Echocardiographic Imaging Challenges in Obesity: Guideline Recommendations and Limitations of Adjusting to Body Size

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According to statistics by the World Health Organization[1] and the Centers for Disease Control,[2] ≈20% of adults in Europe and ≈40% in the United States are obese. In some series nearly half of patients undergoing outpatient echocardiography were noted to have a body mass index (BMI) ≥30 kg/m^2.[3] Obese patients present unique challenges for optimal echocardiographic imaging and interpretation.[3] One such challenge is optimal adjustment for body size in these patients. Guidelines for cardiac imaging frequently recommend adjusting for the body size of the patient for assessment of left atrial (LA) size, left ventricular (LV) mass, and valvular hemodynamics. Several parameters such as height with various allometric powers or body surface area (BSA) have been studied. However, most guidelines recommend indexing to BSA. In this article, we have summarized the guideline recommendations regarding adjustment for body size in the obese, evidence base, potential pitfalls, and clinical implications related to using weight-dependent indexing methods in obese (BMI >30 kg/m^2) and morbidly obese (BMI >40 kg/m^2) individuals (Figure 1A and 1B). Guidelines for various recommendations are summarized in Table.[4–16]

LA Size

Assessment of LA size is prognostically important and is also an integral part of various echocardiographic diagnostic algorithms such as assessment of diastolic function, quantification of mitral valve disease, and assessment of the likelihood of atrial arrhythmias.

Quantification of LA Size: Guideline Recommendations

Society guidelines (American Society of Echocardiography/European Association of Cardiovascular Imaging [ASE/EACVI] chamber quantification guidelines, ASE/EACVI guidelines on assessment of LV diastolic function, and ASE/EACVI guidelines on echocardiography in hypertension) recommend using BSA to index LA volume to assess LA size,[4-6] regardless of the BMI or BSA of the patient. Indexed LA volume is intended to neutralize the effect of sex on LA size. These documents provide no specific recommendations for obese individuals; the threshold of 34 mL/m^2 to define normal is used in all. Only the ASE/EACVI guidelines on echocardiography in hypertension acknowledge that indexing LA volume to BSA corrects for obesity-related LA dilatation, and as a result, obesity-related LA dilatation may remain undetected.[6] On the other hand, the European Society of Cardiology (ESC) guidelines on management of arterial hypertension in adults recommend using LA volume indexed to height^2 to define normal LA size (≤18.5 mL/m^2 for men; ≤16.5 mL/m^2 for women).[7]

Reference LA Indexed Volume: Evidence

Established reference range for LA size is based either on population studies that included normal individuals or studies that have evaluated outcomes based on LA size. The mean BSA in population studies that evaluated LA size in healthy individuals and form the basis of recommendations by the ASE/EACVI chamber quantification guidelines, ranged from 1.44 to 1.84 m^2.[17-19] A study that showed LA volume indexed to BSA to be superior compared with linear diameter (anteroposterior diameter in parasternal view) for prediction of first atrial fibrillation, congestive heart failure, stroke, transient ischemic attack, or other cardiovascular outcomes included patients with a mean BMI around 28 kg/m^2.[20] To

