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ORIGINAL RESEARCH

Impact of Height Exponents on the **Diagnosis and Prognosis of LVH**

The REMODEL Study

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ABSTRACT

BACKGROUND Left ventricular hypertrophy (LVH) is a strong predictor of adverse outcomes. Although normalizing LV mass (LVM) to height exponents reduced variability from body size, specific recommendations for height exponents are lacking due to a scarcity of normal cohorts to define appropriate height exponents.

OBJECTIVES The authors aimed to show the diagnostic and prognostic implications of establishing height exponents specific to sex, ethnicity, and imaging modality.

METHODS Nonoverweight/nonobese Asian healthy volunteers (n = 416) were used to establish appropriate height exponents. The impact of these height exponents was examined in a separate cohort of Asian subjects with hypertension (n = 878). All individuals underwent standardized cardiovascular magnetic resonance imaging. The primary outcome was a composite of acute coronary syndrome, heart failure hospitalization, stroke, and cardiovascular mortality.

RESULTS The height exponents for healthy female subjects and male subjects were 1.57 and 2.33, respectively. LVH was present in 27% of individuals with hypertension when indexed to body surface area and 47% when indexed to sexspecific height exponents. Most individuals reclassified to LVH with height exponents were overweight or obese. There were 37 adverse events over 60 months (37-73 months) of follow-up. Regardless of indexing method, LVH was independently associated with increased adverse events (height exponent HR: 2.80 [95% Cl: 1.25-6.29; P = 0.013]; body surface area HR: 5.43 [95% CI: 2.49-11.8; P < 0.001]).

CONCLUSIONS Reference ranges specific to ethnicity, sex, and imaging modality are necessary to establish appropriate height exponents. Although using height exponents resulted in more LVH reclassification, this did not translate to a notable improvement in event prediction. (JACC Asia. 2025;5:350-357) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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eft ventricular mass (LVM) is a powerful predictor of cardiovascular risk.¹⁻³ LVM strongly relates to body size, indicating the need for appropriate normalization. In adults, LVM is commonly indexed to body surface area (BSA), although this method has been criticized for underestimating left ventricular hypertrophy (LVH) in those who are overweight and obese.⁴

One proposed approach is normalization of LVM by height to some allometric power. For echocardiography, indexing LVM by height to the allometric power of 1.7 or 2.7 has shown the best relation to body size and events prediction.⁵⁻⁷ Although cardiovascular magnetic resonance (CMR) imaging is increasingly used in assessing LVM, the existing body of research on allometric exponents in this context is focused on the MESA (Multi-Ethnic Study of Atherosclerosis) cohort.^{7,8}

Although the MESA study cohort is distinguished by its ethnic diversity, the intrinsic effects of ethnicity may not fully be discerned if certain ethnic groups are underrepresented. Consequently, the determination of appropriate height exponents and reference ranges contingent upon factors such as sex, ethnicity, and imaging modalities remain inadequately elucidated. This underscores the urgent need for more precise diagnostic approaches for LVH. This aim of the current study was to examine the impact of sex-specific height exponents on the diagnosis and prognosis of LVH, leveraging Asian cohorts of health and hypertension.

METHODS

STUDY POPULATION. The study was performed with 2 cohorts. The healthy cohort consisted of volunteers without cardiac symptoms, coronary artery risk factors, and clinical and family history of cardiovascular disease who were prospectively recruited from the community. Healthy volunteers who were overweight/obese (body mass index [BMI] >23.0 kg/m² in Asia) and had abnormal cardiac findings (regional wall motion abnormalities, impaired left ventricular (LV) function and/or cardiomyopathies) on CMR imaging were excluded. This cohort was used to establish reference ranges of LVM indexed to sex-specific height exponents.

