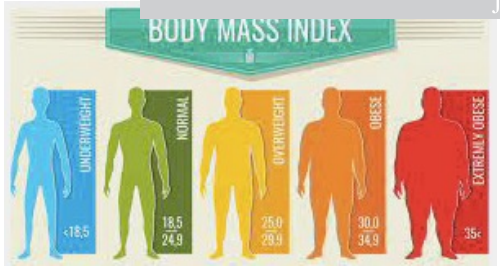
1857 *élite* athletes investigated with ECG and echocardiogram

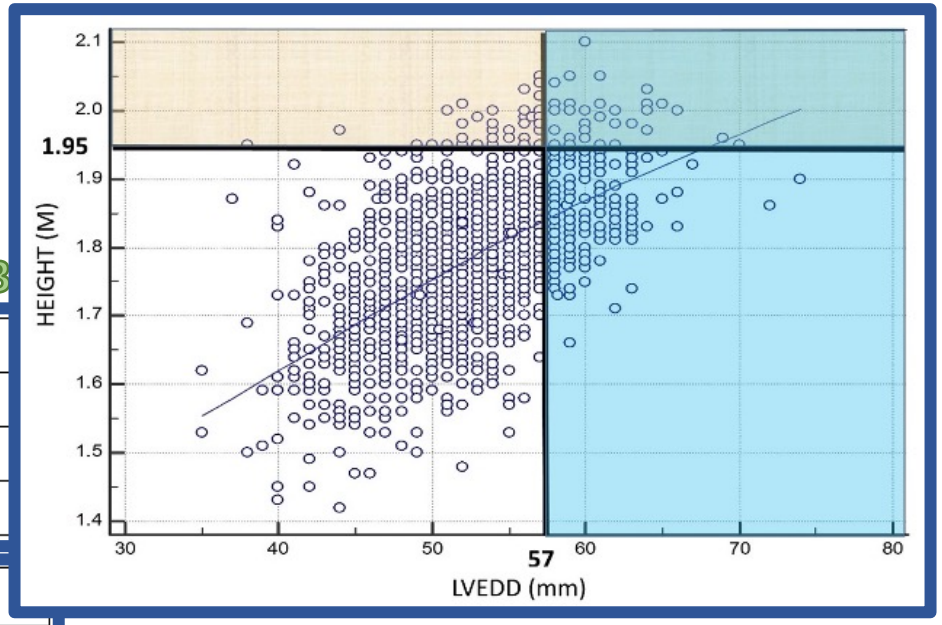
GROUP 1 N=50
BMI≥30 and Height <1.90m

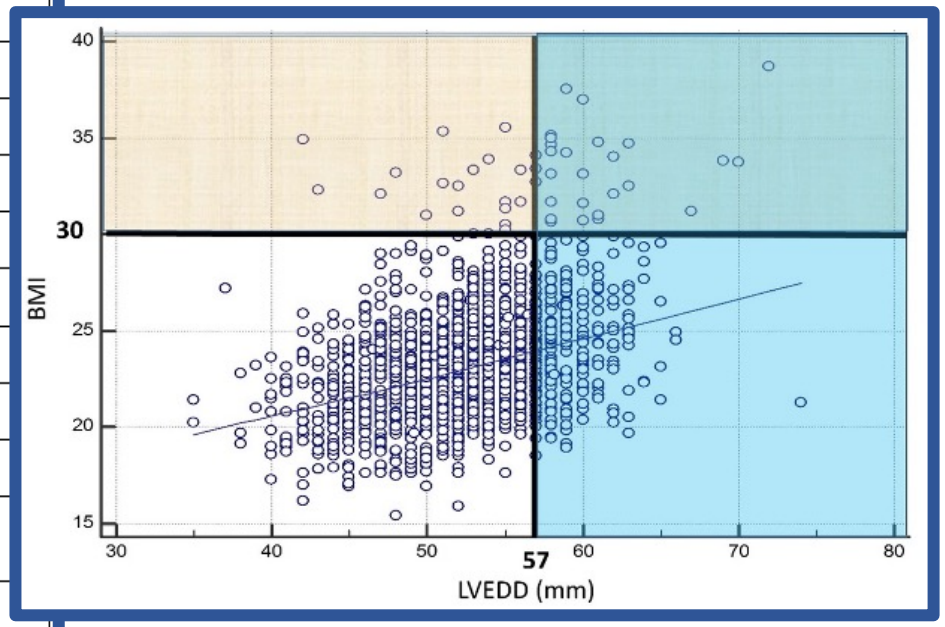
GROUP 2 N=87
BMI<30 and Height ≥1.95 m

GROUP 3 N=243
BMI 20-29 and Height<1.90 m



	GROUP 1	GROUP 2	GROUP 3
Height (m)	1.81±0.09 #*∞	1.98±0.03	1.79±0.12
Weight (Kg)	109±13 #*∞	96±7	77±8
BSA (m^2)	2.3±0.2 #*	2.3±0.1	2.0±0.1
BSA ≤ 2.3 m^2 n (%)	26 (52) #*	41 (47)	220 (90)
LVEDD (mm)	57±6 #*	57±4	53±4
LVEDD > 57 mm n (%)	25 (50) ∞#	33 (38)	31 (13)
LVEDD > 65 mm n (%)	4 (2)	1 (1)	3 (1)
LVESD (mm)	37±6	37±4	36±4
IVS WT (mm)	11±1 #*∞	10±2	9±1
PW WT (mm)	10±1 #*	10±2	9±1
MWT > 11 mm n (%)	12 (24) #*	19 (21)	16 (6)
RWT	0.37±0.05 ∞#	0.35±0.05	0.34±0.05
LA (mm)	40±5 #	38±4	36±1
Normal geometry n (%)	29 (58) #	63 (73)	190 (78)
Concentric hypertrophy/remodelling n (%)	10 (20) #*	12 (14)	16 (6)
Eccentric hypertrophy n (%)	11 (22)	11 (13)	38 (16)





