

Effect of Race on Echocardiographic Measures of Cardiac Structure and Function



Troy M. LaBounty, MD^{a,*}, David S. Bach, MD^a, Eduardo Bossone, MD^{a,b}, and Theodore J. Kolas, MD^a

The relations between race and cardiac structure and function are incompletely understood. We hypothesized that race-specific differences in echocardiography measurements exist. We compared the relation between echocardiography measurements and race among 12,429 nonobese adults without known cardiovascular disease who underwent echocardiography. We compared measurements between whites (n=10,508), blacks (n=792), Asians (n=628), Hispanics (n=315), Native Americans (n=34), and multiracial/other (n=152) cohorts. Multivariate analysis compared measurements indexed to body surface area (BSA) between races and adjusted for variables including age, gender, and mean blood pressure. Mean age was 46.9 ± 17.4 years and 60.5% were women. After multivariable adjustment and using whites as a baseline, there were significant differences (p < 0.05) in left ventricular end-diastolic diameter/BSA for blacks (−0.5 mm/m²), Asians (0.4 mm/m²), Hispanics (0.2 mm/m²), and multiracial/others (0.1 mm/m²); septal wall thickness/BSA for blacks (0.4 mm/m²) and Asians (0.1 mm/m²); posterior wall thickness/BSA for blacks (0.4 mm/m²), Asians (0.1 mm/m²), Hispanics (0.04 mm/m²), and multiracial/others (0.03 mm/m²); left atrial diameter/BSA for Asians (0.2 mm/m²), Hispanics (0.3 mm/m²), and multiracial/others (0.1 mm/m²); septal and lateral e' for blacks (−0.7 cm/s; −0.9 cm/s); and peak tricuspid regurgitation gradient for blacks (4.3 mm Hg) and Asians (−0.9 mm Hg). Race is associated with significant differences in left ventricular size, left atrial size, mitral annular velocity, and tricuspid regurgitation gradient. Normal reference ranges for echocardiography measurements should utilize racially diverse cohorts to prevent misclassification of echocardiography findings based on race. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;124:812–818)

Current guidelines propose normal reference ranges for standard echocardiography measurements,¹ and these thresholds are frequently used to define normal and abnormal findings in clinical practice. These reference ranges are largely based on studies performed in Europe or the United States with a racial makeup that is often mostly white or not reported,^{2–5} and there are limited recommendations in the guidelines specific to race.^{1,6} Although some studies have reported differences in cardiac structure and function between races,^{7–13} other studies have observed no significant differences.^{14,15} We hypothesized that differences exist in cardiac structure and function assessed by echocardiography between patients of different races and ethnicities (described as race for the remainder of this manuscript). We examined a cohort of patients without known risk factors for cardiovascular disease and compared echocardiography measurements between patients stratified as white, black, Asian, Hispanic, Native American, and multiracial/other cohorts.

Methods

We examined echocardiography findings in adult patients referred for a clinically indicated transthoracic echocardiogram. As recommended by guidelines,¹ we examined adults without known cardiovascular disease and without known risk factors for abnormal echocardiogram findings by excluding patients with a systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg (mean of 3 values); obesity; or history of hypertension, diabetes, chronic renal disease, coronary artery disease, tobacco smoking, hyperlipidemia, heart failure, hypertrophic cardiomyopathy, myocardial infarction, or previous valve replacement. Finally, we excluded patients with echocardiographic findings of reduced left ventricular (LV) systolic function (ejection fraction <50%), at least moderate regurgitation of any valve, aortic valve stenosis (peak gradient ≥16 mm Hg), mitral valve stenosis (mean gradient ≥5 mm Hg), tricuspid valve stenosis (mean gradient ≥5 mm Hg), or pulmonary valve stenosis (peak gradient ≥30 mm Hg).¹⁶ From a total population of 87,735 adults with a complete echocardiogram and reported race, the final cohort consisted of 12,429 patients. The first available study was used. The study was approved by the Institutional Review Board with a waiver of informed consent. The study is consistent with the Declaration of Helsinki.

Echocardiograms were performed at a tertiary care academic medical center (University of Michigan Medical Center, Ann Arbor, Michigan), 1 of 6 affiliated satellite clinics located in 5 cities, and an affiliated private practice

^aDepartment of Medicine, University of Michigan, Ann Arbor, Michigan; and ^bHeart Department, University Hospital, Salerno, Italy. Manuscript received April 29, 2019; revised manuscript received and accepted May 23, 2019.

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*Corresponding author: Tel: 734-764-7440; fax: 734-232-4132.