The impact on the diagnosis and prognosis of LVH based on LVM indexed to BSA, height exponents defined from our cohort of healthy volunteers, and those published in previous studies (height^{1.7} and height^{2.7}) were then tested in the REMODEL (Response of the Myocardium to Hypertrophic Conditions in the Adult Population; NCT02670031)

cohort. The REMODEL is a prospective,
observational cohort of asymptomatic pa-
tients with essential hypertension.
9,10,11 The
diagnosis of hypertension was guided by
contemporary recommendations at the time
of study initiation: 1) physician-diagnosed
essential hypertension, receiving at least
one medication for blood pressure control; or
2) newly diagnosed hypertension with office
blood pressure ≥140/90 mm Hg on at least
2 separate clinic visits. Individuals with sec-
ondary causes of hypertension, cardiovascu-
lar diseases, inherited cardiomyopathies,
atrial fibrillation, and contraindications to gadolin-A H
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ium contrast and CMR were excluded.

Ethics approvals were obtained from the Sing-Health Centralised Institutional Review Board, and all participants provided written informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

BMI AND BSA. In all individuals, BMI was computed as $\frac{\text{weight (kg)}}{\text{height (m)}^2}$. Asian BMI thresholds were used to define classifications into normal (BMI <23.0 kg/m²), overweight (BMI 23.0-27.5 kg/m²), and obese (BMI >27.5 kg/m²).¹² BSA was calculated by using the DuBois formula¹³ as follows: BSA = weight (kg)^{0.425} × height (cm)^{0.725} × 0.007184.

CMR IMAGING AND ANALYSIS. All study participants underwent CMR (Siemens Aera 1.5T, Siemens Healthineers) with standardized imaging protocols. Balanced steady-state free precession cine images were acquired in the LV long-axis 2-, 3-, and 4-chamber views and short-axis cines extending from the atrioventricular ring to the apex (acquired voxel size, $1.6 \times 1.3 \times 8.0 \text{ mm}^3$; 30 phases per cardiac cycle).

Deidentified imaging data were analyzed at the National Heart Research Institute Singapore CMR Core Laboratory using a dedicated software (CVI42; Circle Cardiovascular Imaging) by individuals who were blinded to the clinical and outcome data. Cardiac volumes, function, and LVM were analyzed according to published protocols.¹⁴ LVH was defined according to age- and sex-specific reference ranges of LVM indexed to BSA and height exponents.

PRIMARY AND SECONDARY OUTCOMES. The primary outcome in the REMODEL cohort was a composite of hypertension-related events, defined as acute coronary syndromes (ACS), heart failure hospitalization, stroke, and cardiovascular mortality. Secondary outcome was a composite of ACS, heart failure hospitalization, stroke, and all-cause mortality. Recruitment started in February 2016, and

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

BMI = body mass index

BSA = body surface area

CMR = cardiovascular magnetic resonance

LV = left ventricular

LVH = left ventricular hypertrophy

LVM = left ventricular mass

TABLE 1 Baseline Characteristics of Healthy Volunteers and Patients With Hypertension									
	Healthy Volunteers (n = 416)	Patients With Hypertension (n = 878)	P Value						
Clinical characteristics									
Age, y	47.8 ± 15.4	58.0 ± 10.6	<0.001						
Female	257 (62)	336 (38)	<0.001						
Hyperlipidemia	-	429 (49)	-						
Diabetes	-	188 (21)	-						
24-h SBP, mm Hg	-	131 ± 14	-						
24-h DBP, mm Hg	-	79 ± 9	-						
Office SBP, mm Hg	127 ± 19	143 ± 18	< 0.001						
Office DBP, mm Hg	75 ± 12	83 ± 12	<0.001						
Body surface area, m ²	$\textbf{1.60} \pm \textbf{0.10}$	1.80 ± 0.20	<0.001						
Measures on cardiovascular magnetic resonance									
LV mass, g	67 ± 18	96 ± 32	< 0.001						
LV mass, g/m ²	42 ± 9	53 ± 14	< 0.001						
LV mass, g/height	41 ± 10	58 ± 18	<0.001						
LV mass, g/height ^{1.7}	29 ± 6	40 ± 12	< 0.001						
LV mass, g/height ^{2.7}	18 ± 4	24 ± 7	< 0.001						
LV mass, g/height ^{1.57 (F)/2.33 (M)}	27 ± 5	33 ± 9	<0.001						

Values are mean \pm SD or n (%).

