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Variations in indexation of left atrial volume across different races

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ABSTRACT

Background: Left atrial volume (LAV) has prognostic value. Guidelines propose indexation to body surface area (BSA), however studies demonstrate this can overcorrect for body size. Limited studies investigate indexation across different ethnicities. We sought to evaluate the effect of ethnicity on indexation.

Methods: Using data from the World Alliance of Societies of Echocardiography (WASE) cohort, healthy subjects were classified by race as White, Black, Asian, or Other. Biplane LAV was indexed to traditional isometric measurements (BSA, height, weight, ideal body weight (IBW) and IBW derived BSA (IBSA)), as well as previously-derived allometric height exponents (2.7 and 1.72). Additionally, an allometric height exponent for our cohort was derived (linear regression of the logarithmic transformation of LAV $=$ a(height)^{b}) as 1.87. All indices were then assessed using Spearman correlation, with a good index retaining correlation of LAV/index to raw LAV (r$\sim$1), while avoiding overcorrection by the index (r$\sim$0).

Results: There were 1366 subjects (White: 524, Black: 149, Asian: 523, Other: 170; median age 44 years, 653 females (47.8%)). In the entire group, BSA, IBSA, height$^{1.87}$ and height$^{1.72}$ performed well with retaining correlation to raw LAV (r $>$ 0.9 for all), and minimising overcorrection to body size (r $<$ 0.1 for all). On race-specific analysis, BSA overcorrected for body size in the White population (r $=$ 0.128). Height$^{1.72}$ minimised overcorrection for body size in all populations (r $\leq$ 0.1 for all races).

Conclusion: Despite a cohort with normal BMI, there was still disparity in LAV indexation with BSA across races. Allometric height indexation, particularly using height$^{1.72}$, is a possible solution, although further validation studies in BMI extremes are required.

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1. Introduction

Left atrial (LA) size by echocardiography is important in diastolic function evaluation, risk stratification and prognostication of various conditions, including atrial fibrillation, stroke and heart failure. The American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) guidelines [1] recommend that biplane LA volume (LAV), measured from the apical 4 and 2ch views, be indexed to body surface area (BSA). Prior studies have demonstrated that indexing cardiac chamber and aortic size improves prognostic performance [2]. However, recently BSA has been questioned as the best indexation parameter [3,4]. The limitations of BSA in indexation may in part be secondary to racial differences. The EchoNoRMAL study demonstrated that indexation to BSA did not reduce differences in left heart measurements including left ventricular (LV) volumes, LV mass and LAV, and suggested that ethnic-appropriate reference values be utilised [5]. However, having multiple reference values can be tedious for implementation in routine clinical practice.

The allometric model of body size indexation (where the relationship between the body size and cardiac chamber measurement is non-linear), has been shown in various studies to be superior to linear isometric indexation, which is the case with BSA indexation [4,6,7]. The 'theorised' aim for a good indexation marker is to reduce the influence of the body size measurement on the cardiac dimension, whilst still preserving correlation with the cardiac dimension. A recent systematic review demonstrated that allometric indexation to height improved scaling of LAV, maintaining proportionality and reducing overcorrection by body size, especially with the allometric exponent of 2.7 [8–10]. More recently height$^{1.72}$ was proposed, and increased LAV/height$^{1.72}$ was associated with atrial fibrillation (AF) in the general population [11]. However, the utility of allometric indexation of echocardiographic LAV has not been investigated across ethnicities.

Therefore, the present study sought to analyse varying indexation methods of LAV across different ethnicities in a healthy population with 'normal' BMI. The aim was to identify the best indexation parameter that performed well across different races (maintaining correlation to raw LAV, whilst minimising body size dependence).

2. Methods

2.1. Patient selection

The study included participants from the World Alliance of Societies of Echocardiography (WASE) study, the methodology of which has been described previously [12,13]. The WASE normal values study is a multi-centre, cross-sectional study of healthy adult individuals with normal BMI. From September 2016 to January 2019, 19 centres in 15 countries enrolled subjects ≥18 years of age, with no prior history of cardiac disease or risk factors. The study was approved by the local ethics committee of each participating institution, and subjects provided consent as mandated by each of the enrolling centre's institutional review boards or ethics committees.