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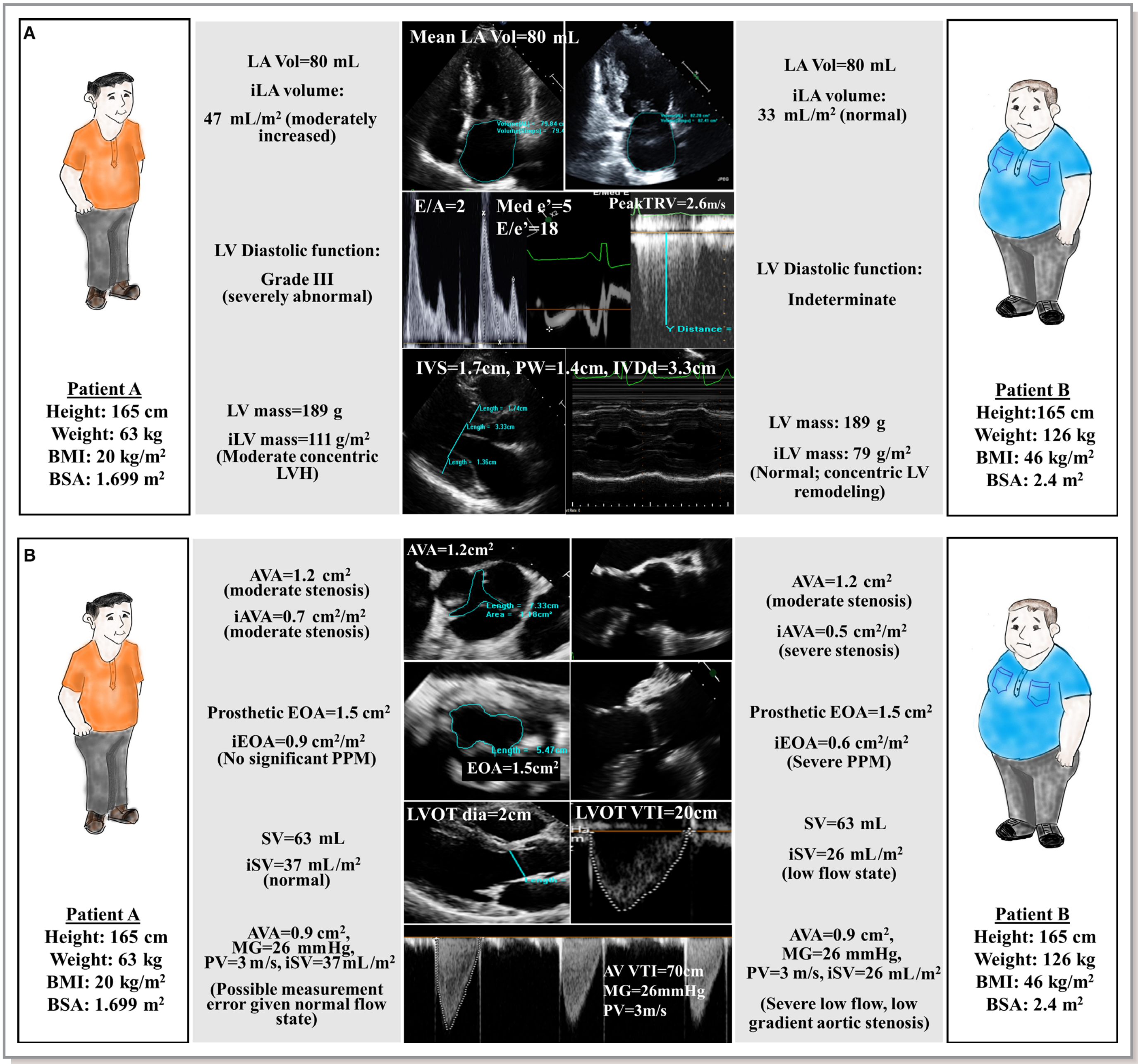

Figure 1. Imaging pitfalls in obese individuals. **A**, Illustration showing discrepancies in assessment of LA volume, diastolic function, and LVH assessment in a lean vs obese patient of similar height. BMI indicates body mass index; BSA, body surface area (Mosteller formula); i, indexed; IVDd, internal left ventricular diameter in diastole; IVS, interventricular septum; LA, left atrial; LV, left ventricle; LVH, left ventricular hypertrophy; PW, posterior wall; TRV, tricuspid regurgitant velocity. **B**, Illustration showing discrepancies in assessment of aortic stenosis, flow state, and assessment of PPM in a lean vs an obese patient of similar height. AVA indicates aortic valve area; BMI, body mass index; BSA, body surface Area; EOA, effective orifice area; i, indexed; MG, mean gradient; PPM, patient prosthesis mismatch; PV, peak velocity; SV, Stroke Volume. In echocardiograms: e′ indicates Mitral Annular Tissue Doppler Velocity; E/A, Ratio of E wave and A wave; E/e′, Ratio of E wave to mitral annular velocity; LVOT, LV outflow tract; VTI, Velocity Time Integral.

the best of our knowledge, no studies have assessed outcomes based on various indexing methods for LA size assessment exclusively in patients with BMI $\geq$30 kg/m^2.

