JACC: CARDIOVASCULAR IMAGING
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PUBLISHED BY ELSEVIER

VOL. 15, NO. 6, 2022

ORIGINAL RESEARCH

Indexing Left Atrial Volumes

Alternative Indexing Methods Better Predict Outcomes in Overweight and Obese Populations

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ABSTRACT

BACKGROUND Left atrial volume (LAV) is often adjusted for body surface area (BSA). In overweight individuals this may result in underestimation of left atrial (LA) dilation. The authors investigated whether alternative indexing techniques better predict mortality and cardiovascular (CV) events.

OBJECTIVES The purpose of this study was to evaluate the efficacy of different methods of indexing LAV in predicting mortality and CV events across a range of body sizes.

METHODS LAV was adjusted for BSA, idealized BSA (iBSA), height, and height-squared (H^2) in patients aged over 50 years who underwent outpatient echocardiography and longitudinal follow-up at our institution. LA dilation was categorized using published criteria. Mortality and CV events were assessed via medical records.

RESULTS LAVs were calculated in 17,454 individuals. In this study, 71.2% were overweight or obese. Indexing using iBSA, height, and H^2 resulted in reclassification of LA size in up to 28.4% ($P < 0.001$) compared with indexing using BSA. In severely obese individuals (body mass index [BMI] $\geq$40 kg/m^2), LA dilation indexed for BSA no longer predicted mortality ($P = 0.70$). Other indexing methods remained predictive of mortality. Height, H^2, and iBSA all had greater performance, compared with BSA, for prediction of mortality and CV events in all overweight patients with H^2 showing the best overall performance ($P < 0.001$). Net reclassification index for mortality was significant for all alternative indexing techniques ($P < 0.001$) and patients whose LA was reclassified from normal to dilated had increased risk of mortality ($P < 0.001$) and CV events ($P < 0.001$) across all BMI categories.

CONCLUSIONS LA dilation based on standard indexing using BSA is nondiscriminatory for prediction of mortality in the severely obese. Indexing using height, H^2, or iBSA to diagnose LA dilation better predicts mortality in this population and has better overall predictive performance across all overweight and obese populations. Using BSA indexing may lead to underappreciation of LA dilation and underestimation of patients at increased risk.
(J Am Coll Cardiol Img 2022;15:989–997) © 2022 by the American College of Cardiology Foundation.

Rates of obesity are increasing worldwide with more than one-third of adults being overweight or obese.[1] In the developed world the prevalence is higher with up to 73.6% of the population overweight and 42.5% obese.[2,3] These rates of obesity are reflected in patients seen in modern echocardiography practices and obesity is recognized as a challenge to the acquisition and accurate

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received August 24, 2021; revised manuscript received February 4, 2022, accepted February 9, 2022.

ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2022.02.006

JACC: CARDIOVASCULAR IMAGING, VOL. 15, NO. 6, 2022
JUNE 2022:989–997

ABBREVIATIONS AND ACRONYMS

ASE = American Society of Echocardiography

AUC = area under the curve

BMI = body mass index

BSA = body surface area

CV = cardiovascular

H^2 = height-squared

iBSA = idealized body surface area calculated for a subject BMI of 25 kg/m^2

IDI = integrated discrimination index

LA = left atria/left atrial

LAV = left atrial volume

NRI = net reclassification index

OR = odds ratio

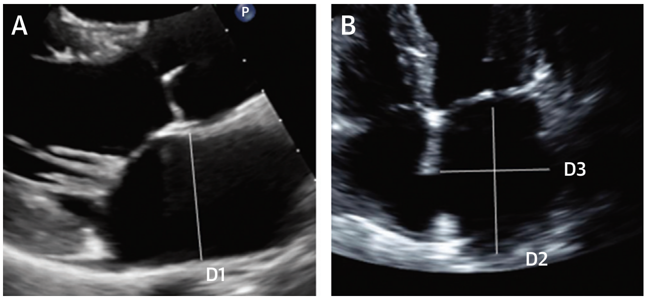
ROC = receiver operator characteristic

interpretation of echocardiographic images.[4,5] This is particularly true where echocardiographic parameters are indexed using body surface area (BSA), which includes both height and weight.[5]

Assessment of left atrial (LA) size is a component of comprehensive transthoracic echocardiography. Current guidelines recommend assessment of LA size by indexing left atrial volume (LAV) to BSA.[6] LAV indexed for BSA performs better than LA area or LA dimension in predicting incident cardiovascular (CV) events.[7] In overweight and obese individuals, indexing LAV for BSA may underestimate the presence and degree of LA dilation.[5,8] Recent hypertension guidelines have suggested height-based indexing of LAV[9] although this has not yet been endorsed by major echocardiographic societies.[6,10] Much of the data underlying current indexing recommendations are based on studies[7,11] in patients whose body mass index (BMI) was <30 kg/m^2, which may not accurately reflect a large percentage of the population seen in echocardiographic practices. There is a paucity of data examining how best to index LAV in obese or severely obese individuals.