Title: Left ventricular morphology and geometry in élite athletes characterized by extreme anthropometry

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Left ventricular morphology and geometry in élite athletes characterized by extreme anthropometry

INTRODUCTION

Long-term exercise results in cardiac electrical and morphological adaptation. [1] The most common finding in highly trained sports participants is enlargement of all cardiac chambers and increased left ventricular (LV) mass. [1,2] In some cases, marked morphological changes pose a *dilemma* in distinguishing physiological cardiac adaptation to exercise from potentially fatal cardiac conditions such as cardiomyopathies. [3–7] The challenges in the differential diagnosis are particularly critical in assessing athletes with a large body size. [8] However, a limited number of studies involving athletes with extreme body anthropometry are currently available with a lack of reference values for normality in this subset of individuals. Moreover, most data are inherent to athletes with large body surface area (BSA >2.3 m^2), not considering other parameters such as body mass index (BMI), which is an index of corporeal density. Recent studies provided normative data for basketball players. [9] Although these studies shed some light on athletes with height above average, the effect of other indices of extreme body anthropometry such as high BMI on cardiac dimensions in athletes are largely unknown. In addition, the normal cardiac values in athletes with above-average height engaged in sports other than basketball is unclear. The aim of this study was to explore if there is any individual impact of BMI and height on LV size and geometry in a cohort of healthy athletes.

MATERIAL AND METHODS

The UK does not support a state sponsored cardiac screening program in athletes. However, the charitable organisation Cardiac Risk in the Young (www.c-ry.org.uk) has an established cardiac screening program for young individuals that also serves many professional sporting organisations in the UK. Details of the cardiac screening programme have been previously described. [10,11]

Between 2007 and 2014, 2081 consecutive young highly trained athletes were evaluated with a health questionnaire, electrocardiogram (ECG) and echocardiogram for screening purposes. Of these, 2031 were not affected by a cardiomyopathy or a major valvular/congenital/electrical disease after an

electrocardiogram (ECG) and echocardiogram. Complete anthropometric data were available in a total of 1857 athletes, which constituted the study cohort (study protocol summarized in Figure 1).

In the attempt to investigate the different contribution of BMI and height in cardiac remodelling in athletes, we focused mainly on 3 subgroups of athletes. The first (Group 1, n=50, 3%) was constituted by athletes with high BMI and normal height (BMI ≥ 30 and height < 1.90 m); the second (Group 2, n=87, 5%) included athletes who were particularly tall but had a normal BMI (height ≥ 1.95 m and BMI < 30); the third group (Group 3, n=243, 13%) served for comparison and included age-matched athletes characterized by height < 1.90 m and normal BMI (between 20 and 29). A BMI value of 30 was used as a cut-off because it is an established threshold to define obesity. The threshold of 1.95 m of height was arbitrarily chosen as the value equated to mean plus 2 standard deviations in our cohort. BMI and body surface area (BSA) were calculated as previously described. [12,13] We used the previously utilized threshold of BSA > 2.3 m^2 to define extreme anthropometry [8].

Two-dimensional echocardiography was performed using either a GE Vivid I (Tirat, Israel), Philips Sonos 7500, Philips iE33 or Philips CPX50 (Bothell, Washington). The echocardiographic protocol consisted of parasternal long axis views of the ventricles, long axis view of the aortic root and ascending aorta, basal short axis view of the origin of the coronary arteries, mid papillary short axis view of the left ventricle, apical 4-chamber, and 2-chamber views of the left ventricle and pulsed tissue Doppler of the lateral mitral annulus. Digitized images of 2 beats were stored. Digitized images were analysed offline according to the European Society of Echocardiography (ESC) guidelines by cardiologists and expert sonographers. LV mass was automatically calculated by the machine using the Devereux formula (0,8 x 1.04 x [(DTd + SIV + PP)^3 – DTd^3] + 0,6gr. Isometric scaling of LV mass to BSA was chosen, as per American Society of Echocardiography (ASE) and ESC recommendations [14]. LV internal diameter, septal wall thickness, posterior wall thickness and left atrial (LA) diameter were measured from two-dimensional (2D) images in the parasternal long-axis view at both end-diastole and end-systole. Relative wall thickness (RWT) was calculated as the ratio of the sum of the interventricular septum (IVS) and posterior wall (PW) thickness in end-diastole to the left ventricular end-diastolic diameter (LVEDD); care was taken to exclude right

ventricular septal bands and posterior wall chordae when measuring IVS and PW thickness, respectively. According to international guidelines, the RWT upper threshold of normality was 0.42. [14] Calculation of RWT permits categorization of an increase in LV mass as either concentric (RWT >0.42) or eccentric (RWT <0.42) hypertrophy and allows identification of concentric remodelling (normal mass with RWT >0.42) vs normal geometry (normal mass and RWT <0.42).

Finally, systolic function was measured by using the biplane Simpson's rule from the apical four- and two-chamber views, fractional shortening, and visual assessment. LV ejection fraction was considered to be normal when > 50%.

Ethical approval was granted by the National Research Ethics Service, Essex 2 Research Ethics Committee in the UK. Written consent was obtained from individuals ≥16 years and from a parent/guardian for those <16 years.

Statistical analysis was performed using the PASW software (PASW 18.0 Inc, Chicago, IL). Results are expressed as mean ± SD for continuous variables or as number of cases and percentage for categorical variables. Comparison between continuous variables among groups were performed with the analysis of variance (ANOVA) – using the Brown-Forsythe statistic when the assumption of equal variances did not hold – while the proportions were compared by means of the Chi-square test, using Fisher's exact test when necessary. Statistical analysis was performed using PASW software (PASW 18.0 Inc, Chicago, IL, USA).