Obesity is known to be associated with LA structural and functional remodeling[21] and a higher prevalence of conditions that are mediated by LA enlargement such as diastolic heart failure and atrial fibrillation. When LA size was indexed based on methods that were not weight dependent, a higher prevalence of LA enlargement was noted in obese patients.[22,23] Stritzke and colleagues[23] studied 1212 individuals who had an ECG at baseline and 10 years later. They assessed LA size indexed to height and found that obesity was the strongest risk factor beside aging for LA enlargement. The prevalence of LA enlargement was significantly lower when LA enlargement was assessed using the traditional method of indexing LA size to BSA, especially in obese individuals. Another study showed that obesity was the strongest predictor of LA enlargement (measured as a linear diameter in parasternal view) in hypertensive patients.[22]

Clinical Implications

Besides hypertension and age, obesity is the main determinant for LA enlargement[6] and represents a pathological process, not just a physiological increase. Using weight-dependent methods such as BSA to index LA volume in obese and morbidly obese patients may underestimate the magnitude of LA dilatation and underestimate the effect of obesity on LA remodeling. Clinically, this may translate into underestimation of diastolic dysfunction, prediction of future cardiovascular events, and prevalence of LA enlargement in obese patients.

Clinicians can consider using BSA to estimate LA size in obese individuals. If LA is dilated based on this method, it is reasonable to quantify LV diastolic dysfunction based on this. However, the report should mention that the LA size may be underestimated. If LA size is normal when indexed to BSA in obese individuals, we recommend using height-based indexing as recommended by the ESC hypertension guidelines.[7] Alternatively, clinicians should consider using recommendations from ESC/ASE 2005 guidelines,[24] which provided lower thresholds for defining LA dilatation (normal $\leq$28 mL/m^2) (Figure 2).

LV Mass

Assessment of LV mass by echocardiography or other imaging modalities is clinically and epidemiologically important. Clinically, LV hypertrophy (LVH) is associated with adverse clinical events in patients. Epidemiologically, prevalence of LVH and risk of associated adverse cardiovascular events are important public health measures and are useful to identify the burden of hypertension.

Adjusting LV Mass to Body Size: Guideline Recommendations

ASE/EACVI 2015 chamber quantification guidelines[4] acknowledge that height-based indexing has advantages over BSA-based indexing in obese individuals but still recommend reporting LV mass values indexed to the BSA to define LV hypertrophy in all patients, as most of the population studies reported LV mass indexed to BSA. These guidelines also do not provide height-specific cutoffs for defining LVH. Another ASE/EACVI guideline published in 2015 regarding use of echocardiography in hypertension[6] provides height-specific cutoffs for quantification of LVH. Although this document also suggests that height-based indexing preserves the effect of obesity on LV mass, it does not provide specific recommendations on the best method for indexing in obese patients. On the other hand, the ESC guidelines on management of arterial hypertension recommend height-based indexing to define LVH (LV mass/height in m$^{2.7}$), whereas indexing LV mass to BSA is only recommended for patients with normal weight.[7]

Pathological LVH and Cardiac Risk

The ideal method to adjust to body size for LV mass remains controversial in obese subjects, but studies have tended to favor height-based indexing. Some studies have shown that LV mass indexed to BSA best identifies clinical events as compared with other methods,[25] whereas other studies have favored height-based indexing, especially in overweight and obese subjects.[26,27] Another study showed that height-based indexing predicted mortality and cardiovascular outcomes better than BSA-based indexing in dialysis patients.[28]

Outcome studies comparing the best indexing method in obese patients are limited. Also, no population studies have exclusively studied echocardiographic characteristics in "otherwise healthy" obese individuals. Most observational studies in obese and morbidly obese patients have reported LVH using LV mass indexed to height, with various allometric powers (most commonly 2.7).[29] Studies in patients undergoing bariatric surgery have shown a significant regression in LV mass and LVH after weight loss. One study that indexed LV mass to BSA in morbidly obese subjects did not show any significant change in LVH after weight loss, even though there was a significant decrease in LV mass after bariatric surgery.[30] These studies suggest that indexing LV mass to BSA tends to attenuate the effect of obesity on LVH.