We investigated the efficacy of various methods of indexing for LA dilation to predict mortality and CV events across a range of BMI categories. We hypothesized LA dilation determined using height, height-squared (H^2), or ideal BSA (iBSA) based indexing techniques would better predict mortality and incident CV events among the overweight and obese.

FIGURE 1 Calculation of LAV Using the Ellipsoid Method



Three left atrial (LA) measurements were obtained from images optimized for the LA at end systole. D1 is the anterior-posterior (A-P) dimension measured perpendicular to the aortic root long axis in the parasternal long axis view, D2 is the superior inferior (S-I) dimension measured between the mitral annulus and the back wall of the left atrium, and D3 is the medial lateral (M-L) dimension orthogonal to D2 measured from the apical 4-chamber. Left atrial volume (LAV) was calculated using the following formula: (D1(A-P) × D2(S-I) × D3(M-L)) × (0.523).

METHODS

STUDY POPULATION. Our institutional echocardiography database was assessed for patients older than 50 years of age who underwent outpatient echocardiography where 3 measurements of LA dimension and the patients height and weight were recorded. Patients with history of valve surgery, congenital heart disease, or cardiac transplantation or with mechanical circulatory assist devices were excluded. To maximize clinical data, from this cohort ($n = 34{,}962$), we limited analysis to patients receiving the majority of their care at our center ($n = 17{,}454$).[12,13] Follow-up was calculated from a patient's earliest eligible transthoracic echocardiography. Patients were defined as overweight (BMI ≥25 and <30 kg/m^2), obese (BMI ≥30 and <40 kg/m^2), and severely obese (BMI ≥40 kg/m^2) based on BMI.

ECHOCARDIOGRAPHIC DATA. All quantitative echocardiographic data was derived from the clinical echocardiographic report performed by attending cardiologists with level III certification in echocardiography. Echocardiographic protocols and quality assurance programs exist to minimize measurement error and inter-reader variability in our institution. Three LA measurements were obtained as demonstrated in Figure 1. LAV was derived using the formula: (D1(A-P) × D2(S-I) × D3(M-L) × (0.523)).[14] Biplane LAV by disk summation algorithm was available in a subgroup of individuals. Measurements of left ventricular function were derived from the clinical echocardiogram report and reported in compliance with American Society of Echocardiography (ASE) recommendations.[6] Height and weight were recorded at the time of echocardiography.

INDEXING OF LAV MEASUREMENTS. LAVs were indexed for BSA, iBSA, height, and H^2. BSA was calculated using the Mosteller formula,[6,15] and repeated using 2 alternative formulae to ensure consistency.[16,17] We calculated iBSA using standard BSA formula but using a derived weight that would correspond to a BMI of 25 kg/m^2 for each patient. Indexed LAVs were categorized as dilated or nondilated using ASE criteria for BSA and iBSA (dilated >34 mL/m^2),[6] and published reference values by gender for height (dilated male >35.7 mL/m, female >33.7 mL/m)[18] and H^2 (dilated male >18.5 mL/m^2, female >16.5 mL/m^2).[9] Individuals were considered to have LA size reclassified if there was discrepancy between size indexed for BSA and either iBSA, height,