E-mail address: labt@med.umich.edu (T.M. LaBounty).

Table 1
Differences in patient characteristics by race

Variable	White (n = 10,508)	Black (n = 792)	Asian (n = 628)	Hispanic (n = 315)	Native American (n = 34)	Multiracial/Other (n = 152)	p
Age (years)	49 (33-61)	42 (28-54)	43 (32-53)	38 (27-53)	45 (32-54)	40 (28-54)	<0.001
Women	60.1%	62.0%	65.8%	63.8%	55.9%	51.3%	0.008
Body mass index (kg/m ²)	24.4 (22.0-26.9)	24.9 (22.2-27.6)	23.3 (21.2-25.7)	22.9 (20.9-25.3)	25.2 (22.7-27.3)	24.5 (21.9-27.2)	<0.001
Body surface area (m ²)	1.80 (1.66-1.96)	1.79 (1.67-1.94)	1.65 (1.55-1.80)	1.74 (1.61-1.89)	1.80 (1.71-1.99)	1.77 (1.61-1.93)	<0.001
Systolic blood pressure (mm Hg)	117 (109-126)	118 (110-126)	112 (104-120)	116 (107-123)	124 (112-128)	1164 (107-124)	<0.001
Diastolic blood pressure (mm Hg)	67 (62-73)	68 (63-74)	67 (62-73)	67 (61-72)	69 (61-77)	67 (62-73)	0.006

Percentage or median value with interquartile range provided.

primary care hospital in a sixth city. All studies were performed by experienced registered cardiac sonographers and interpreted at a core laboratory by 1 of 10 highly experienced nonblinded cardiologists with Level III training in echocardiography. A standardized protocol followed recommended guidelines and included a comprehensive study of all cardiac structures.¹⁷ Echocardiograms were performed using Philips EPIQ 7 and iE33 systems (Philips Healthcare, Andover, Massachusetts); Acuson Sequoia 512 systems (Siemens, Malvern, Pennsylvania); or GE Vivid 7, Vivid 9, or Vivid E9 systems (GE Healthcare, Wauwatosa, Wisconsin). Images were archived in standard DICOM format and reviewed using contemporary versions of Synapse Cardiovascular Client (Fujifilm Medical Systems, Valhalla, New York). Clinical data were extracted from the electronic medical record. Race was self-reported.

Consistent with guideline recommendations, LV dimensions were indexed to body surface area (BSA) given their established relations with this marker of body size.¹ Data were tested for normal distribution using the Kolmogorov-Smirnov test. Normally distributed data are presented as mean \pm 1 standard deviation; data that are not normally distributed are presented as median (interquartile range). Comparisons of continuous variables without normal distribution were made using the Kruskal-Wallis Test. Comparisons of continuous variables with a normal distribution were made using ANOVA. Categorical variables were compared using the Chi-square test.

Multivariable analyses were performed using stepwise linear regression with comparisons between races using whites as a baseline and were adjusted for age, gender (except for gender-specific analyses), BSA (for nonindexed values), and mean arterial blood pressure. Subgroup analyses were performed comparing differences by race in patients with a normal body mass index (<25 kg/m²), with additional subgroup analyses performed in younger patients (<45 years of age).

p values <0.05 were considered significant. Statistical analyses were performed using IBM SPSS version 25 for Mac (IBM Corporation; Armonk, New York).

Results

Mean age was 46.9 ± 17.4 years and 60.5% were female. Among patients stratified by race, there were

differences in age, gender, and other patient characteristics (Table 1). On adjusted comparisons (Figure 1), there were significant differences between races in LV end-diastolic and end-systolic diameters indexed to BSA; septal and posterior wall thickness indexed to BSA; and left atrial diameter and volume indexed to BSA. There were also significant differences between races in unadjusted mitral E/A ratio and peak tricuspid regurgitation gradient; but not global longitudinal strain, E velocity, or e' velocities (Table 2).

Adjusted comparisons in echocardiography measurements between blacks and whites (Table 3) demonstrated smaller indexed LV diameters, increased indexed LV wall thicknesses, lower e' velocities, and a higher peak tricuspid regurgitation gradient. In comparison to whites, Asians were observed to have increased indexed LV end-diastolic diameter and LV wall thicknesses, increased indexed left atrial diameter, and a decreased peak tricuspid regurgitation gradient on adjusted analyses. Hispanics, in comparison to whites and after adjusting for other variables, had increased indexed LV end-diastolic diameter, posterior wall thickness, and left atrial diameter. Subgroup analyses by gender are also provided in these tables and demonstrate similar patterns to the overall groups.