For the purposes of this report, "normal" or "acceptable risk" BMI was defined as 18.5–27.5 kg/m^2 for Asian populations, and 18.5–30 kg/m^2 for other populations, as per recommendations of the World Health Organisation (WHO) expert consultation [14]. Enrolled subjects were classified into different race groups: White, Asian, Black and Other (mixed race and middle eastern Asian).

2.2. Echocardiographic measurements and indexation

A comprehensive transthoracic echocardiogram was acquired for all patients following ASE/EACVI guidelines [1,12]. LAV was measured at end-systole from the 4 and 2-chamber apical views, using the Simpson biplane method of discs. All 2 dimensional (2D) image analysis was performed using a vendor-neutral workstation (Image Arena, TOMTEC, Munich, Germany) in one Core Laboratory in the US (MedStar Health Research Institute, Washington, DC). For this study, only biplane 2D LA volumes were analysed.

LAV indexation parameters that were evaluated included isometric parameters such as BSA, height (m), weight (kg), ideal body weight (IBW), and BSA from ideal body weight (IBSA). IBW was used as it was considered similar to lean body mass [15], and was calculated using the Knoben method [16] with the formula IBW (kg) = 50 + 0.91 (height (cm) - 152.4) in males and IBW (kg) = 45.5 + 0.91 (height (cm) - 152.4) in females. BSA was calculated using the DuBois & DuBois method [17], with the formula BSA [m^2] = weight [kg]$^{0.425}$ × height (cm)$^{0.725}$ × 0.007184. Allometric indexation to height was performed, including the previously proposed allometric height exponents of 2.7 and 1.72 [8–11] as well as our newly-derived exponent (see below).

2.3. Statistical analysis

We derived the ideal allometric indexation marker for height in our cohort similar to previous studies [6]. Firstly, the equation $Y = aX^b$ was considered, where Y is LAV, X is height, a is the scaling factor and b is the scaling exponent. Logarithmic transformation of this equation, i.e. $Ln(Y) = Ln(a) + b*Ln(X)$, was performed to derive the exponent. A linear regression model was then used to estimate the appropriate value of b and 95% confidence interval for the dataset.

Categorical variables are expressed as count (percentage) and continuous variables are expressed as median (interquartile range), due to them being non-normally distributed. LAV values using various indexation markers were expressed across different races and sexes. Categorical variables were compared using a Chi-Square test. Continuous variables of various LA indexation measurements were compared across races using non-parametric tests (Mann-Whitney and Kruskal-Wallis tests). The threshold for significance was determined as $p < 0.05$.

Correlation coefficients (Spearman's correlation) were obtained of the indexed LAV to 1) raw LAV and 2) body size marker, and these were plotted across the whole group (Fig. 1) and across races (Fig. 2). Absolute r values are presented for comparison (as the direction of the correlation is less relevant, whilst the degree of correlation is). As such, absolute 95% confidence intervals (CI) are presented in the figures; if the 95% CI crossed 0, the CI was presented from 0 to the highest absolute magnitude to represent greatest possible variability. The original Spearman's r values, 95% CI and p-values are presented in the supplementary data. An ideal indexation parameter was expected to scale proportionally to LA size (r closest to 1 being the best model), whilst remaining independent of body size (r closest to 0 being the best model) [8]. Whilst there are no previous studies reporting an exact threshold for these correlations, in our study $r > 0.9$ for indexed LAV: raw LAV and $r < 0.1$ for indexed LAV: indexation marker were considered ideal for an indexation parameter.

As a WHO recommended definition for BMI range was used for the Asian population, a subgroup analysis was performed with all races being BMI 18.5–27.5 kg/m^2, to assess for consistency of the results.