 $\mathsf{DBP}=\mathsf{diastolic}\ \mathsf{blood}\ \mathsf{pressure};\ \mathsf{LV}=\mathsf{left}\ \mathsf{ventricular};\ \mathsf{SBP}=\mathsf{systolic}\ \mathsf{blood}\ \mathsf{pressure}.$

participants were followed up until December 2023. Data of patients lost to follow-up and who did not have an event were censored at the date when patient was last known to be alive.

STATISTICAL ANALYSIS. Continuous variables were assessed for normal distribution by using the Shapiro-Wilk test. Data are presented as either mean \pm SD or median (IQR), as appropriate. Analyses were performed by using R version 4.3.1 (R Foundation for Statistical Computing) and SPSS version 24 (IBM SPSS Statistics, IBM Corporation), assuming a two-sided test with a 5% level of significance.

Healthy volunteer cohort. The relationship between LVM and body height was modeled according to the allometric equation $y = a \cdot x^b$, where y is LVM in grams, a is a constant, x is height in meters, and b represents the height power exponent. The x and y variables were logarithmically transformed: $\ln (y) = \ln (a) + b \cdot \ln (x)$.¹⁵ Subsequently, ordinary least squares linear regression was performed to estimate the allometric scaling exponent, b.

Separate simple linear regression analyses were used to model the association between LVM and age in male and female subjects. Reference ranges were defined by using the 95% prediction interval: mean \pm $t_{0.975, n-1}$ ($\sqrt{(n+1)/n}$)·(SD). To account for the sample size, 95% CIs of the upper and lower reference limits were also estimated. Values within these confidence intervals were considered "indeterminate abnormal/ borderline normal."¹⁶

REMODEL cohort. Time-to-event analysis of primary and secondary outcomes in hypertensive patients with LVH (unindexed, indexed to BSA, and height exponents) was performed by using multivariable Cox proportional hazards models adjusted for diabetes, hyperlipidemia, and systolic blood pressure. The model of unindexed LVM was additionally adjusted for height and weight. The assumption for proportional hazards was assessed by using the log (–log[survival]) plots.

RESULTS

The study included 416 healthy volunteers (mean age 48 \pm 15 years; female, n = 257) and 878 patients with hypertension (mean age 58 \pm 11 years; female, n = 336; systolic blood pressure 131 \pm 14 mm Hg) (Table 1).

DERIVATION OF HEIGHT EXPONENTS AND REFER-ENCE RANGES. Simple linear regression was performed after logarithmic transformation of LVM and height. The height exponents for healthy female and male subjects were 1.57 and 2.33, respectively (**Figure 1**). Sex-specific reference ranges in LVM, both unindexed and indexed to BSA and height exponents, were established (**Table 2**). When normalized to height exponents, female subjects had higher LVM compared with male subjects ($28 \pm 5 \text{ g/h}^{1.57}$ vs $24 \pm 4 \text{ g/h}^{2.33}$; P < 0.001). Conversely, when normalized to BSA, female subjects had lower LVM compared with male subjects ($38 \pm 6 \text{ g/m}^2$ vs $49 \pm 8 \text{ g/m}^2$; P < 0.001).

IMPACT ON THE DIAGNOSIS OF LVH IN INDIVIDUALS WITH HYPERTENSION. In the REMODEL cohort, LVH was present in 236 (27%) and 409 (47%) individuals when LVM was indexed to BSA and sex-specific height exponents, respectively. Across BMI categories, classification of LVH was concordant in 80% of individuals (n = 701) between LVM indexed to BSA and sex-specific height exponents. LVM indexed to height exponents reclassified 175 individuals to having LVH, with more reclassifications across higher BMI categories: normal BMI, n = 4 (2.3%); overweight, n = 58 (33%); and obese, n = 113 (65%). Conversely, only 2 individuals (both with normal BMI) were reclassified as having LVH when LVM was indexed to BSA (Figure 2).

PROGNOSTIC VALUE OF LVH USING SEX-SPECIFIC HEIGHT EXPONENTS. There were 37 primary and 47 secondary outcomes over median 60 months (37-73 months) of follow-up: ACS, n = 12; heart



failure hospitalization, n = 8, stroke, n = 12; cardiovascular deaths, n = 5; and noncardiovascular deaths, n = 10.

of the method of diagnosis, LVH was independently associated with increased primary and secondary outcomes. LVH diagnosed based on LVM indexed to BSA was associated with the highest numerical HR, but its 95% CIs overlapped with those of other LVH measures (Figure 3).