Using the variables from HYPERLINK \l "tbl0003" Table 3, Native Americans (vs whites) had smaller adjusted EA ratios (-0.05 , 95% confidence interval [CI] -0.01 to -0.09 , $p = 0.009$); no other variables were significantly different ($p > 0.05$ for each). Using these same variables, multiracial/other patients (vs whites) had increased adjusted left atrial diameter/BSA (0.11 mm/m², 95% CI 0.02 to 0.21 , $p = 0.02$), posterior wall thickness/BSA (0.03 mm/m², 95% CI 0.01 to 0.06 , $p = 0.02$), and LV end-diastolic diameter/BSA (0.10 mm/m², 95% CI 0.01 to 0.20 , $p = 0.04$); there were no other significant differences between groups ($p > 0.05$ for each). These smaller cohorts were not stratified by gender.

Discussion

This study observes many significant differences in echocardiography measurements of cardiac structure and function between races in a cohort with normal blood pressure and without cardiovascular risk factors. We observed small but potentially meaningful differences in a wide variety of echocardiography measurements including LV

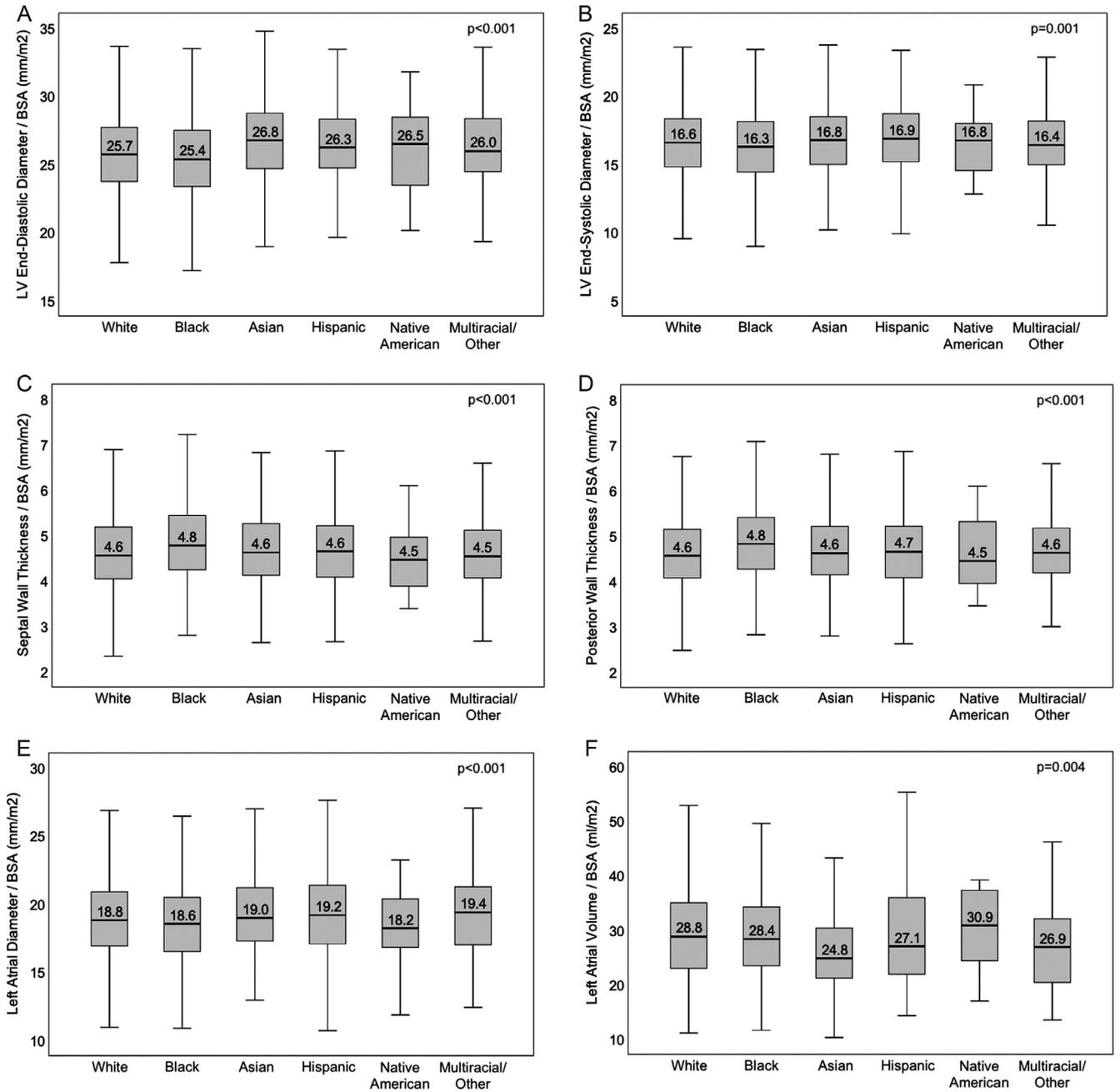


Figure 1. (A to F) There were significant differences between races for LV end-diastolic diameter/BSA (A), LV end-systolic diameter/BSA (B), septal wall thickness/BSA (C), posterior wall thickness/BSA (D), left atrial diameter/BSA (E), and left atrial volume/BSA (F). p values are provided on the figures. The black horizontal lines represent median values which are numerically labelled on the figure, the box the interquartile range, and the vertical lines extend up to 1.5 times the interquartile range and represent nonoutlier cases. Left atrial volume was only available in a subgroup of patients (n = 1,964). BSA = body surface area; LV = left ventricular.

diameter and wall thickness, LV mass, left atrial size, diastolic parameters, and peak tricuspid regurgitation gradient.

We observed smaller LV diameters, increased wall thickness, and increased LV mass in blacks. Although these differences are small, the adjusted differences in wall thickness and LV diameter could result in meaningful differences in patients with borderline values. These findings are similar to reports of increased LV wall thicknesses in African male soccer players.¹⁸ We also observed increased LV

diameter and wall thickness in Asians and Hispanics, although differences were smaller than in blacks.

In contrast to our findings, the Multi-Ethnic Study of Atherosclerosis observed no differences by magnetic resonance imaging in indexed LV volumes or mass between whites and blacks or Hispanics.¹¹ Other studies using echocardiography or magnetic resonance imaging have observed increased LV wall thickness and/or LV mass in blacks,^{9,10,12,13,19} which are consistent with our results. In

Asians, indexed LV diameter and wall thickness were higher as has been reported in the Multi-Ethnic Study of Atherosclerosis study.¹¹ Although limited by our small sample size, we observed no differences in LV dimensions or mass in Native Americans, consistent with findings from the Strong Heart Study.¹⁵