TABLE 1 Baseline Clinical Characteristics and Echocardiographic Parameters

	Whole Cohort (N = 17,454)	BMI <25 kg/m^2 (N = 4,818)	Overweight (N = 6,541)	Obese (N = 5,192)	Severely Obese (N = 903)	*P* Value
Age at echo, y	68.63 ± 10.56	70.69 ± 11.07	69.30 ± 10.54	66.87 ± 9.81	63.12 ± 8.48	<0.001
Female, %	47.2% (n = 8,230)	58.0 (n = 2,795)	38.5 (n = 2,520)	46.0 (n = 2,388)	58.4 (n = 527)	<0.001
BMI, kg/m^2	28.76 (6.2)	22.43 ± 1.93	27.36 ± 1.43	33.51 ± 2.61	45.34 ± 6.36	<0.001
Height, cm	169.07 ± 10.62	168.04 ± 10.33	170.47 ± 10.51	168.76 ± 10.81	166.2 ± 10.60	<0.001
Weight, kg	82.49 ± 20.19	63.68 ± 10.16	79.82 ± 10.76	95.79 ± 14.15	125 ± 6.53	<0.001
BSA, m^2	1.96 ± 0.27	1.72 ± 0.19	1.94 ± 0.19	2.12 ± 0.22	2.40 ± 0.27	<0.001
Baseline factors						
Hypertension, %	84.1 (n=14,675)	75.7 (n = 3,649)	84.4 (n = 5,522)	89.7 (n = 4,655)	94.0 (n = 849)	<0.001
Hypercholesterolemia, %	80.6 (n = 14,074)	74.3 (n = 3,579)	82.3 (n = 5,383)	84.2 (n = 4,374)	81.7 (n =738)	<0.001
Diabetes, %	31.0 (n = 5,406)	20.0 (n = 963)	28.2 (n = 1,847)	40.5 (n = 2,101)	54.8 (n = 495)	<0.001
Myocardial infarction, %	24.3 (n = 4,240)	21.4 (n = 1,029)	25.0 (n = 1,635)	26.5 (n = 1,374)	22.4 (n = 202)	<0.001
Cardiac revascularization, %	12.6 (n = 2,193)	10.7 (n = 516)	14.0 (n = 919)	12.9 (n = 672)	9.5 (n = 86)	<0.001
Atrial fibrillation, %	27.0 (n = 4,707)	27.6 (n = 1,332)	28.0 (n = 1,830)	26.0 (n = 1,348)	21.8 (n = 197)	<0.001
Stroke/TIA, %	27.9 (n = 4,871)	29.5 (n = 1,442)	29.5 (n = 1,930)	26.1 (n = 1,354)	18.3 (n = 165)	<0.001
Current smoking, %	7.6 (n = 1,325)	6.5 (n = 314)	7.0 (n = 456)	9.1 (n = 471)	6.3 (n = 84)	<0.001
Echocardiographic characteristics						
Ejection fraction, %	64.84 ± 10.19	64.78 ± 10.40	64.62 ± 10.17	65.09 ± 10.07	65.36 ± 9.83	0.035
LA dimension AP, mm	38.75 ± 6.04	36.20 ± 6.27	39.16 ± 5.60	40.21 ± 5.68	40.92 ± 5.42	<0.001
LA dimension SI, mm	54.67 ± 7.60	52.1 ± 8.07	54.93 ± 7.33	56.24 ± 6.97	57.29 ± 6.80	<0.001
LA dimension ML, mm	42.43 ± 6.52	41.39 ± 6.68	42.53 ± 6.29	43.07 ± 6.56	43.46 ± 6.37	<0.001
LA volume, mL	48.82 ± 19.45	42.86 ± 19.38	49.45 ± 18.60	52.55 ± 19.4	54.65 ± 18.55	<0.001

AP = anterior-posterior; BMI = body mass index; BSA = body surface area; LA = left atrial; ML = medial-lateral; SI = superior-inferior; TIA = transient ischemic attack.

or H^2. Clinically significant reclassification was considered to have occurred in individuals whose LA size was nondilated when indexed for BSA and dilated when indexed for iBSA, height, or H^2.

OUTCOME VARIABLES. Demographics, baseline comorbidities at the time of echocardiography, and outcome measures were determined using the electronic health record to November 2020. The primary outcome variable was all-cause mortality obtained from the electronic health record, which integrates clinical records and the social security death index to identify dates of death. The secondary outcome variable was incident CV events including the following: myocardial infarction, unstable angina, coronary revascularization, heart failure, ventricular arrythmia, stroke, transient ischemic attack, and atrial fibrillation. Data on CV events were obtained from institutional coding data and time to CV events was determined by the first eligible event. All aspects of this study comply with the Declaration of Helsinki and were approved by the Institutional Review Board. The need for informed consent was waived.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD, or median (IQR), and compared using independent samples *t* tests and 1-way analysis of variance or Wilcoxon signed rank and Kruskal-Wallis tests. Categorical variables are reported as absolute numbers and percentages and compared using chi-square test. The association between LA dilation and outcome measures was explored using binary logistic regression and Cox proportional hazard models adjusted for age, sex, baseline CV risk factors (hypertension, hypercholesterolemia, diabetes and smoking), and diagnosis of atrial fibrillation at the time of echocardiography. Based on an a priori hypothesis that the effect alternative indexing techniques would be greatest at extremes of body size, the effect of BMI category on the relationship between LA dilation and mortality was explored using an interaction variable and analysis stratified by BMI category was undertaken. The impact of reclassification on outcome variables was examined using binary logistic regression, net

TABLE 2 Reclassification of LA Size Based on Alternative Indexing Techniques

	iBSA	Height	H^2
% reclassified (whole cohort)	5.0% (n = 866)	11.7 (n = 2,049)	28.5% (n = 4,977)
% reclassified BMI <25 kg/m^2	0% (n = 0)	2.6% (n = 124)	15.2% (n = 732)
% reclassified overweight	2.7% (n = 175)	10.1% (n = 659)	25.7% (n = 1,678)
% reclassified obese	10.1% (n = 520)	19.0% (n = 988)	39.8% (n = 2,067)
% reclassified severely obese	18.9% (n =171)	30.8% (n = 278)	55.4% (n = 500)

H^2 = height-squared; iBSA = idealized body surface area; other abbreviations as in Table 1.