IBM SPSS Statistics version 28 (Chicago, IL, USA) and R Studio Version 4.2 (Vienna, Austria) were used to analyse the data.

3. Results

Table 1 demonstrates the demographic, anthropometric and LAV measurements across the 4 race groups. The original cohort was 1946; 580 were excluded due to unmeasurable 2D biplane LAV. A total of 1366 subjects were thus evaluated, including White: 524, Black: 149, Asian: 523, Other: 170. The median age was 44 years (IQR 31–64) with 653 females (47.8%). Sex and age distribution were similar across all 4 race groups ($p = 0.828$ and $p = 0.256$ respectively). Systolic and diastolic blood pressure measurements varied across the race and sex groups ($p < 0.001$ by Kruskal-Wallis test); however, clinically the median values remained in the normal range (approximately 120/80).

All anthropometric markers (BMI, BSA, IBW, IBSA) were significantly different between the race groups (Table 1). Asian people had the lowest average measurements, whereas White people had the highest. All indexed values were significantly different between the race groups, except indexation to weight, which demonstrated no difference ($p = 0.118$).

Figs. 1 and 2 illustrate the correlation coefficients for each indexation marker to raw LAV and to body size, (exact (non-absolute) correlation values and 95% CI included in the supplementary data). Fig. 1 schematically demonstrates the balance between the two correlations for all subjects, whilst Fig. 2 demonstrates the correlation across the 4 race groups. In both Figs. 1 and 2, a good indexation marker is represented in the bottom right corner (representing increased correlation to raw LAV and inverse correlation to body size marker, maintaining the parameter's size-independence). The derived allometric exponent for height in our cohort was 1.87 (1.58–2.15, $p < 0.01$). In the entire group, BSA, IBSA, height, height$^{1.87}$ and height$^{1.72}$ performed well with retaining correlation to raw LAV ($r > 0.9$ for all). With respect to correlation to body size, IBSA, BSA, height$^{1.87}$ and height$^{1.72}$ performed well ($r < 0.1$ for all). Height$^{1.87}$ removed the effect of body size to a greater extent than BSA (LAV/height$^{1.87}$ to height$^{1.87}$ = 0.004 (0–0.058) vs LAV/BSA to BSA = 0.083 (0.029–0.137)) and so did height$^{1.72}$ ((LAV/height$^{1.72}$ to height$^{1.72}$ = 0.023 (0–0.077)). Furthermore, height$^{1.72}$ was similar to our derived exponent height$^{1.87}$ (r to raw LAV = 0.949 (0.943–0.954) for $H^{1.72}$ and 0.940 (0.933–0.946) for $H^{1.87}$ and r to