We examined the prognosis of LVH diagnosed with unindexed LVM, indexed to BSA and height exponents (including height^{1.7} and height^{2.7}). Regardless

TABLE 2 Sex-Specific Reference Ranges in LV Mass																
	All	Age 20-29, y (n = 32)		Age 30-39, y (n = 41)		Age 40-49, y (n = 62)		Age 50-59, y (n = 70)			Age >60, y (n = 52)					
Female Subjects	(N = 257)	Lower	Mean	Upper	Lower	Mean	Upper	Lower	Mean	Upper	Lower	Mean	Upper	Lower	Mean	Upper
LV mass	58 ± 10	38-43	58	73-78	38-43	58	73-78	37-42	58	73-78	37-42	57	73-78	37-42	57	72-78
Indexed LV mass, g/m ²	$\textbf{38} \pm \textbf{6}$	25-28	37	46-50	25-28	37	47-50	25-28	38	47-50	26-29	38	47-51	26-29	38	48-51
Indexed LV mass, g/h ^{1.57}	28 ± 5	18-20	27	34-37	18-20	27	35-37	18-21	28	35-37	19-21	28	35-37	19-21	28	35-38
Indexed LV mass, g/h ^{1.7}	26 ± 4	17-19	26	32-34	17-19	26	32-35	17-20	26	33-35	18-20	26	33-35	18-20	27	33-35
Indexed LV mass, g/h ^{2.7}	17 ± 3	10-12	16	20-22	10-12	16	20-22	11-12	16	21-22	11-12	17	21-22	11-13	17	21-23
Indexed LV mass, g/h	36 ± 6	24-27	36	45-48	24-27	36	45-48	24-27	36	45-48	24-27	36	46-49	24-27	37	46-49
	All	Age 20-29, y (n = 37)		Age 30-39, y (n = 16)		Age 40-49, y (n = 27)		Age 50-59, y (n = 34)		Age >60, y (n = 45)						
Male Subjects	(N = 159)	Lower	Mean	Upper	Lower	Mean	Upper	Lower	Mean	Upper	Lower	Mean	Upper	Lower	Mean	Upper
LV mass	83 ± 16	60-68	93	117-125	57-65	89	114-122	53-62	86	110-118	50-58	83	107-115	47-55	79	104-112
Indexed LV mass, g/m ²	49 ± 8	35-39	52	64-68	34-38	51	63-67	33-37	50	62-66	32-36	48	61-65	31-35	47	60-64
Indexed LV mass, g/h ^{2.33}	24 ± 4	17-19	25	31-33	16-18	25	31-33	16-18	24	31-33	16-18	24	30-32	15-17	24	30-32
Indexed LV mass, g/h ^{1.7}	34 ± 6	24-27	36	44-47	23-26	35	44-47	23-25	34	43-46	22-25	33	42-45	21-24	33	42-44
Indexed LV mass, g/h ^{2.7}	20 ± 3	13-15	20	26-27	13-15	20	25-27	13-15	20	25-27	13-15	20	25-27	13-14	20	25-26
Indexed LV mass, g/h	49 ± 9	35-40	53	66-70	34-38	51	64-69	32-37	50	63-67	31-35	49	62-66	30-34	47	60-65

Values given in the upper and lower confidence intervals of the reference limits are considered "indeterminate abnormal/borderline normal." The lower bound of the upper reference limit was used as the diagnostic cutoff for left ventricular (LV) hypertrophy in this study.



DISCUSSION

Despite the potential merit of allometric scaling, current guidance on appropriate scaling coefficients is lacking. Furthermore, there is a paucity of studies to critically assess the influence of ethnicity on allometric scaling and outcomes. In this CMR study,5-7 height exponents in Asian subjects differed between sexes (2.33 in male subjects and 1.57 in female subjects), contrasting with the single height exponent of 1.7 or 2.7 reported in previous echocardiographic studies. Utilizing these exponents in individuals with hypertension resulted in increased reclassification of individuals with hypertensive LVH, particularly among those who were overweight and obese. However, this alternative approach of indexing LVM did not translate to significant improvement in event prediction (Central Illustration).