TABLE 3 Odds Ratio for All-Cause Mortality Based on Different Indexing Methods

	BSA			iBSA			Height			H^2		
	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value
Whole cohort	2.34	2.09-2.62	<0.001	2.10	1.90-2.33	<0.001	2.08	1.89-2.28	<0.001	1.99	1.82-2.17	<0.001
BMI <25 kg/m^2	2.46	2.02-2.99	<0.001	2.17	1.75-2.68	<0.001	2.47	2.05-2.97	<0.001	2.29	1.94-2.70	<0.001
Overweight	2.61	2.18-3.13	<0.001	2.60	2.20-3.08	<0.001	2.40	2.06-2.80	<0.001	2.08	1.79-2.41	<0.001
Obese	1.92	1.54-2.41	<0.001	1.78	1.48-2.14	<0.001	1.74	1.47-2.07	<0.001	1.89	1.59-2.24	<0.001
Severely obese	1.16	0.55-2.44	0.70	1.97	1.28-3.04	0.002	1.67	1.11-2.51	0.013	2.12	1.34-3.37	0.001

Abbreviations as in Tables 1 and 2.

reclassification index (NRI), and integrated discrimination indices (IDI).[19] In exploratory analysis, sensitivity and specificity of different methods of classifying LA size for predicting mortality and CV events were explored using receiver operator characteristic (ROC) curves and compared by assessing the area difference under the ROC curve using nonparametric assumptions. Statistical analyses were undertaken using IBM SPSS Statistics Subscription (IBM Corporation) and SAS (SAS Institute).

RESULTS

PATIENT POPULATION AND BASELINE DEMOGRAPHICS. In this study, 17,454 patients aged older than 50 years who underwent outpatient echocardiography at our institution between June 2008 and March 2020 were included in this analysis. Baseline demographic characteristics at the time of echocardiogram are listed in Table 1; 47.2% of the cohort was female and average age was 68.6 years. Mean BMI was 28.8 ± 6.2 kg/m^2 and 71.2% were overweight or obese (26.4% overweight, 37.5% obese, and 5.2% severely obese). Baseline CV risk factors were highly prevalent with hypertension in 84.1%, hypercholesterolemia in 80.6%, and diabetes in 31.0% and showed expectedly higher rate with increasing BMI ($P < 0.001$). Also, 27.0% of patients had a diagnosis of atrial fibrillation, 27.9% had a previous stroke or transient ischemic attack, and 24.3% had prior myocardial infarction. The association of these factors with increasing BMI was less consistent (Table 1). Indications for echocardiography are summarized in Supplemental Table 1.

BASELINE ECHOCARDIOGRAPHIC CHARACTERISTICS. Echocardiographic characteristics are presented in Table 1. Mean ejection fraction was 64.8 ± 10.2%. Mean LAV was 48.8 ± 19.5 mL. Where LAV by both biplane and ellipsoid method were available there was a strong correlation between methods ($r = 0.83$; $P < 0.001$). LA image quality was limited in 0.67% of individuals.