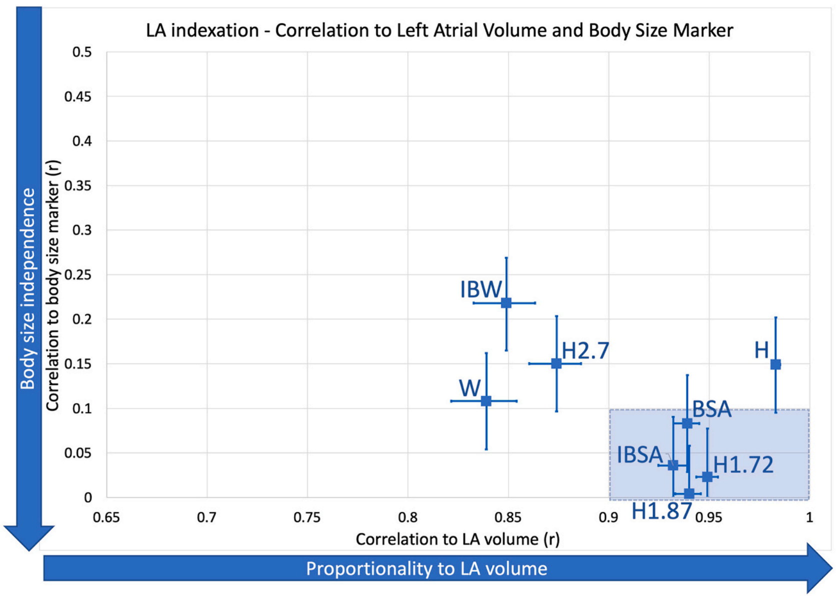

Fig. 1. Schematic illustration of Correlation of Indexed LAV to raw LAV and body size marker (r with 95% CI*) across the whole group. A good indexation marker retains good correlation to LAV (r~1) and avoids overcorrection by body size marker (r~0). This is represented by the blue box where $r > 0.9$ and $r < 0.1$ respectively. *BSA: body surface area, H: Height, W: Weight, IBW: Ideal body weight, IBSA: Ideal body surface area (calculated from IBW), LA: left atrial.* * Absolute r values and 95% confidence intervals (CI) are presented; if the 95%CI crossed 0, the CI is represented from 0 to the highest absolute magnitude to represent greatest possible variability.

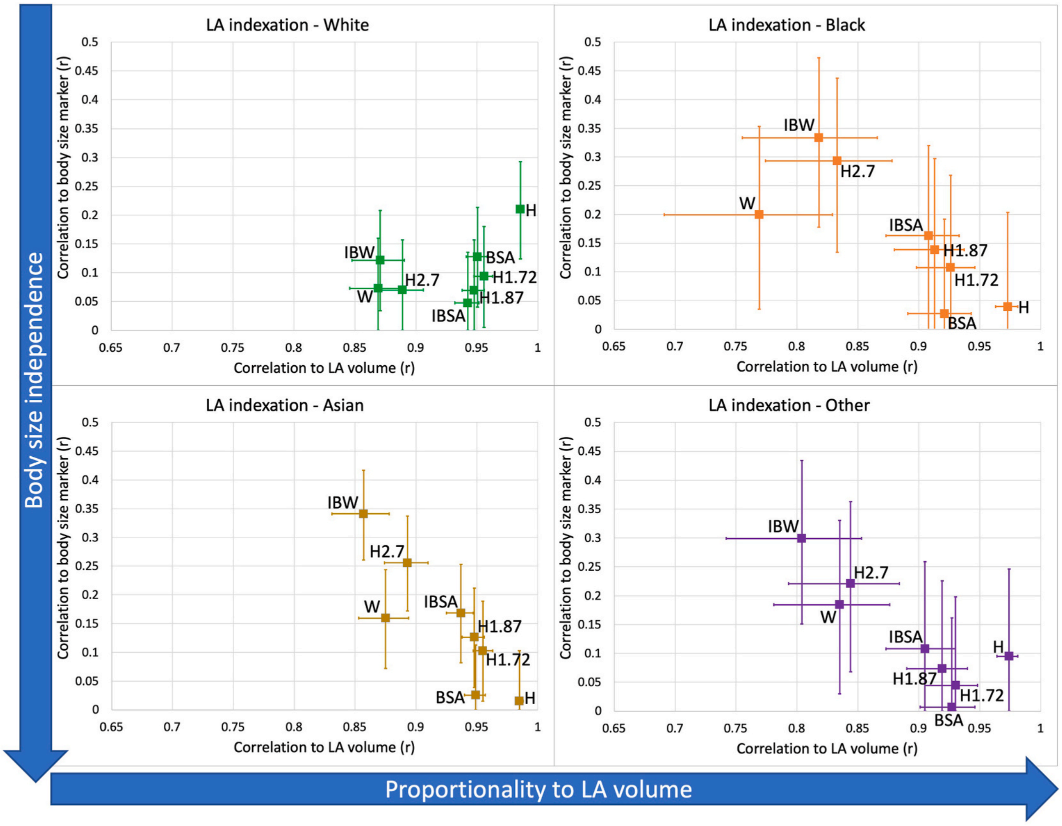

Fig. 2. Schematic illustration of Correlation of Indexed LAV to raw LAV and body size marker (r with 95% CI*) across different races. A good indexation marker is which retains good correlation to LAV (r~1), and avoids overcorrection by body size marker (r~0). In all graphs, this is represented by the bottom right corner. *BSA: body surface area, H: height* *Absolute r values and 95% confidence intervals (CI) are presented in the figures; if the 95%CI crossed 0, the CI is presented from 0 to the highest absolute magnitude to represent greatest possible variability.