RESULTS

Baseline demographic features are shown in Table 1. Mean age of athletes was 25±7, 24±5 and 25±1 years, in group 1, 2 and 3, respectively. Athletes were predominantly males (n=45, 90% in group 1, n=86, 99% in group 2, n=219, 90% in group 3). The average hours of exercise per week were 17±6 in group 1, 22±7 in group 2 and 19±7 in group 3 ($p<0.001$ between group 2 and 3). BSA was similar in group 1 and 2 (2.3±0.2 m^2 in group 1 vs 2.3±0.1 m^2 in group 2) but was significantly lower in group 3 (2.0±0.1 m^2, $p <0.001$ between group 1 and 3 and between group 2 and 3). BSA was ≤ 2.3 m^2 in 52% of cases in group 1, 47% in group 2 and 90% of cases in group 3.

In athletes of group 1 the top 5 sports were rugby (n=40, 80%), shooting (n=3, 6%), athletics (n=3, 6%), cricket (n=1, 2%), swimming (n=1, 2%). In athletes of group 2 the top 5 sports were rowing (n=19, 22%), volleyball (n=11, 13%), cricket (n=11, 13%), football (n=10, 11%) and rugby (n=10, 11%).

Table 1 shows the echocardiographic characteristics of the study population. Both athletes of group 1 and group 2 showed an enlarged LV end-diastolic diameter (LVEDD) in comparison with athletes of group 3 (57±6 mm in group 1 *vs* 57±4 mm in group 2 *vs* 53±4 mm group 3, p <0.05 between group 1 and 3 and group 2 and 3, p non-significant between group 1 and 2). Twenty-five (50%) athletes of group 1 *vs* 33 (38%) of group 2 and 31 (13%) of group 3 exhibited a LVEDD > 57 mm (p < 0.001 between group 1 and group 3, p = 0.23 between group 1 and group 2). Figure 2 represents the relationship between LVEDD and BMI and height.

LV maximum wall thickness (MWT) was significantly higher in athletes of group 1 (11±1 mm *vs* 10±2 mm in group 2, p = 0.001, *vs* 9±1 mm in group 3, p < 0.001). Similarly, relative wall thickness RWT was significantly higher in athletes of group 1 (0.37±0.05) *vs* athletes in group 2 (0.35±0.05) and group 3 (0.34±0.05), p < 0.05 between group 1 and 2 and between group 1 and group 3).

Twelve (24%) athletes in group 1 *vs* 19 (21%) in group 2 and 16 (6%) in group 3 exhibited a MWT > 11 mm (p <0.001 between group 1 and group 3, p =0.85 between group 1 and 2 - Figure 3).

Concentric hypertrophy or concentric remodelling was found in 10 athletes of group 1 (20%), in 6 athletes of group 2 (7%) (p =0.04 between group 1 and group 2), and in 16 (6%) athletes in group 3 (Figure 4). On the other hand, 11 athletes (22%) in group 1 *vs* 11 (13%) in group 2 and 38 (16%) in group 3 showed eccentric hypertrophy (p non-significant between the three groups). Normal geometry was found in 29 athletes (58%) in group 1 *vs* 63 (73%) in group 2 and 190 (78%) in group 3 (p =0.07 between group 1 and group 2, p =0.003 between group 1 and group 3, p=0.344 between group 2 and group 3).

We found that 26 (52%) of athletes of group 1 and 41 (47%) of group 2 had a BSA ≤ 2.3 m^2. We compared LVEDD, MWT and the prevalence of concentric remodelling or hypertrophy in athletes of Group 1 with BSA > 2.3 m^2 and athletes from the same Group with BSA ≤ 2.3 m^2. Athletes with BSA ≤ 2.3 m^2 showed smaller LVEDD (53±5 vs 60±5 mm, p <0.001), similar wall thickness (10±1 mm *vs* 11±1 mm, p =0.128), higher RWT

(0.39±0.05 *vs* 0.35±0.04, p=0.006) and higher prevalence of concentric hypertrophy or remodelling (31% vs 8%, p =0.04).

Most athletes were further followed-up (with ECG and echocardiogram) as per Sport organizations screening protocols and none of them developed pathological findings.

The average difference between two independent readers (inter-observer variability based on 80 echocardiograms) was of 1.8±0.4 mm for LVEDD (Kappa inter-observer coefficient of 0.86), 0.6±0.2 mm for interventricular septal thickness (Kappa inter-observer coefficient of 0.79) and 0.5±0.2 mm for posterior wall thickness (Kappa inter-observer coefficient of 0.79).

DISCUSSION

This study provides data on LV dimensions and geometry in a cohort of young *élite* athletes with extreme body anthropometry defined as either high BMI or above-average height. Although previous studies considered BSA as the only marker of large body size, we sought to establish the contribution of both increased BMI and height to LV dimensions and geometry in athletes.

The main findings of our study are: a) both athletes with high BMI/normal height and athletes with normal BMI/above average- height exhibit larger LV dimension and thicker walls than athletes with normal BMI/normal height, meaning that both BMI and above-average height have an impact on LV size and geometry; b) half of athletes with high BMI/normal height has a dilated LV (LVEDD >57mm) and nearly a quarter has a MWT above 11mm; similarly, more than a third of athletes with normal BMI/above average-height a dilated LV and 20% of them has a MWT >11mm; c) athletes with high BMI/normal height exhibit a thicker IVS (11mm) and higher RWT (0.37) and more frequently have concentric hypertrophy/remodelling than athletes with normal BMI/above-average height, while they share similar values of LV dimensions; d) within the group of high BMI/normal height athletes, those with BSA <2.3 mq have similar wall thickness but smaller diameters, greater RWT and higher prevalence of concentric hypertrophy/remodelling compared to those with BSA >2.3 mq.

Regular physical exercise results in physiological electrical, functional and structural cardiac adaptations. [15] These changes may overlap with pathological conditions, such as cardiomyopathies, where strenuous exercise is associated with an increased risk of adverse events including sudden cardiac death. [16–19] It is well established that *élite* athletes exhibit on average a 10–20% increase in LV wall thickness and LVEDD. [1] Electrical and structural changes are determined by a variety of factors including age, gender, type of sport, ethnicity and body size. [8,20–24]

The relationship between body size, long-term exercise and cardiac dimensions is complex. Extreme body anthropometry is supposed to be a key determinant of cardiac adaptation to exercise, but few studies have attempted to address this specific issue.