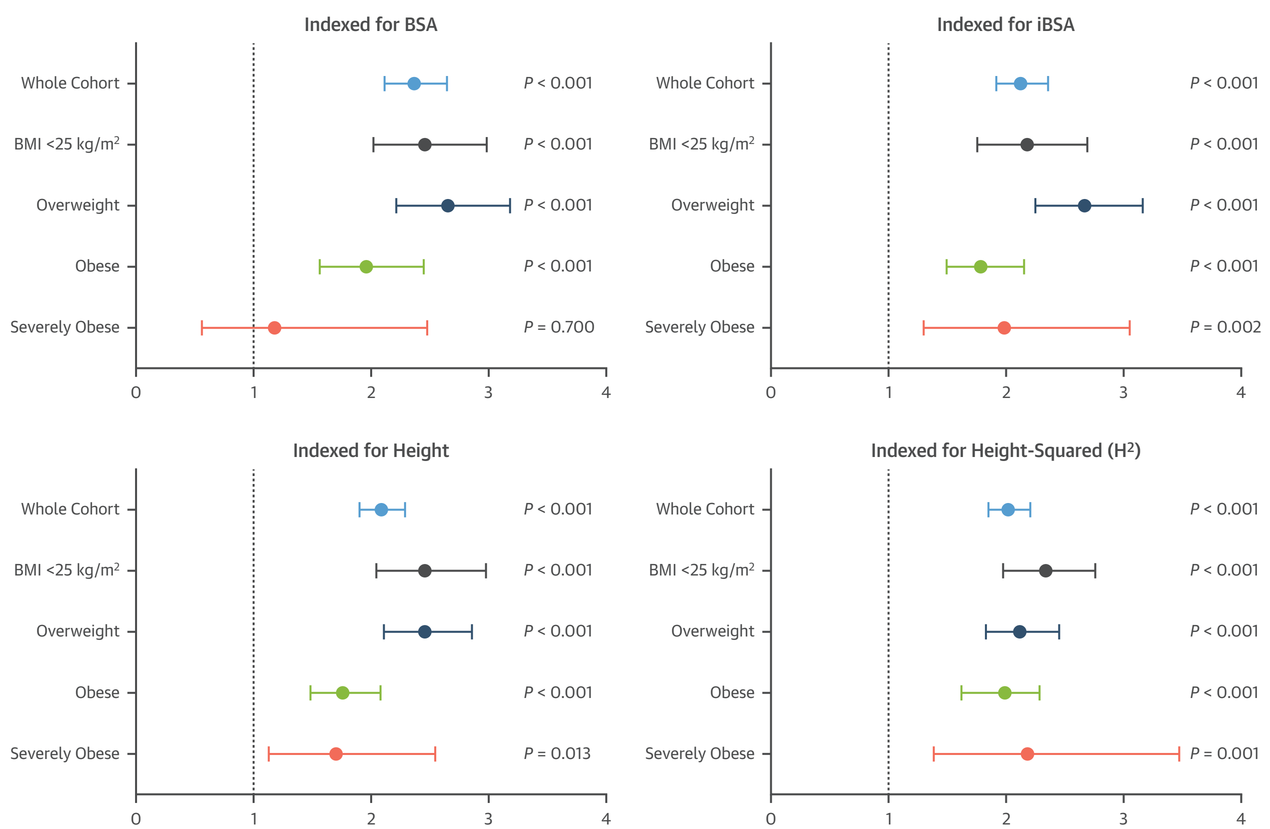
OUTCOME EVENTS. Median follow-up was 1,723 days (IQR: 840-3,026 days). There were 3,033 deaths at a median of 1,605 days (IQR: 834-2,604 days). Incident CV events were experienced by 38.5% (n = 6715) at a median of 641 days (IQR: 181-1,420).

ALTERATION OF LA SIZE CLASSIFICATION. Indexing for iBSA, height, and H^2 all led to clinically significant reclassification of LA size from normal to dilated. The greatest degree of reclassification occurred with indexing for H^2 (28.5%; $P < 0.001$), with relatively less reclassification with indexing for height (11.7%; $P < 0.001$) and iBSA (5.0%; $P < 0.001$). The chance of reclassification varied depending on BMI with the greatest impact in the severely obese, where as many as 55.4% of individuals were reclassified. Rates of reclassification from normal to dilated by each indexing method are presented in Table 2.

PREDICTION OF MORTALITY. LA dilation was predictive of incident mortality whether indexed for BSA (odds ratio [OR]: 2.34; $P < 0.001$), iBSA (OR: 2.10; $P < 0.001$), height (OR: 2.08; $P < 0.001$), or H^2 (OR: 1.99; $P < 0.001$). BMI category significantly modified the interaction between LA dilation and mortality (interaction variable $P = 0.001$) and, therefore, the analysis was stratified by BMI category. ORs for mortality associated with LA dilation are presented in Table 3. Among the severely obese (BMI ≥40 kg/m^2), LA dilation based on indexing based on BSA no longer predicted mortality (OR: 1.16; $P = 0.70$). Dilation based on indexing using iBSA (OR: 1.97; $P = 0.002$), height (OR: 1.67; $P = 0.013$), and H^2 (OR: 2.12; $P = 0.001$) continued to predict mortality in this population (Figure 2). When analysis was repeated using Cox proportional hazard models, similar trends were seen, with a slight attenuation of the predictive value of height in the severely obese. Association of BSA/iBSA and mortality was consistent regardless of which BSA formula was used (Supplemental Table 2).

For prediction of mortality both NRI and IDI were significant for LA dilation using iBSA ($P < 0.001$),

FIGURE 2 **Odds Ratio of All-Cause Mortality Associated With LA Dilation Based on Different Indexing Methods**



Odds ratio of all-cause mortality associated with LA dilation based on different indexing methods. When LA dilation is determined using indexing for BSA **(top left)** among the severely obese (BMI >40 kg/m^2) LA dilation no longer predicted mortality ($P = 0.70$). Dilation determined using indexing for iBSA **(top right)**, height **(bottom left)**, and H^2 **(bottom right)** continued to predict mortality in these individuals. Abbreviation as in Figure 1.

height ($P < 0.001$), and H^2 ($P < 0.001$) compared with LA dilation using BSA. In exploratory analyses, when the overall sensitivity and specificity of different methods of classifying LA size as dilated for predicting mortality were examined using ROC curves, the area under the curve (AUC) for H^2 was the greatest (AUC: 0.62) and was significantly greater than BSA (AUC: 0.59; $P < 0.001$), iBSA (AUC: 0.59; $P < 0.001$), and height (AUC: 0.61; $P = 0.001$). Indexing using height or H^2 had greater AUCs compared with BSA in every weight category, and indexing using iBSA had greater AUCs compared with BSA in all overweight individuals (Supplemental Table 3).