Even fewer studies have assessed the effect of indexing methods on yet another important epidemiological parameter, the population-attributable risk percentage (PAR%). The PAR% is important from a population health standpoint as it better defines the proportion of disease in the population that can be attributed to a particular risk factor. Two studies in 2005 compared PAR% associated with LVH with various indexing methods. In 1 cohort with a low prevalence of obesity (22%),[31] the PAR% attributable to LVH was similar for various indexing methods (BSA, height, height$^{2.13}$, height$^{2.7}$), even though prevalence of LVH was higher when LV mass was adjusted by height-based indexing methods in comparison to BSA. The other study included a cohort of patients with a high prevalence of obesity (56%)[32] and showed that height-based

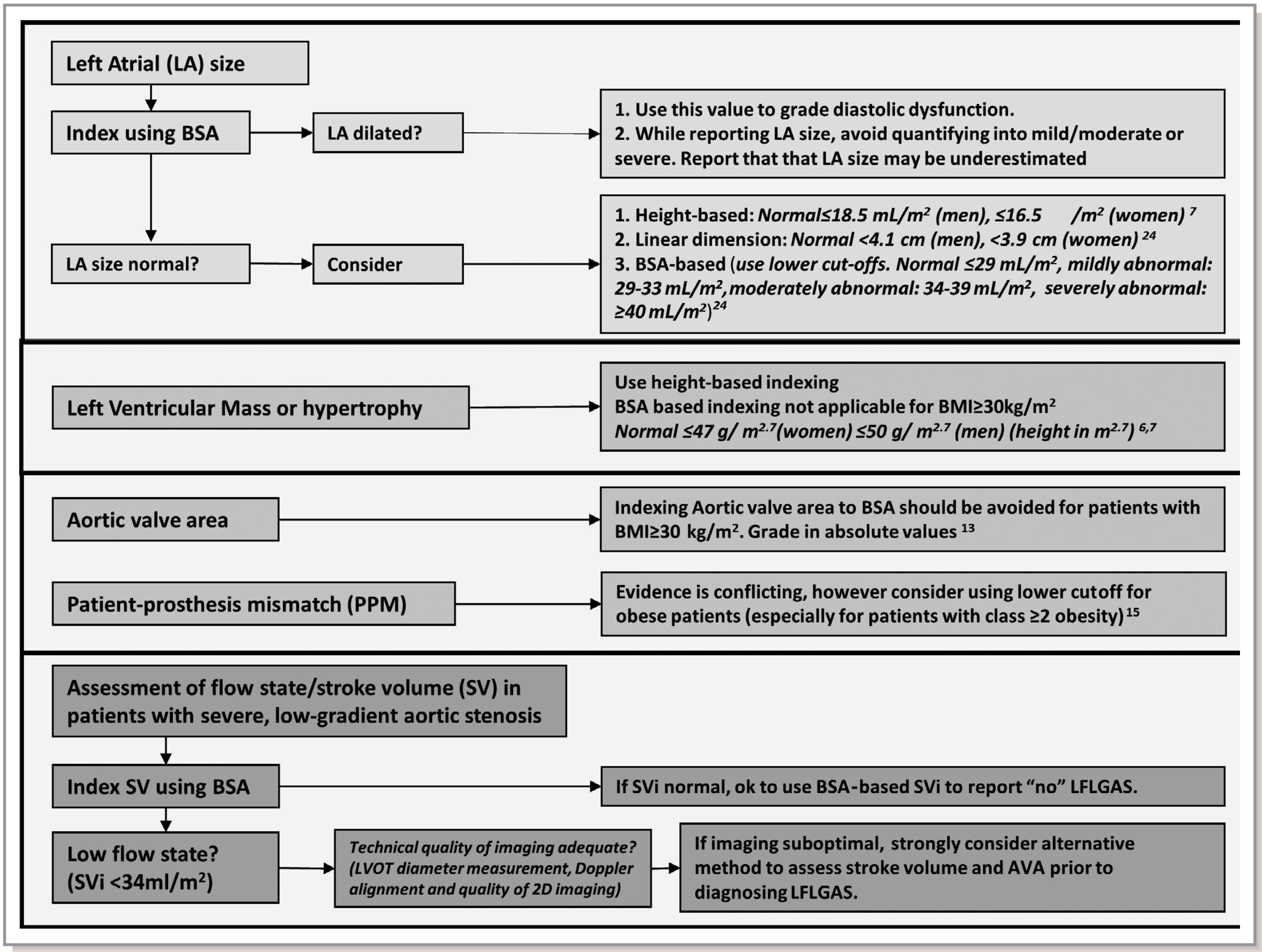

Figure 2. Proposed indexing methods for chamber quantification in obese individuals. A schematic showing proposed alternative indexing methods for obese individuals to avoid misclassification. 2D indicates 2-dimensional; abn, abnormal; AVA, aortic valve area; BMI, body mass index; BSA, body surface area; LVOT, left ventricular outflow tract; SVi, Stroke Volume (indexed); SV, stroke volume.

indexing was superior to BSA in assessing PAR% attributable to LVH and prevalence of LVH in this population.

Physiological LVH

Certain physiological conditions such as pregnancy and endurance training can lead to morphological LVH, which in these cases, is benign and reversible. In athletes, LVH has commonly been described in terms of absolute wall thickness, rather than indexed values.