In the largest study on athletes with extreme anthropometry to date, Riding et al.[8] showed that established upper limits for physiological cardiac hypertrophy of 14 mm for MWT and 65 mm for LVEDD are clinically appropriate for all athletes (including the ones with BSA >2.3m^2). These results have important clinical implications especially in terms of screening, because they define the physiological upper limits of exercise-induced cardiac adaptation in athletes with large BSA, even though the 2.3 m^2 cut-off for definition of extreme anthropometry was arbitrarily established. In our study 52% of athletes with BMI>30 and 47% of extremely tall athletes (height ≥ 1.95 m) had a BSA ≤2.3 m^2. Although most American and European guidelines suggest reference values normalized per BSA, some caution should be exercised when considering BSA as the only measure of anthropometry. The use of allometric scaling as opposed to simple ratio scaling has been suggested by several studies, supporting the thesis that the latter doesn't allow for relationships between body size and cardiovascular variables that accommodate different relative geometries. [25,26]

Our study on a cohort constituted predominantly by male, Caucasian *élite* athletes shows that high BMI is associated with dilated LV, increased LV wall thickness and concentric hypertrophy/remodelling respectively in 50%, 24% and 20% of the cases. These data have useful implications, for example, in the assessment of rugby players, whose body *habitus* is almost invariably defined by elevated BMI (greater body weight and standard-height). We found that particularly in these individuals the echocardiographic findings pose a

diagnostic *dilemma* and several athletes fall in the diagnostic overlap with cardiomyopathies as DCM and HCM (Figure 5). In our series, the upper limits of normality were 72 mm for LVEDD and 14 mm for MWT.

The gaps in knowledge are not limited to athletes with high BMI, but also to athletes with height above average. In this subset of individuals, data on basketball players are the only available. Cardiac adaptation is determined by a mixture of factors and type of sport is likely to represent one of them. Therefore, data limited on only one sport may not apply to the whole spectrum of sporting disciplines. In our cohort, just a minority of athletes with height ≥ 1.95 m and BMI < 30 was a basketball player. Our data confirm that these athletes may develop significant dilatation and physiological hypertrophy, even though RWT was rarely above thresholds of normality, in keeping with a harmonic increase in LV size and wall thickness. The degree of cardiac morphological changes was similar to the one described by Engel et al.[9] in a cohort of National Basketball Association (NBA) professional athletes with comparable average height and BSA.

Our data confirms that no direct linear relationship exists between both high BMI and above-average height and LV size and wall thickness. From our results, speculations can be made about high BMI (intended as weight prevailing over height) having an impact on both LV linear dimensions (LVEDD) and LV wall thickness, resulting in more frequent LV dilatation and increased MWT and higher prevalence of LV hypertrophy/remodelling, while above-average height and BSA influencing more LV dimensions rather than wall thickness, generating a more harmonic adaptation to exercise. This in further corroborated by the fact that in those athletes with BMI>30 and BSA >2.3 LVEDD is larger than those with BSA <2.3 and that these athletes have similar values of RWT and less concentric hypertrophy, suggesting that height might influence primarily LV size.

Nevertheless, BMI is a measure used to determine a person's degree of overweight, on the contrary BSA measures the total surface area of the body. When the height value is fixed, a strong correlation exists between BSA and BMI as only weight values vary. However, when the two parameters change, no correlation exists between BSA and BMI.

Our study has some limitations. Nearly all athletes in our cohort are males. This issue has been raised and discussed in previous studies and reflects mainly social and cultural aspects of sports participation. We

considered only young *élite* athletes of Caucasian ethnicity. Therefore, these results may not be applicable to recreational or veteran athletes and further series including athletes of other ethnicities may show different results in terms of LV geometric remodelling and cut-offs for LV size and physiological hypertrophy. Moreover, we acknowledge that our control group was not matched for type of sports/exercise and there is the possibility that LV remodelling was determined by the sporting discipline, rather than anthropometry solely. Finally, this analysis is cross-sectional, thus we cannot derive any inference about changes in cardiac structure during follow-up.

CONCLUSIONS

Athletes with high BMI and above-average height exhibit more pronounced LV physiological adaptive changes compared to normal BMI/normal height athletes. In particular, athletes with high BMI have similar LV dimensions but greater wall thickness and higher prevalence of concentric remodelling compared to very tall athletes. Athletes with high BMI and large BSA have the widest LV dimensions. Global LV remodelling in response to exercise is complex and multifactorial and no single body-size parameter can predict LV morphology.

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REFERENCES:

1. Pelliccia A, Maron BJ, Spataro A, Proschan MA, Spirito P. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. *N Engl J Med* [Internet]. 1991;324:295–301. Available from: http://www.ncbi.nlm.nih.gov/pubmed/1824720

2. Rawlins J, Carre F, Kervio G, Papadakis M, Chandra N, Edwards C, Whyte GP, Sharma S. Ethnic differences in physiological cardiac adaptation to intense physical exercise in highly trained female athletes. *Circulation* [Internet]. 2010;121:1078–85. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20176985

3. Sharma S, Merghani A, Gati S. Cardiac screening of young athletes prior to participation in sports: difficulties in detecting the fatally flawed among the fabulously fit. *JAMA Intern Med* [Internet]. 2015;175:125–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25384176

4. Sharma S, Merghani A, Mont L. Exercise and the heart: the good, the bad, and the ugly. *Eur Heart J* [Internet]. 2015;1445–1453. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25839670

5. D'Silva A, Sharma S. Management of young competitive athletes with cardiovascular conditions. *Heart* [Internet]. 2016;Available from: http://www.ncbi.nlm.nih.gov/pubmed/27888210

6. Maron BJ. Distinguishing hypertrophic cardiomyopathy from athlete's heart physiological remodelling: clinical significance, diagnostic strategies and implications for preparticipation screening. *Br J Sports Med*. 2009;43:649–656.