ALLOMETRIC SCALING INCREASES THE DIAGNOSIS

OF LVH. Ideally, LVM should be normalized to lean/ fat-free muscle mass. A clinically practical and convenient surrogate of fat-free mass is body height, and allometric height-exponent indexing of LVM potentially overcomes the limitation of underestimating LVH in overweight or obese individuals. Indeed, the study found nearly a 2-fold increase in LVH prevalence when height-exponent indexing of LVM was used. These results were consistent with previous studies that reported how LVM indexed to height, height^{2.13}, or height^{2.7} diagnosed significantly more LVH than when indexed to BSA.^{4,17-20} Also consistent with previous studies, a large proportion of the patients who were reclassified as having LVH based on height-exponent indexing were overweight or obese.^{4,8,21}

PROGNOSTIC IMPACT OF DIFFERENT LVH MEASURES. In echocardiographic studies, indexing LVM to height^{1.7} or height^{2.7} has shown the best relationship to body size and event prediction.⁵⁻⁷ CMR is widely recognized as an important imaging modality in diagnosing LVH because of its superior accuracy and precision in assessing LVM.²² The two CMR studies used the MESA cohort to examine the importance of LVM indexed to height exponents and reported a higher prevalence of LVH for measures that did not account for weight, but there were no important differences in prognostic value among the indices studied.^{7,8}



Compared with these contemporary CMR studies, the current study had a larger cohort of a homogeneous ethnicity and with a wider age range (20-88 years vs 45-84 years in the MESA cohort). We showed that LVH diagnosed based on height-exponent and BSA indexing was similar in predicting adverse outcomes. Although the HR of LVH indexed to BSA was numerically higher, the CI overlapped with those indexed to height exponents. This agrees with studies that reported similar cardiovascular events and mortality risk regardless of either BSA or height-exponent indexing being used.^{7,17,18,20}

CLINICAL IMPLICATIONS. In nonobese individuals, the approach of normalization will likely not have a significant impact on the diagnosis of LVH. In contrast, in populations with a high prevalence of obesity, indexing with BSA underestimates the effects of obesity and reduces the prevalence of LVH.

Our findings endorse the importance of normalizing LVM by height exponents in such a scenario. For this application, it is crucial that the appropriate reference ranges specific to the ethnicity, sex, and imaging modality be established.

The current study found that the diagnosis of LVH, whether based on either BSA or height-exponent indexing, was concordant in 80% of patients with hypertension. Moreover, the distribution of adverse outcomes related to LVH across BMI categories was similar regardless of the indexing approach. Although height-exponent indexing maximizes the populationattributable risk, this consideration must also be balanced against the lack of a significant improvement in event prediction. These findings resonant with a recent real-world echocardiography study, which showed that height-based indexing of cardiac dimensions (including LVM) did not improve prognostication beyond BSA.²³



In this cardiovascular magnetic resonance study, the appropriate height exponents were 1.57 in Asian female (F) subjects and 2.33 in Asian male (M) subjects. Normalizing to height exponents increased the diagnosis of hypertensive left ventricular hypertrophy (LVH), predominantly in those who were overweight and obese. Regardless of the method of indexing, LVH was associated with adverse primary and secondary outcomes. BMI = body mass index; BSA = body surface area; LV = left ventricular; LVM = left ventricular mass.

STUDY LIMITATIONS. We acknowledge the study was limited by a relatively small number of events. However, the observed findings are consistent with existing knowledge of the prognostic value of height exponents. Although our investigations showed that indexing LVM to height exponents reduced variability attributed to body size and sex, the allometric exponents established in Asian subjects warrant further validation and comparison with other ethnicities using the same imaging modality. Such efforts will enhance the generalizability and robustness of the findings across different demographic profiles.

CONCLUSIONS

Normal reference ranges specific to the ethnicity, sex, and imaging modality are necessary to establish appropriate height exponents. The current study reported that Asian male and female subjects have unique height exponents, differing from those observed in earlier studies. Although the adoption of height exponents resulted in increased reclassification of individuals with LVH, this did not translate to a notable improvement in event prediction.

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