PREDICTION OF CV EVENTS. LA dilation was predictive of incident CV events when indexed for BSA (OR: 2.40; $P < 0.001$), iBSA (OR: 2.34; $P < 0.001$), height (OR: 2.26; $P < 0.001$), or H^2 (OR: 2.14; $P < 0.001$), and all methods remained predictive throughout all BMI categories (Table 4). Effect was similar when analysis was repeated using Cox proportional hazard models. For prediction of CV events, the NRI were significant for LA dilation height ($P < 0.0001$) and H^2 ($P = 0.0004$) compared with LA dilation using BSA, but not for iBSA ($P = 0.17$). IDI was significant for prediction of mortality for all alternative models compared with BSA ($P < 0.001$). In exploratory analysis, when sensitivity and specificity of different methods of classifying LA dilation for predicting CV events were examined, the AUC for H^2 was the greatest (AUC: 0.60) and was significantly greater than the AUC for BSA (AUC: 0.56; $P < 0.001$), iBSA (AUC: 0.57; $P < 0.001$), and height (AUC: 0.59; $P = 0.001$). Indexing using height-based methods (height or H^2) was associated with significantly larger AUC compared with BSA in every weight category (Supplemental Table 4). Indexing for iBSA was associated with a significantly larger AUC in all overweight individuals.

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TABLE 4 Odds Ratio for Cardiovascular Events Based on Different Indexing Methods

	BSA			iBSA			Height			H^2		
	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value
BMI <25 kg/m^2	2.43	2.03-2.91	<0.001	2.18	1.79-2.66	<0.001	2.50	2.11-2.96	<0.001	2.34	2.04-2.69	<0.001
Overweight	2.37	2.01-2.79	<0.001	2.25	1.94-2.62	<0.001	2.10	1.85-2.39	<0.001	2.04	1.83-2.29	<0.001
Obese	2.48	2.03-3.02	<0.001	2.48	2.14-2.87	<0.001	2.32	2.04-2.64	<0.001	2.22	1.96-2.50	<0.001
Severely obese	2.22	1.20-4.13	0.012	1.99	1.44-2.75	<0.001	1.77	1.33-2.36	<0.001	1.64	1.22-2.19	<0.001

Abbreviations as in Tables 1 and 2.

RECLASSIFICATION OF LA SIZE AND OUTCOME EVENTS. In view of NRI and IDI analyses showing significant association between reclassification and outcomes, we considered the risk of mortality and CV events among those patients whose LA size was classified as normal (n = 15,442) using BSA-based indexing but reclassified using alternative techniques. Those whose LA was reclassified as dilated based were at increased risk of mortality (iBSA OR: 1.70; $P < 0.001$; height OR: 1.63; $P < 0.001$; H^2 OR: 1.67; $P < 0.001$) and CV events (iBSA OR: 2.07; $P < 0.001$; height OR: 1.92; $P < 0.001$; H^2 OR: 1.88; $P < 0.001$). The relationship between reclassification and increased risk was seen across all BMI categories including nonoverweight individuals (BMI <25 kg/m^2; Table 5).

DISCUSSION

Our study has identified several novel and clinically important findings. Among a large cohort of outpatients we have demonstrated: 1) use of height, H^2, or iBSA rather than BSA-based indexing methods leads to reclassification of LA size from normal to dilated in a substantial portion of individuals; 2) at extremes of body size LA dilation based on BSA indexing loses the ability to predict mortality, however, other methods remain predictive; 3) the overall performance for the prediction of mortality and CV events was greatest for H^2-based indexing; and 4) reclassification unmasks a cohort at increased risk of mortality and CV events.