7. Finocchiaro G, Dhutia H, Gray B, Ensam B, Papatheodorou S, Miles C, Malhotra A, Fanton Z, Bulleros P, Homfray T, Witney AA, Bunce N, Anderson LJ, Ware JS, Sharma R, Tome M, Behr ER, Sheppard

MN, Papadakis M, Sharma S. Diagnostic yield of hypertrophic cardiomyopathy in first-degree relatives of decedents with idiopathic left ventricular hypertrophy. *Europace* [Internet]. 2020;Available from: http://www.ncbi.nlm.nih.gov/pubmed/32011662

8. Riding NR, Salah O, Sharma S, Carré F, O'Hanlon R, George KP, Hamilton B, Chalabi H, Whyte GP, Wilson MG. Do big athletes have big hearts? Impact of extreme anthropometry upon cardiac hypertrophy in professional male athletes. *Br J Sports Med* [Internet]. 2012;46 Suppl 1:i90-7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23097487

9. Engel DJ, Schwartz A, Homma S. Athletic Cardiac Remodeling in US Professional Basketball Players. *JAMA Cardiol* [Internet]. 2016;1:80–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27437659

10. Finocchiaro G, Dhutia H, D'Silva A, Malhotra A, Steriotis A, Millar L, Prakash K, Narain R, Papadakis M, Sharma R, Sharma S. Effect of Sex and Sporting Discipline on LV Adaptation to Exercise. *JACC Cardiovasc Imaging*. 2017;10.

11. Malhotra A, Dhutia H, Gati S, Yeo T-J, Dores H, Bastiaenen R, Narain R, Merghani A, Finocchiaro G, Sheikh N, Steriotis A, Zaidi A, Millar L, Behr E, Tome M, Papadakis M, Sharma S. Anterior T-Wave Inversion in Young White Athletes and Nonathletes: Prevalence and Significance. *J Am Coll Cardiol* [Internet]. 2017;69:1–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28057231

12. Khosla T, Lowe CR. Indices of obesity derived from body weight and height. *Br J Prev Soc Med* [Internet]. 1967;21:122–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/6033482

13. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. 1916. *Nutrition* [Internet]. 5:303–11; discussion 312-3. Available from: http://www.ncbi.nlm.nih.gov/pubmed/2520314

14. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt J-U. Recommendations for cardiac chamber quantification by echocardiography in

adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* [Internet]. 2015;16:233–70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25712077

15. Pelliccia A, Kinoshita N, Pisicchio C, Quattrini F, Dipaolo FM, Ciardo R, Di Giacinto B, Guerra E, De Blasiis E, Casasco M, Culasso F, Maron BJ. Long-term clinical consequences of intense, uninterrupted endurance training in olympic athletes. *J Am Coll Cardiol* [Internet]. 2010;55:1619–25. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20378081

16. Finocchiaro G, Papadakis M, Robertus J-L, Dhutia H, Steriotis AK, Tome M, Mellor G, Merghani A, Malhotra A, Behr E, Sharma S, Sheppard MN. Etiology of Sudden Death in Sports: Insights From a United Kingdom Regional Registry. *J Am Coll Cardiol* [Internet]. 2016;67:2108–15. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27151341

17. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden Deaths in Young Competitive Athletes: Analysis of 1866 Deaths in the United States, 1980-2006. *Circulation* [Internet]. 2009;119:1085–1092. Available from: http://circ.ahajournals.org/cgi/doi/10.1161/CIRCULATIONAHA.108.804617

18. Harmon KG, Asif IM, Maleszewski JJ, Owens DS, Prutkin JM, Salerno JC, Zigman ML, Ellenbogen R, Rao AL, Ackerman MJ, Drezner JA. Incidence, Cause, and Comparative Frequency of Sudden Cardiac Death in National Collegiate Athletic Association AthletesCLINICAL PERSPECTIVE. *Circulation* [Internet]. 2015;132:10–19. Available from: http://circ.ahajournals.org/lookup/doi/10.1161/CIRCULATIONAHA.115.015431

19. Finocchiaro G, Papadakis M, Dhutia H, Zaidi A, Malhotra A, Fabi E, Cappelletto C, Brook J, Papatheodorou E, Ensam B, Miles CJ, Bastiaenen R, Attard V, Homfray T, Sharma R, Tome M, Carr-White G, Merlo M, Behr ER, Sinagra G, Sharma S. Electrocardiographic differentiation between "benign T-wave inversion" and arrhythmogenic right ventricular cardiomyopathy. *Europace*. 2019;21.

20. Sheikh N, Sharma S. Impact of ethnicity on cardiac adaptation to exercise. *Nat Rev Cardiol* [Internet]. 2014;11:198–217. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24569362

21. Utomi V, Oxborough D, Ashley E, Lord R, Fletcher S, Stembridge M, Shave R, Hoffman MD, Whyte G, Somauroo J, Sharma S, George K. Predominance of normal left ventricular geometry in the male "athlete's heart". *Heart* [Internet]. 2014;100:1264–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24916049

22. Papadakis M, Carre F, Kervio G, Rawlins J, Panoulas VF, Chandra N, Basavarajaiah S, Carby L, Fonseca T, Sharma S. The prevalence, distribution, and clinical outcomes of electrocardiographic repolarization patterns in male athletes of African/Afro-Caribbean origin. *Eur Heart J* [Internet]. 2011;32:2304–2313. Available from: http://eurheartj.oxfordjournals.org/cgi/doi/10.1093/eurheartj/ehr140

23. Basavarajaiah S, Boraita A, Whyte G, Wilson M, Carby L, Shah A, Sharma S. Ethnic differences in left ventricular remodeling in highly-trained athletes relevance to differentiating physiologic left ventricular hypertrophy from hypertrophic cardiomyopathy. *J Am Coll Cardiol* [Internet]. 2008;51:2256–62. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18534273