Clinical and Public Health Implications

LVH in obese patients is a pathological process (Figure 3) and has been shown to be associated with important clinical events.[29] Using BSA-based indexing may result in underestimation of the prevalence of LVH in obese patients. Moreover, in a population with high prevalence of obesity, LV mass indexed to height is a better method compared with BSA-based indexing from an epidemiological standpoint to assess prevalence of LVH and PAR%.

We recommend indexing LV mass to height$^{2.7}$ in obese individuals as recommended by the ESC hypertension guidelines[7] (Figure 2). BSA should not be used to index LV mass when BMI is $\geq$30 kg/m^2.

Assessment of Stroke Volume

Stroke volume indexed to body surface area is particularly important in patients suspected to have heart failure or deemed to have severe aortic stenosis by the continuity method, but with low transaortic gradients (mean gradient <40 mm Hg and peak velocity <4 m/s). Major society guidelines recommend assessment of indexed stroke volume

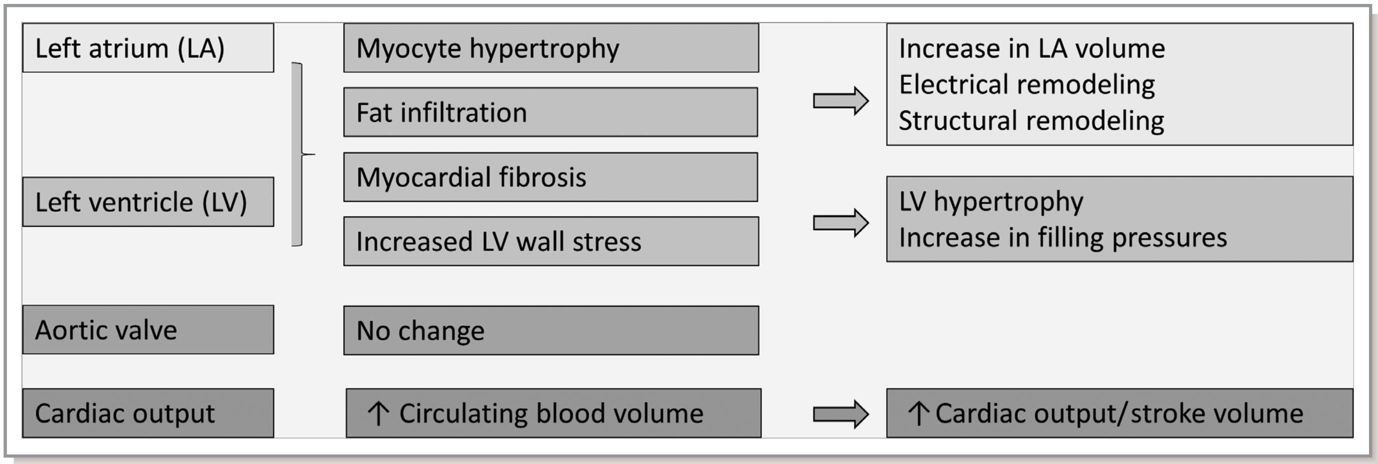

Figure 3. Myocardial adaptations in obesity. Illustration showing some of the physiological and pathological myocardial adaptations relevant to indexing in obese individuals. LA indicates left atrium; LV, left ventricle; ↑, increase.

in these situations to define the flow state as a possible explanation for low gradients, or low-flow, low-gradient aortic stenosis.