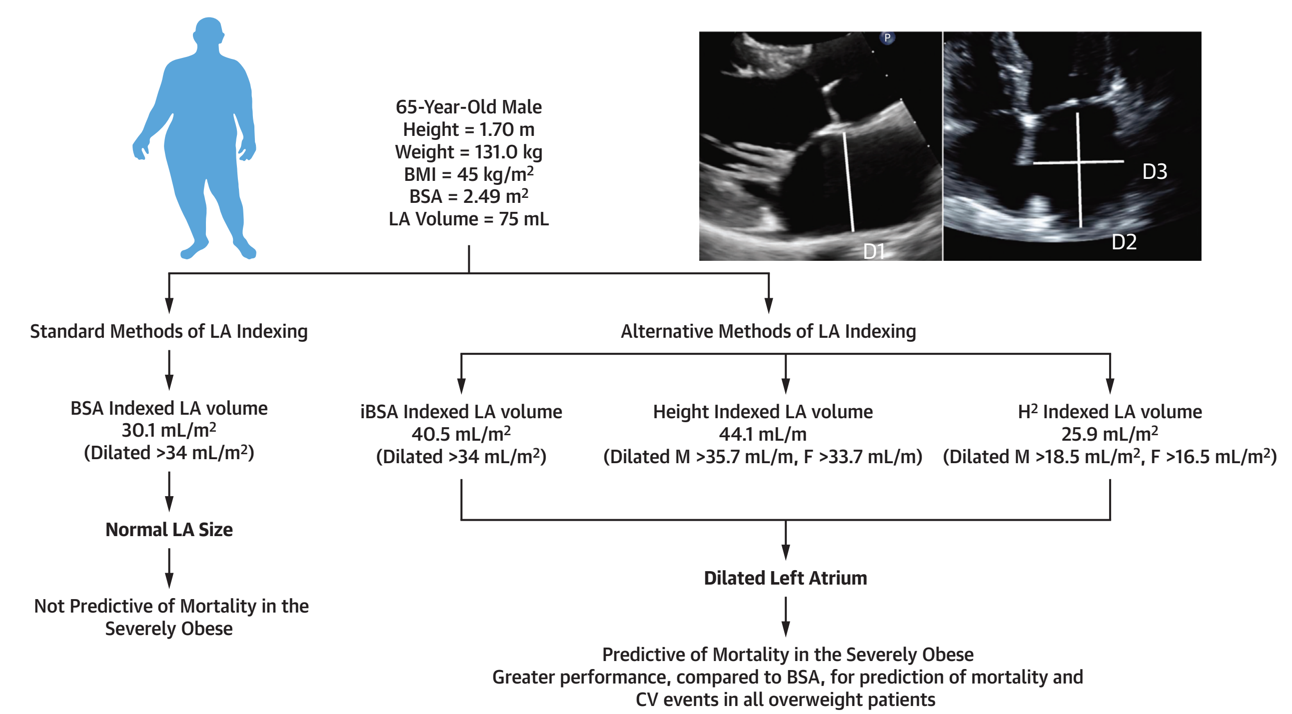
This data suggests that current, standard indexing using BSA potentially underestimates LA dilation and may fail to identify patients at increased risk (Central Illustration).

CLINICAL RELEVANCE OF FINDINGS. LA size has been shown to predict mortality and incident CV events in a wide range of diseased and high-risk patient populations.[20-24] Previous data has shown the superiority of LAV indexed for BSA compared with area or linear measurements of LA dilation[7] and this has formed the basis for current recommendations on echocardiographic assessment of LA dilation.[6] LA dilation is recognized to provide prognostic information,[22] and is incorporated into clinical decision making.[25,26]

The prevalence and severity of obesity continue to increase in the developed world. Between 1999 and 2018 the prevalence of obesity increased from 30.5%-42.4% and severe obesity increased from 4.7%-9.2% in the United States.[27] Our data suggest that BSA-based indexing for LA dilation is a poor discriminator in the severely obese and, therefore, diagnosing LA dilation using BSA-based indexing is suboptimal in close to 10% of the population. In our study alternative indexing techniques, particular H^2, were associated with better overall performance for prediction of mortality and CV events in all overweight individuals and potentially unmasked an unrecognized group of patients at increased risk. The superiority of height-based indexing over BSA is supported by a significantly greater AUC in all BMI categories and significant NRIs and IDI for reclassification of height-based indexing methods for prediction of mortality. Additionally, patients whose LA size was reclassified were at increased risk of mortality and CV events in all BMI categories including in those of normal or near normal weight. These findings suggest that, in a subgroup of normal or near normal weight individuals, current indexing techniques may underestimate LA dilation and misidentify a group at increased risk.

We have investigated multiple alternative indexing strategies. There are practical reasons to favor H^2-based indexing due to its relative ease of application compared with the more complicated technique of calculating an iBSA and the strength of predictive ability in the severely obese. Additionally, the use of height-based indexing technique would be consistent with a move toward this approach for other echocardiographic parameters, most notably aortic dimensions.[10] Our results should lead to caution in using BSA-based indexing to determine LA dilation in the severely obese. In this population clinicians should consider alternative methods of indexing. Among less

CENTRAL ILLUSTRATION The Impact of Alternative Indexing Techniques in Diagnosis of LA Dilation in a Severely Obese Patient



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This figure demonstrates the impact of alternative indexing techniques on the diagnosis of left atrial (LA) dilation in a severely obese patient. BSA-based indexing suggests normal LA size, however, alternative indexing techniques reclassify the LA size from normal to dilated. Reclassification will occur in up to 55.4% of severely obese individuals and unmasks patients at increased risks of mortality and cardiovascular events. In severely obese patients, LA dilation when indexed for BSA no longer predicts mortality; however other indexing methods remain predictive. Height, height-squared (H^2), and iBSA-based diagnosis of LA dilation had greater overall performance, compared with BSA, for prediction of mortality and CV events.

severely obese individuals BSA-based indexing may still underestimate LA dilation and risk, and further validation using volumetric based techniques may clarify which method of indexing best predicts mortality and CV outcome in these individuals.