Among diastolic parameters, blacks had lower tissue Doppler e' velocities than whites. In comparison, Russo et al observed lower e' velocities in black and Hispanic volunteers in New York City, but these differences became non-significant after adjusting for co-morbidities.²⁰ Differences from our study may reflect different racial backgrounds in our cohort as well as the lack of significant co-morbidities. Our findings suggest that the current definitions for low e' velocities used to help define diastolic dysfunction may be too high for blacks.

Many of the observed differences between races were small and often may not result in a clinically meaningful difference. However, using current thresholds for normal ranges,¹ even a 1 mm difference in LV dimensions or wall thickness could affect whether a measurement is classified normal or abnormal in borderline cases (Figure 2), and could result in further diagnostic testing and diagnoses that could have been prevented if normal reference values based on a racially diverse cohort were available and utilized. Similarly, even the small differences of under 1 cm/s in e' velocity that we observed could result in a difference in classification of diastolic function using current guidelines,¹ which could affect downstream patient management. Although significant differences in reader variability have also been reported,²¹ the addition of potential differences by race may exacerbate this problem by adding a race-related difference on top of measurement variability.

Our observed differences in echocardiographic measurements between races raises concerns about whether current thresholds used to define normal and abnormal measurements – largely based on studies performed in Europe or the United States and with a racial makeup that is mostly white or not reported²⁻⁵ – are applicable to non-white patients. Our findings suggest the need for prospective research to establish reference ranges for echocardiographic findings that include a racially and geographically diverse population.²²

A limitation of this study is that it examined subjects within a limited geographic area, which would be expected to impact the races examined in this study. We also had relatively small non-white cohorts which limits our ability to identify differences between groups. In addition, whereas we excluded patients with known risk factors for changes in echocardiography findings, unmeasured variables may be present. Further, we examined patients referred for clinically indicated echocardiography, which may introduce selection bias. Although studies of normal volunteers may avoid these biases,^{5,23} these studies would also be susceptible to volunteer bias, and would lack the statistical power of this cohort. In addition, studies were not blindly interpreted, which could also introduce bias. Race was self-reported, which may introduce error,²⁴ and the limited race categories that were available may not permit accurate classification of all patients and do not provide detailed characterization of race. Finally, there are established interactions