24. Finocchiaro G, Dhutia H, D'Silva A, Malhotra A, Steriotis A, Millar L, Prakash K, Narain R, Papadakis M, Sharma R, Sharma S. Effect of Sex and Sporting Discipline on LV Adaptation to Exercise. *JACC Cardiovasc Imaging* [Internet]. 2016;Available from: http://www.ncbi.nlm.nih.gov/pubmed/27865722

25. George K, Sharma S, Batterham A, Whyte G, McKenna W. Allometric analysis of the association between cardiac dimensions and body size variables in 464 junior athletes. *Clin Sci (Lond)* [Internet]. 2001;100:47–54. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11115417

26. Chantler PD, Clements RE, Sharp L, George KP, Tan L-B, Goldspink DF. The influence of body size on measurements of overall cardiac function. *Am J Physiol Heart Circ Physiol* [Internet]. 2005;289:H2059-65. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15964929

Table 1. Demographic and echocardiographic characteristics.

	Group 1 (n=50)	**Group 2 (n=87)**	**Group 3 (n=243)**
Age (years)	25±7	24±5	25±1
Males n (%)	45(90)	86 (99)	219(90)
Caucasian n (%)	39 (78) ∞	80 (92)	217 (89)
Height (m)	1.81±0.09 ∞#*	1.98±0.03	1.79±0.12
Weight (Kg)	109±13 ∞#*	96±7	77±8
BSA (m^2)	2.3±0.2 #*	2.3±0.1	2.0±0.1
BSA ≤ 2.3 m^2 n (%)	26 (52) #*	41 (47)	220 (90)
Hours per week	17±6 *	22±7	19±7
LVEDD (mm)	57±6 #*	57±4	53±4
LVEDD > 57 mm n (%)	25 (50) #*	33 (38)	31 (13)
LVEDD > 65 mm n (%)	4 (2)	1 (1)	3 (1)
LVESD (mm)	37±6	37±4	36±4
IVS WT (mm)	11±1 ∞#*	10±2	9±1
PW WT (mm)	10±1 #*	10±2	9±1
MWT > 11 mm n (%)	12 (24) #*	19 (21)	16 (6)
RWT	0.37±0.05 ∞#	0.35±0.05	0.34±0.05
Normal geometry n (%)	29 (58) #	63 (73)	190 (78)
Concentric hypertrophy/remodelling RWT > 0.42 n (%)	10 (20) #*	12 (14)	15 (6)
Eccentric hypertrophy n (%)	11 (22)	11 (13)	38 (16)

Legends: BSA: body surface area; IVS: interventricular septum; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; PW: posterior wall; RWT: relative wall thickness; MWT: maximal wall thickness; WT: wall thickness
Group 1: athletes with BMI ≥ 30 and height < 1.90 m
Group 2: athletes with height ≥1.95 m and BMI <30
Group 3: athletes with BMI between 20 and 29 and height < 1.90 m.
∞ $p < 0.05$ between Group 1 and Group 2
# $p < 0.05$ between Group 1 and Group 3
* $p < 0.05$ between Group 2 and Group 3

FIGURES LEGEND

Figure 1: Study protocol.

Figure 2: Relationship of LV size with BMI and height. Upper panel: a BMI cut-off of 30 was used as per methods; lower panel: a height cut-off of 1.90 was used as per methods. **Abbreviations:** LVEDD: left ventricular end-diastolic diameter.

Figure 3: Maximal left ventricular wall thickness in the three groups and percentages of athletes exceeding normal values. A cut-off of 11 mm was considered to define increased wall thickness. Group 1: athletes with BMI ≥ 30 and height <1.90; Group 2: athletes with height ≥1.90 m and BMI <30; Group 3: athletes with BMI 20-29 and height < 1.90 m. **Abbreviations:** MWT: maximal wall thickness.

Figure 4: Prevalence of geometric patterns in the three groups. Yellow horizontal line identifies LV mass index upper cut-offs in women, while the blue horizontal line identifies the same cut-offs in men. Vertical blue line identifies the values of 0.42. **Abbreviations:** LVMI: left ventricular mass index, RWT: relative wall thickness.

Figure 5: Diagnostic overlap between cardiomyopathies and physiological cardiac adaptation.

Abbreviations: DCM: dilated cardiomyopathy; HCM: hypertrophic cardiomyopathy

Figure 1.