Supporting Evidence

Multiple studies have shown worse cardiovascular outcomes in patients with low-flow, low-gradient aortic stenosis and paradoxical low-flow, low-gradient aortic stenosis based on a stroke volume index cutoff of 35 mL/m^2. However, obese patients were underrepresented in most of these studies.[33-35] Limited echocardiographic data regarding stroke volume in obese patients come from studies that evaluated patients undergoing bariatric surgery. However, stroke volume index was not consistently reported in these studies.[36,37] Studies using modalities such as cardiac catheterization in morbidly obese patients have reported higher stroke volume.[30,38] A study based on cardiac catheterization data suggested that indexing stroke volume to BSA can eliminate the effects of increased body size on stroke volume, and a uniform cutoff can be used for a wide range of BMI and BSA.[39]

Clinical Implications

Cardiac output and stroke volume increase with increased body weight and BMI, which represent a physiological adaptation to increased circulating blood volume and metabolic needs (Figure 3). Unlike other pathological changes in cardiac structure, increased stroke volume in obese patients does not seem to correlate independently with adverse cardiac outcomes, and hence, using a single cutoff to define a normal flow state across a wide range of body size and BMI is feasible.

Clinicians can consider using stroke volume indexed to BSA to define the flow state in obese individuals. However, if a low-flow state is present, we recommend confirming cardiac output by other methods, especially in the setting of technically limited studies (suboptimal 2D imaging or Doppler alignment), which are not uncommon in obese individuals (Figure 2).

Quantification of Aortic Stenosis Severity

In addition to several Doppler-based and nonindexed parameters, the American College of Cardiology/American Heart Association (ACC/AHA) valve guidelines[8] and the appropriate use criteria for treatment of severe aortic stenosis[9] also suggest a cutoff of $\leq$0.6 cm^2/m^2 to define severe aortic stenosis. However, the ACC/AHA guidelines or the appropriate use criteria do not clarify whether this approach of using indexed aortic valve area (AVA) in making treatment decisions is applicable to patients with obesity. On the other hand, the ASE/EACVI guidelines[10] recommend using indexed valve area to quantify aortic stenosis primarily in patients with small body size. ASE/EACVI guidelines recognize that the role of indexing is controversial, particularly in obese patients. The ESC guideline recommendations have changed over time. The previous version of ESC 2007 guidelines[11] recommended indexing AVA in patients with “unusually small” or “unusually large” body size. This was subsequently changed to include only “unusually small” body size in the ESC 2012 version.[12] The latest version of the ESC guidelines published in 2017, does not provide any recommendations for quantifying aortic stenosis based on indexed AVA.[13]

Evidence Base

Autopsy studies have shown that AVA in infants and children is directly related to age, weight, and the BSA.[40] However, this is not true in adults. In an autopsy study by Westaby

Table. Comparison of Various Guideline Recommendations for Indexing Left Atrial Size, Left Ventricular Mass, Aortic Stenosis, and Patient-Prosthesis Mismatch

Left Atrial Size

	ASE/EACVI-2015 Chamber Quantification Guidelines[4]	ASE/EACVI-2016 Left Ventricular Diastolic Function Guidelines[5]	ASE/EACVI-2015 Echocardiogra-phy in Hypertension[6]	ESC-2018 Guidelines on Hypertension Management[7]	ACC/AHA
LA volume (indexed to BSA)	Normal ≤34 mL/m^2	Normal ≤34/m^2	Normal ≤34/m^2 (obesity-related LA enlargement may remain undetected)	None	None
LA volume (indexed to height^2)	None	None	None	≤18.5 mL/m^2 (men) ≤16.5 mL/m^2 (women)	None