STUDY LIMITATIONS. These data are a retrospective review of data derived from a large outpatient echocardiography laboratory and may be subject to selection bias. This database does, however, represent a large population representative of those routinely referred to echocardiography laboratories and increases the generalizability of our findings. Institutional coding data was used to identify outcome events in our population and individual adjudication of events by review of the clinical record was not feasible. We have limited our analysis to patients receiving longitudinal care at our institution maximizing completeness of clinical data. To minimize the impact of any missing data we have focused on all-cause mortality as our primary outcome measure and treated CV events as a secondary outcome. The ellipsoid method was used to calculate LAV because linear measurements have been used at our center for a prolonged period, whereas biplane volumetric assessment using the disk summation algorithm, the current ASE standard,[6] has been used for a shorter time. Although the ellipsoid method is limited by potential inaccuracy of linear measurements, our institution uses quality control mechanisms to minimize measurement error, and our data show good correlation between methods. Additionally, our primary aim was to compare different methods of indexing. Because the same method of assessing LAV was used for all indexing techniques, we feel the comparison between indexing techniques is valid. Finally, the ellipsoid method leads to smaller LAVs compared with the biplane volumetric assessment[28] and will potentially lead us to underestimate both LA

JACC: CARDIOVASCULAR IMAGING, VOL. 15, NO. 6, 2022
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TABLE 5 Risk of Mortality and Cardiovascular Events in Patients Whose Left Atrium Was Reclassified by Different Indexing Methods

	iBSA			Height			H^2		
	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value	Odds Ratio	95% CI	*P* Value
Whole cohort									
Mortality	1.70	1.43-2.3	<0.001	1.63	1.44-1.85	<0.001	1.67	1.51-1.85	<0.001
Cardiovascular events	2.09	1.81-2.40	<0.001	1.92	1.74-2.12	<0.001	1.88	1.74-2.02	<0.001
BMI <25 kg/m^2									
Mortality	-	-	-	1.95	1.28-3.00	0.002	1.84	1.49-2.27	<0.001
Cardiovascular events	-	-	-	2.50	1.72-3.63	<0.001	1.96	1.66-2.33	<0.001
Overweight									
Mortality	2.07	1.46-2.94	<0.001	1.84	1.50-2.26	<0.001	1.65	1.40-1.95	<0.001
Cardiovascular events	1.64	1.21-2.24	0.002	1.68	1.42-1.99	<0.001	1.77	1.56-2.00	<0.001
Obese									
Mortality	1.51	1.18-1.92	<0.001	1.53	1.26-1.86	<0.001	1.74	1.45-2.09	<0.001
Cardiovascular events	2.15	1.78-2.60	<0.001	2.01	1.74-2.33	<0.001	1.98	1.74-2.25	<0.001
Severely obese									
Mortality	2.21	1.39-3.52	<0.001	1.76	1.15-2.69	0.009	2.20	1.38-3.52	0.001
Cardiovascular events	1.83	1.28-2.61	<0.001	1.66	1.22-2.24	0.001	1.55	1.15-2.09	0.004

Abbreviations as in Tables 1 and 2.

dilation and the effect of alternative indexing techniques.

CONCLUSIONS

Using height (height or H^2) or iBSA-based indexing methods to determine LA dilation allows better prediction of mortality in severely obese populations. These techniques have better performance in predicting mortality across overweight and obese populations, suggesting that current, standard indexing using BSA underestimates LA dilation and may fail to identify patients at increased risk.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Hung is supported in part by National Institutes of Health-National Heart, Blood, and Lung Institute RO1HL103723-05. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: LA dilation based on BSA-based indexing does not predict mortality in severely obese populations presumably caused by underestimation of LA dilation. Alternative indexing techniques remain predictive in this population and demonstrate predictive performance in all overweight populations.

COMPETENCY IN PATIENT CARE: Echocardiographers should consider using non–BSA-based indexing to diagnose LA dilation, particularly in the severely obese, and recognize the potential for underestimation of LA dilation in overweight and obese populations.

TRANSLATIONAL OUTLOOK: Further research is needed to consider indexing of other echocardiographic parameters in overweight and obese populations. Prospective studies may help refine our understanding of which is the superior indexing technique for predicting CV mortality and events.

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KEY WORDS body mass index (BMI), body surface area, echocardiography, height, indexing, left atrium, obesity

APPENDIX For supplemental tables, please see the online version of this paper.