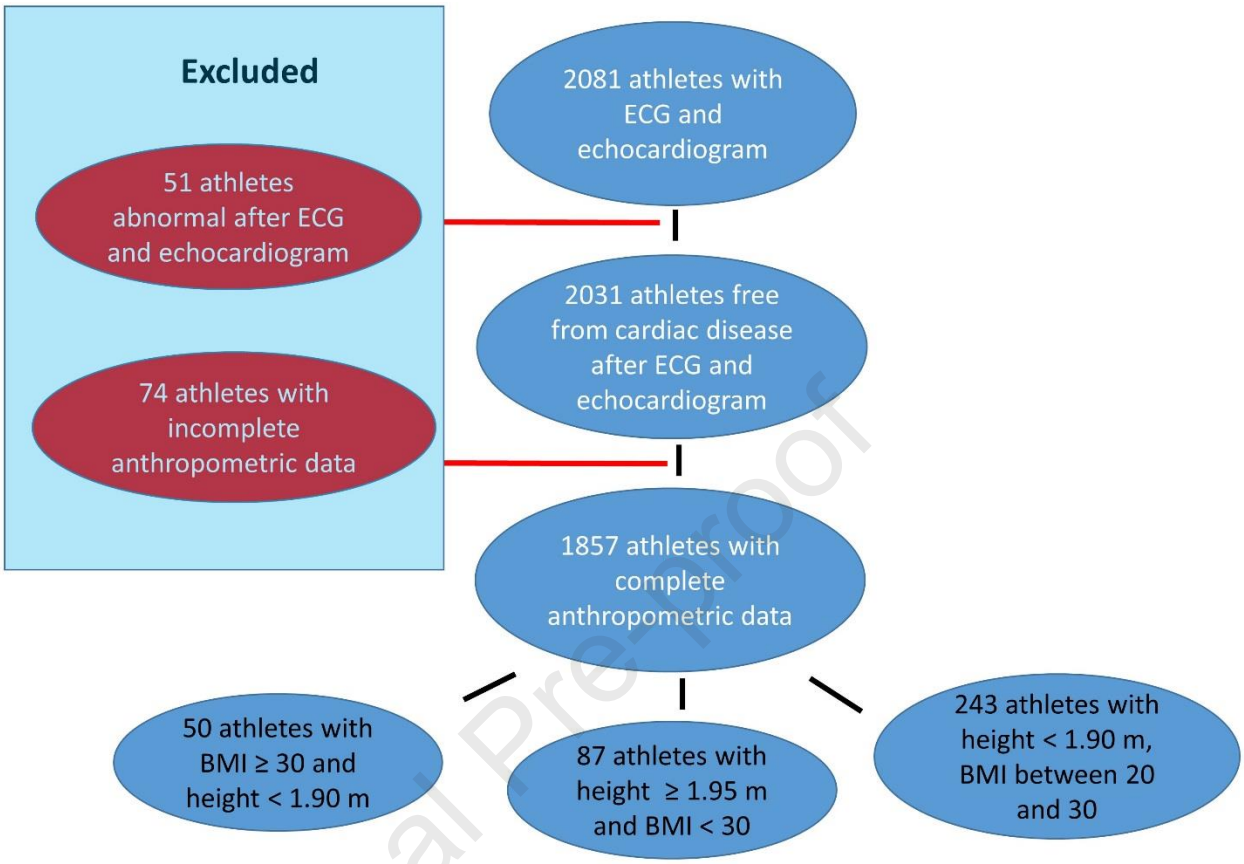

Figure 2.

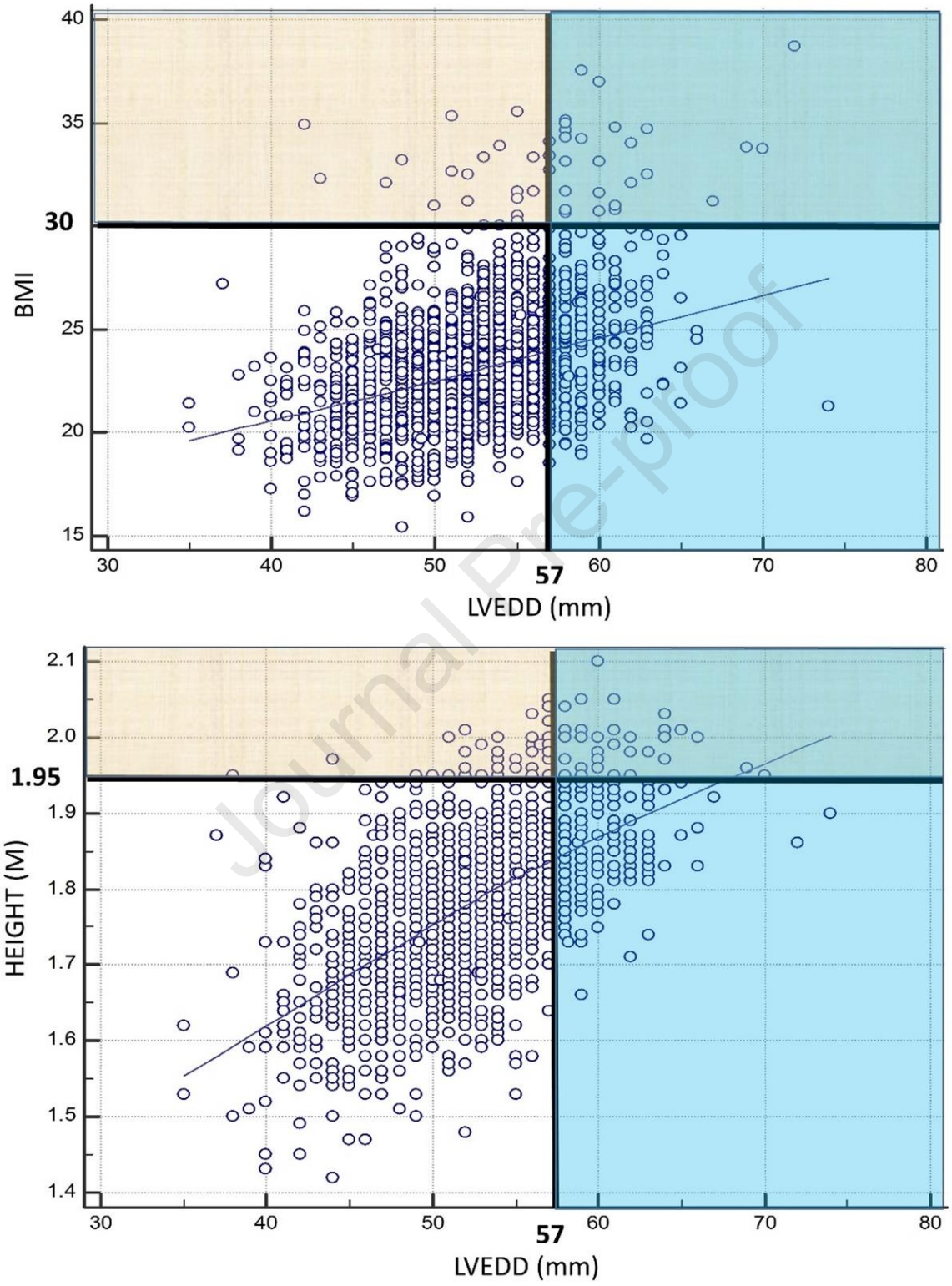

Figure 3.