Left Ventricular Hypertrophy

	ASE/EACVI-2015 Chamber Quantification Guidelines[4]	ASE/EACVI-2015 Echocardiography in Hypertension[6]	ESC-2018 Guidelines on Hypertension Management[7]	ACC/AHA
LV mass by linear method (indexed to BSA)	≤95 g/m^2 (women) ≤115 g/m^2 (men)	≤95 g/m^2 (women) ≤115 g/m^2 (men) (obesity-related LVH may remain undetected)	≤95 g/m^2 (women) ≤115 g/m^2 (men) May be used in normal-weight patients	None
LV mass by linear method (indexed to height)	None	≤44 g/m$^{2.7}$ (women) ≤48 g/m$^{2.7}$ (men) ≤99 g/m (women) ≤126 g/m (men)	≤47 g/m$^{2.7}$ (women) ≤50 g/m$^{2.7}$ (men) (height in m$^{2.7}$)	None

Classification of Aortic Stenosis Based on Indexed Values

	ACC/AHA 2014/2017 Valve Guidelines[8]/AUC-2017 for Treatment of Aortic Stenosis[9]	ASE/EACVI-2017 Guidelines on Assessment of Aortic Stenosis[10]	ESC-2007 Valve Guidelines[11]	ESC-2012 Valve Guidelines[12]	ESC-2017 Valve Guidelines[13]
Severe aortic stenosis based on BSA	≤0.6 cm^2/m^2	<0.6 cm^2/m^2 controversial in obese, important for children, adolescents and small adults	<0.6 cm^2/m^2 for unusually small or unusually large individuals	<0.6 cm^2/m^2 for unusually small individuals	No recommendations provided

Patient-Prosthesis Mismatch

	ACC/AHA 2014/2017 Valve Guidelines[8]	ASE-2009 Guidelines on Echo Evaluation of Prosthetic Valve[14]	EACVI-2016 Guidelines for Imaging of Prosthetic Valves[15]	VARC-2-2012 Consensus Document[16]	ESC
PPM	≤0.85 cm^2/m^2	≤0.85 cm^2/m^2	≤0.85 cm^2/m* ≤0.70 cm^2/m†	≤0.85 cm^2/m^2* ≤0.70 cm^2/m^2†	None
Severe PPM	<0.65 cm^2/m^2	<0.65 cm^2/m^2	<0.65 cm^2/m* <0.55 cm^2/m†	<0.65 cm^2/m^2* <0.60 cm^2/m^2†	None

ACC/AHA indicates American College of Cardiology/American Heart Association; ASE, American Society of Echocardiography; AUC, appropriate use criteria; BMI, body mass index; BSA, body surface area; EACVI, European Association of Cardiovascular Imaging; ESC, European Society of Cardiology; LA, left atrium; LV, left ventricle; LVH, left ventricular hypertrophy; PPM, patient-prosthesis mismatch; VARC, Valve Academic Research Consortium.

*BMI <30 kg/m^2.

†BMI ≥30 kg/m^2.

et al, the correlation between AVA and BSA in adults (16-83 years) was poor.[41]

Multiple studies have shown that indexing AVA by BSA overclassifies aortic stenosis as severe without improving predictive accuracy for adverse events in comparison to nonindexed valve area.[42-45] This is especially true in obese individuals.[44,45] Some studies[43] have suggested a height-based indexed cutoff of <0.45 cm^2/m or a lower cutoff of <0.4 cm^2/m^2 to be better predictive of adverse events at 2 years in contrast to the recommended cutoff of <0.6 cm^2/m^2.