body size = 0.023 (0–0.077) for $H^{1.72}$ vs 0.004 (0–0.058) for $H^{1.87}$). IBSA was slightly better than standard BSA, with less influence of body size (r = 0.036 (0–0.09) vs 0.083 (0.029–0.137) respectively).

For differences between races (Fig. 2), BSA indexation appeared better for Black, Asian and Other compared to White groups. Isometric height was the best index for Black and Asian people, whereas allometric $height^{1.72}$ was better than isometric height for White and Other groups. In general, $height^{1.72}$ performed better than $height^{2.7}$ for all races. IBSA was a particularly good index in the White population, whereas in the other race groups, it retained body size dependence ($r > 0.1$). $Height^{1.72}$ was a reasonably good indexation parameter across all races, and performed better than $height^{2.7}$ that was previously proposed. In Black and Asian populations there was only a minor influence of body size, r = 0.107 (0–0.268) and 0.103 (0.015–0.189) respectively, and $Height^{1.72}$ performed slighter better than $Height^{1.87}$ in these populations.

In the subgroup analysis of BMI 18.5–27.5 kg/m2 across all races (Total n = 1228; 446 White, 114 Black, 523 Asian, 145 Other), the derived indexation parameter for height was 1.70 (1.40–2.00, $p < 0.01$). As this was similar to previously analysed parameter of 1.72, the latter was retained for the analysis for comparison purposes. The supplementary figure demonstrates the correlation coefficients for each indexation marker to raw LAV and to body size. The results were similar to the general analysis with good correlations for $Height^{1.72}$ (r to raw LAV 0.948 (0.942–0.953), r to body size 0.005 (0–0.062)), BSA (r to raw LAV 0.942 (0.935–0.948), r to body size 0.057 (0–0.114)) and $Height^{1.87}$ (r to raw LAV 0.938 (0.931–0.945), r to body size 0.031 (0–0.088)).

4. Discussion

This is the first study to examine different methods of LAV indexation across ethnicities at a large scale. Our results reveal the complexity of LAV indexation across different races, even in a normal BMI cohort. We demonstrate that allometric indexation to height (particularly $height^{1.72}$) performed well across races at minimising body size correction, whilst retaining correlation to raw LAV.

4.1. Problems with BSA indexation

The goal of indexation is to eliminate the effect of the subject's body size on cardiac chamber size, whilst retaining correlation to the

Table 1
Characteristics including anthropometric measurements and indexed LAV across different Races.