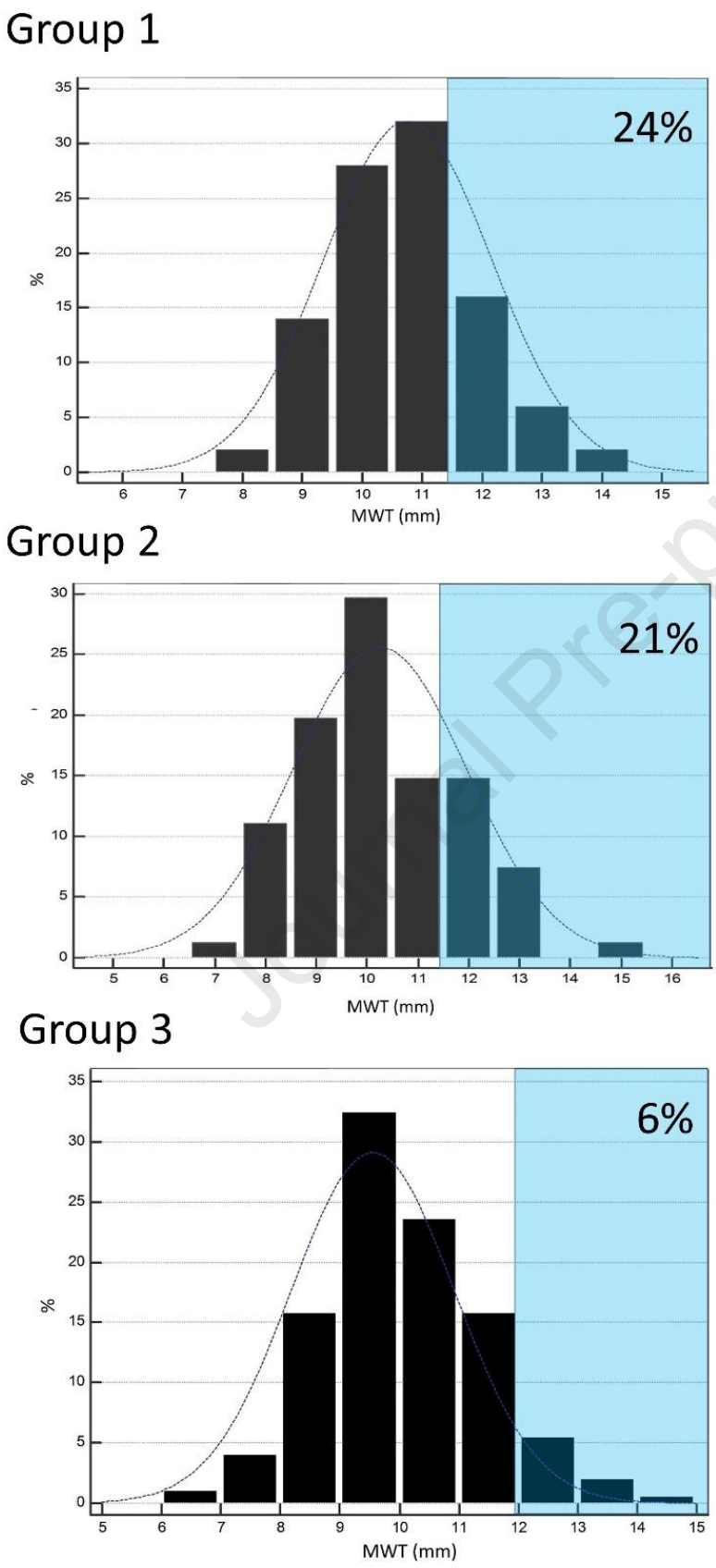

Figure 4.

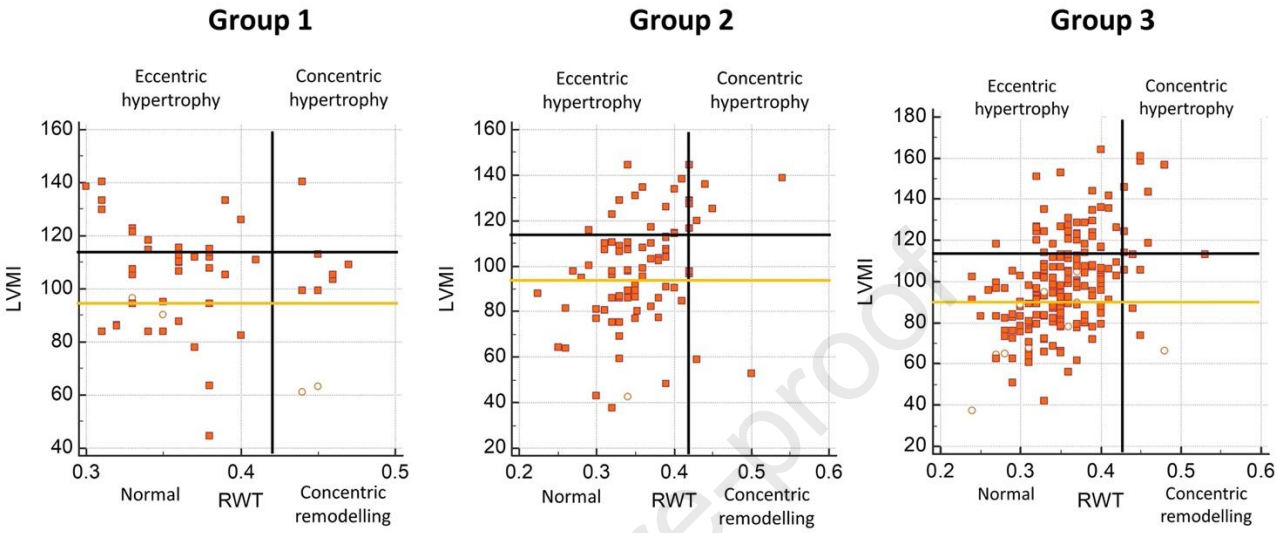

Figure 5