Clinical Implications

Based on the above evidence, it can be concluded that classification of aortic stenosis based on BSA is arbitrary in the absence of any definite physiological correlation between the BSA and the normal aortic valve area in adults. This is especially true in obese patients, where excess weight accounts for an increase in BSA. Using a cutoff of <0.6 cm^2/m^2 to define severe aortic stenosis may inadvertently overestimate the true severity and prevalence of aortic stenosis in obese patients, and it does not provide any additive prognostic information in these patients. Based on this, we do not recommend indexing AVA in obese patients to make treatment decisions. Indexing AVA should be reserved in patients with smaller body size.[10]

Patient-Prosthesis Mismatch

Presence of a patient-prosthesis mismatch (PPM) is an important adverse prognostic indicator in patients with prosthetic valves and is defined by effective orifice area (usually derived by echocardiography) indexed to BSA. Some guideline documents provide different thresholds to define PPM in obese and lean patients, whereas other documents provide uniform threshold regardless of body size. The ACC/AHA[8] and the ASE guidelines[14] provide a uniform threshold of indexed effective orifice area <0.85 and <0.65 cm^2/m^2 to define PPM and severe PPM, respectively, regardless of the BSA or BMI. The EACVI[15] and the Valve Academic Research Consortium-2[16] guidelines recommend different thresholds for obese patients to define PPM (severe PPM defined as <0.55 cm^2/m^2 and <0.60 cm^2/m^2 respectively). Similarly, some documents have recommended different thresholds to define normal prosthetic effective orifice area in patients with BSA >1.6 m^2.[16] These recommendations are summarized in Table.

Evidence Base

Older studies that showed that patients with PPM have adverse prognosis mostly included individuals with average BMI and BSA, ranging from 1.56±0.12 to 1.84±0.20 m^2.[46,47] Studies that included obese individuals have shown conflicting findings. In a study by Mohty and colleagues[48] PPM was noted to be associated with a higher mortality only in patients with a BMI <30 kg/m^2. In obese patients PPM was not a predictor of higher mortality. Similar findings were reported by another study[49] in which PPM was a predictor of adverse events in lean and overweight patients but not in obese patients. In a meta-analysis of 58 studies a BMI >28 kg/m^2 had a weaker impact on mortality (hazard ratio 1.14; 95% CI 1.07-1.22, P=0.0001) compared with BMI <28 kg/m^2 (hazard ratio 2.37; 95% CI 1.42-3.95; P=0.003).[50]

The above findings contrast with some recent studies from national database registries. Two studies from the Society of Thoracic Surgeons/Transcatheter Valve Therapy,[51] and the Society of Thoracic Surgeons adult cardiac surgery database[52] registries showed that PPM (effective orifice area <0.65 cm^2/m^2) was also associated with poor outcomes in patients with BMI ≥30 kg/m^2. However, these studies did not assess the effect of worsening severity of obesity (class 2 or greater) on clinical outcomes or whether the association of PPM with worse outcomes is applicable across all BMI ranges. It would be helpful to know if there is an upper limit of BMI beyond which there is no association of poor outcomes with PPM, and a lower threshold as suggested by Valve Academic Research Consortium-2 and EACVI guidelines may be more appropriate.

Clinical Implications

Using the thresholds as recommended by the ACC/AHA guidelines to define PPM may overestimate the severity and prevalence of PPM in obese patients. However, evidence for use of these thresholds to assess long-term outcomes is conflicting.

It is probably reasonable to use lower thresholds to define PPM (Figure 2) (especially in patients with class 2 and class 3 obesity) as recommended by the Valve Academic Research Consortium-2 and EACVI guidelines. This is particularly important when a valve intervention is considered due to PPM. However, more studies with head-to-head comparison of differing thresholds recommended by various guidelines are needed to better define the optimal cutoff in obese patients.

Conclusions

Optimal adjustment of echocardiographic parameters for body size in obese individuals remains a challenge. In obese individuals excess weight contributes to an increased BSA and using weight-based indexing methods (BSA) for chamber quantification, LV diastolic function assessment and quantification of valvular hemodynamics may result in misclassification and misleading conclusions. We also found multiple disagreements among various guideline recommendations regarding adjustment for body size in obese individuals. Although a uniform threshold can be used to define parameters that are physiological in obesity such as stroke volume index, indexing to BSA for other morphological changes in the cardiac structures that represent a pathological change such as LA dilatation or LVH should be avoided. Similarly, classifying aortic stenosis based on BSA and defining PPM in obese patients should be used with caution. Further research is needed to better define the best way to adjust for body size in obese individuals.

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