RACE	Total N=1366	White n=524	Black n=149	Asian N=523	Other N=170	p-value*
Sex (female)	653 (47.8)	253 (48.3)	67 (45)	248 (47.4)	85 (50)	0.828
Age (years)	44 (31–64)	48 (31–66)	43 (32–58)	43 (31–63)	44 (34–58)	0.256
SBP (mmHg)	120 (110–129)	119 (110–125)	122 (114–129)	122 (114–130)	120 (110–126)	<0.001
DBP(mmHg)	73 (69–80)	71 (66–80)	73 (67–81)	76 (70–81)	70 (60–80)	<0.001
Height (m)	1.67 (1.6–1.75)	1.7 (1.63–1.78)	1.68 (1.62–1.75)	1.63 (1.57–1.7)	1.68 (1.6–1.73)	<0.001
Weight (kg)	66 (58–75)	72 (62–80)	70 (62–81)	60 (54–68)	69 (61–76)	<0.001
BMI (kg/m^2)	23.8 (21.9–25.9)	24.6 (22.7–26.6)	25.1 (22.1–27.4)	22.7 (21.1–24.5)	24.7 (23.1–26.7)	<0.001
BSA (m^2)	1.75 (1.61–1.9)	1.83 (1.68–1.97)	1.8 (1.67–1.95)	1.64 (1.53–1.79)	1.77 (1.64–1.91)	<0.001
IBW (kg)	61.5 (52.4–69.7)	64.2 (56.9–73.3)	62.4 (56.1–70.6)	57 (49.7–66)	61.5 (52.4–67.8)	<0.001
IBSA (m^2)	1.68 (1.53–1.84)	1.76 (1.6–1.91)	1.71 (1.6–1.85)	1.6 (1.48–1.77)	1.69 (1.53–1.8)	<0.001
Height$^{1.72}$ (m$^{1.72}$)	2.42 (2.24–2.62)	2.49 (2.33–2.7)	2.44 (2.29–2.62)	2.32 (2.17–2.49)	2.44 (2.24–2.57)	<0.001
Height$^{1.87}$ (m$^{1.87}$)	2.61 (2.41–2.85)	2.7 (2.51–2.94)	2.64 (2.46–2.85)	2.49 (2.32–2.7)	2.64 (2.41–2.79)	<0.001
Height$^{2.7}$ (m$^{2.7}$)	3.99 (3.56–4.53)	4.19 (3.77–4.74)	4.06 (3.68–4.53)	3.74 (3.38–4.19)	4.06 (3.56–4.39)	<0.001
LAV (mL)	43.9 (35.3–54.6)	46.8 (37–58)	48.1 (40.8–60.1)	39.8 (31.4–49.3)	46.1 (36.5–54.7)	<0.001
LAV/BSA (mL/m^2)	25.2 (20.5–30.7)	25.3 (20.7–31.6)	26.6 (23–32.7)	24.6 (19–29.5)	25.9 (21.8–30.9)	<0.001
LAV/height (mL/m)	26.5 (21.2–32.7)	27.5 (22.1–34)	28.6 (24.6–35.6)	24.6 (19.1–30)	27.1 (22–33.1)	<0.001
LAV/height$^{1.72}$ (mL/m$^{1.72}$)	18.2 (14.7–22.4)	18.7 (15.2–23.3)	19.7 (16.7–24.4)	17.3 (13.5–20.9)	19.2 (15.4–22.6)	<0.001
LAV/height$^{1.87}$ (mL/m$^{1.87}$)	16.82 (13.63–20.85)	17.21 (14.02–21.48)	18.27 (15.44–22.5)	16.02 (12.59–19.57)	17.83 (14.21–21.01)	<0.001
LAV/height$^{2.7}$ (mL/m$^{2.7}$)	11.09 (8.9–13.59)	11.1 (8.97–13.66)	11.83 (9.7–14.41)	10.68 (8.25–13.11)	11.55 (9.44–13.84)	<0.001
LAV/weight (mL/kg)	0.661 (0.54–0.801)	0.651 (0.533–0.812)	0.693 (0.598–0.801)	0.665 (0.53–0.801)	0.66 (0.549–0.788)	0.118
LAV/IBW (mL/kg)	0.73 (0.585–0.898)	0.735 (0.591–0.906)	0.786 (0.636–0.942)	0.694 (0.55–0.866)	0.762 (0.613–0.914)	<0.001
LAV/IBSA (mL/m^2)	26.3 (21.2–32.3)	26.8 (21.7–33.3)	28.3 (24.3–35.1)	24.7 (19.3–30.5)	27.7 (21.8–32.8)	<0.001

*p-value for sex was derived from Chi-squared test, the remaining variables were Kruskal-Wallis for different races. Data presented as median and interquartile range for continuous variables and number and percentage for categorical variables. BMI: body mass index, BSA: body surface area, DBP: diastolic blood pressure, IBW: Ideal body weight, IBSA: Ideal body surface area (calculated from IBW), LAV: left atrial volume, SBP: systolic blood pressure.

original measurement. Overall, BSA was a reasonable indexation marker across races, albeit in a cohort with normal BMI. However, this was less so for White persons due to overcorrection by body size, as demonstrated by retention of a correlation of LAV/BSA to BSA ($r = 0.128$). Previous studies, albeit in predominant Caucasian populations, demonstrated that indexation to BSA overcorrects for body size [6,8,18], with overcorrection particularly evident at a higher BMI. A recent study demonstrated that with a BMI ≥40 kg/m^2, LAV indexed to BSA loses prognostic value [18]. This is likely because organ size does not vary much based on weight fluctuations [19]. As such, using BSA is problematic as there is an assumed linear relationship between cardiac structures and body size, that fails to account for the fact that body composition affects cardiac size [20]. Moreover, it is considered that cardiac size is determined by fat-free mass [21,22], indicating the relationship between skeletal and cardiac muscle. Therefore, obesity and body composition have a significant impact on LA size indexation.

BSA derived from IBW (IBSA) was a better indexation marker than standard BSA in the overall cohort, as it reduced overcorrection by body size. However, on race-specific analysis, this was predominantly in the White population (with other races retaining size-dependence). The superiority of IBSA over BSA is likely because the former correlates better with fat-free mass [23]. Moreover, an enlarged left atrium based on IBSA indexation was a better predictor of mortality than BSA indexation in obese populations [18]. This is also likely because indexation to IBSA is similar mathematically to indexing to allometric height [13].

4.2. Allometric height indexation across races

Overall, the derived allometric height indexation marker in the entire cohort (height$^{1.87}$) was better than BSA indexation as it reduced the influence of body size. The previously proposed parameter of Height$^{1.72}$ was similar to our derived parameter height$^{1.87}$ in the overall cohort, and was slightly better in Black and Asian populations with respect to correction for body size. Moreover, Height$^{1.72}$ was consistently a good parameter in both the WHO definition of 'acceptable risk' BMI (where Asians were considered as 18.5–27.5 kg/m^2, and the rest as 18.5–30 kg/m^2) as well in the subgroup when all races were considered the same BMI 18.5–27.5 kg/m^2 (and was similar to the derived allometric height exponent in the subgroup of height$^{1.70}$).

Importantly, studies report various ideal height exponents for LAV indexation. Previous reports demonstrate that exponents closer to 1.7–2 are ideal for LAV indexation [10,11,24], though other studies report ideal LAV indexation with height exponents closer to 1 [25–27], and this may represent the inherent variability in ethnicity, as demonstrated in our study. Moreover, previous studies reporting higher exponents likely had a greater proportion of Caucasian/White populations.

4.3. Ethnic variation in cardiac chamber indexation

There are limited studies that examine LAV indexation across races. Our results are consistent with previous studies where BSA indexation did not remove cardiac chamber size (including LAV) difference between ethnicities [5]. Moreover, using cardiac magnetic-resonance-imaging derived LA volumes, Chinese American (Asian) people consistently had lower LAV despite indexation to BSA, height or height$^{1.7}$ [28]. Prior reports have shown that LV mass is highest in African-Americans, and lowest in Asian-Americans [29], suggesting inherent differences in cardiac structures between races. Furthermore, cardiac adaptation to exercise differs between White and Black athletes [30]. Multiple factors likely affect the relationship between body size and cardiac chamber size, including cardiac output, oxygen consumption and heart-rate during development [31]. Therefore, it would seem intuitive that metabolically active tissue mass such as fat-free mass would best correlate to cardiac size, and fat-free mass varies significantly between sexes and ethnicities, providing an explanation for ethnic differences [32]. Furthermore, in a small study, indexation by fat-free mass as compared to height and BSA improved the integration of LA and left ventricular volumes across different ethnicities [33].

4.4. Clinical implications

The current study demonstrates that indexing to allometric height, particularly Height$^{1.72}$, as previously proposed [11], performed well in minimising correction by body size, whilst maintaining correlation to raw LAV for all races. However, further studies are required to assess its applicability in extremes of BMI across different races. Further outcome data is also required, although Olsen et al. has already demonstrated that LAV/Height$^{1.72}$ was a better predictor of AF than LAV/BSA [11]. Having a single indexation parameter that is applicable across all races minimises the complexity and inefficiency of utilising different reference values for each race (i.e., EchoNoRMAL study - [5]). An alternative solution, as mentioned previously, may be indexation to fat-free mass. However, a feasible and accurate measurement of body composition is still a challenge, although this may improve with technological advancements. Other studies have suggested the potential utility of waist circumference or waist-hip ratio, which have a better relationship to LA phasic volumes and reservoir function than BMI, likely because they are a better reflector of adiposity [34].

4.5. Study limitations

Only subjects with normal BMI were studied, as they comprised the WASE cohort. We did not have access to obese subjects to investigate BMI extremes across race groups. However, this is also a strength of our study, because despite 'homogeneity' of the cohort with respect to BMI, we still demonstrated race-based differences. Despite attempts to achieve equal group recruitment by the WASE investigators, certain groups e.g. Black and Other groups were under-represented. In addition, we acknowledge the addition of the race group "other", which consisted predominantly of mixed race groups, would pose difficulty in clinical application. A number of patients had to be excluded (n = 580, 235 White, 18 Black, 216 Asian, and 111 other) as they had suboptimal biplane LA views for volume calculation, and this may have resulted in selection bias. Moreover, it is important to note that intra-race variations in body composition may exist (e.g. south Asians versus east Asians versus southeast Asians), however it was beyond the scope of this study to examine these subgroups. We did not have outcome data to determine which LAV indexation parameter had prognostic value. Whilst fat-free mass could be a powerful marker of indexation, this was not measured and hence was unavailable for comparison with allometric height in this study cohort.

5. Conclusion

Despite a population with normal BMI, there was disparity with LAV indexation across races. Indexation with allometric height raised to an exponent of 1.72, performed well as it minimised body size correction, and maintained proportionality to LAV across all races. Further validation studies including varying BMI groups with outcome data are required to determine the clinical utility of this indexation parameter across races.

Declarations

The study was approved by the local ethics committee of each participating institution, and subjects provided consent as mandated by each enrolling centre's institutional review boards or ethics committees. For the Medstar core lab, ethics was approved by The MedStar Health Institutional Review Board (approval number 2016-266). The WASE study was supported by the American Society of Echocardiography. There was no particular funding source for this manuscript.

Author contribution statement

Conceived and designed the experiments: AF, LT, FP, RL, FA, EK.

Performed the experiments: AF, LT, JE.

Analysed and interpreted the data: AF, LT, JE, FP, EK.

Contributed reagents, materials, analysis tools or data: RL, FA, AS, CS, TM, WASE investigators (Aldo D Prado, Karima Addetia, Michele Bellino, Masao Daimon, Pedro Gutierrez Fajardo, Ravi R Kasliwal, James N Kirkpatrick, Mark J Monaghan, Denisa Muraru, Kofo O Ogunyankin, Seung Woo Park, Ricardo E Ronderos, Anita Sadeghpour, Gregory M Scalia, Masaaki Takeuchi, Wendy Tsang, Edwin S Tucay, Ana Clara Tude Rodrigues, Amuthan Vivekanandan, Yun Zhang).

Wrote the paper: AF (first draft), LT, FP, EK, RL, FA

Data availability statement

Data will be made available on request.

WASE contribution

The WASE (World Alliance Societies of Echocardiography) group consists of investigators from international centres who enrolled normal subjects and performed echocardiograms. They contributed the echocardiographic images for this study. RL and FA are the principal investigators of the WASE group. The raw measurements on these echocardiographic images were performed by the core lab group (listed authors - AS, CS, TM, FA, RL). These measurements were provided for subsequent indexation and analysis for this study, which was performed by AF, LT, JE, FP, EK.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20334.

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