Table 2
Other echocardiography measurement differences by race

Variable	n	White (n = 10,508)	Black (n = 792)	Asian (n = 628)	Hispanic (n = 315)	Native American (n = 34)	Multiracial/ Other (n = 152)	p
LV mass index (g/m ²)	12204	69.2 (58.8-81.7)	72.2 (61.1-84.9)	64.5 (54.9-76.3)	68.9 (58.7-79.5)	75.4 (62.7-85.5)	69.1 (57.5-79.9)	<0.001
[GLS]	710	20.9 (19.3-22.5)	20.8 (18.8-22.3)	21.6 (20.4-23.0)	20.2 (18.6-22.1)	-	21.0 (17.5-23.0)	0.23
E velocity (m/s)	2439	0.80 (0.67-0.90)	0.80 (0.70-0.90)	0.81 (0.70-1.00)	0.80 (0.69-0.94)	0.88 (72-1.00)	0.70 (0.64-0.90)	0.04
Septal e' (cm/s)	3727	10.0 (7.8-12.0)	9.7 (8.0-11.8)	10.0 (8.2-12.2)	10.2 (8.9-12.0)	8.9 (7.8-9.8)	9.3 (7.6-11.5)	0.35
Lateral e' (cm/s)	2867	12.3 (9.6-15.6)	12.0 (9.8-15.0)	12.2 (10.3-15.2)	13.4 (11.3-16.3)	13.2 (9.5-16.9)	12.1 (10.1-15.0)	0.28
E/A ratio	11096	1.3 (1.0 to 1.7)	1.4 (1.0 to 1.8)	1.4 (1.2 to 1.8)	1.4 (1.1 to 1.8)	1.1 (0.9 to 1.6)	1.4 (1.1 to 1.7)	<0.001
E/septal e' ratio	2925	8.1 (6.8-10.0)	8.1 (6.9-9.9)	8.1 (6.9-10.1)	8.4 (6.5-9.6)	7.8 (6.1-8.5)	7.8 (6.6-9.7)	0.88
E/lateral e' ratio	2826	6.2 (5.0-7.9)	6.2 (5.2-7.6)	6.2 (5.0-8.1)	6.2 (4.9-7.5)	6.3 (5.1-7.7)	5.7 (5.0-7.2)	0.57
TAPSE (mm)	5655	23 (20-26)	22 (19-25)	23 (19-25)	23 (20-25)	22 (19-25)	24 (21-27)	0.06
TR PPG (mm Hg)	5448	22 (18-27)	23 (19-30)	20 (18-2)	21 (18-26)	22 (19-26)	21 (18-25)	0.001

Percentage or median value with interquartile range provided. GLS = global longitudinal strain; LV = left ventricle; PPG = peak pressure gradient; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

Table 3
Adjusted differences echocardiographic findings by race compared with whites

	Blacks		Asians		Hispanics	
	Adjusted difference (95% CI)	p	Adjusted difference (95% CI)	p	Adjusted difference (95% CI)	p
<i>Overall</i>						
LV end-diastolic Diameter/BSA (mm/m ²)	-0.46 (-0.25 to -0.68)	<0.001	0.35 (0.23 to 0.47)	<0.001	0.17 (0.05 to 0.28)	0.004
LV end-systolic Diameter/BSA (mm/m ²)	-0.45 (-0.25 to -0.65)	<0.001	-	0.50	-	0.54
Septal wall thickness/BSA (mm/m ²)	0.35 (0.29 to 0.42)	<0.001	0.08 (0.05 to 0.12)	<0.001	-	0.08
Posterior wall thickness/BSA (mm/m ²)	0.36 (0.29 to 0.42)	<0.001	0.07 (0.03 to 0.10)	<0.001	0.04 (0.01 to 0.07)	0.01
Left atrial diameter/BSA (mm/m ²)	-	0.58	0.23 (0.11 to 0.36)	<0.001	0.31 (0.20 to 0.43)	<0.001
Left atrial volume/BSA (ml/m ²)	-	0.95	-1.30 (-0.36 to -2.23)	0.007	-	0.12
LV mass/BSA (g/m ²)	4.46 (3.14 to 5.78)	<0.001	-1.51 (-0.79 to -2.23)	<0.001	-	0.27
Global longitudinal strain	-	0.45	-	0.13	-	0.65
E velocity (m/s)	-	0.60	-	0.11	-	0.77
Septal e' (cm/s)	-0.66 (-0.33 to -0.99)	<0.001	-	0.18	-	0.25
Lateral e' (cm/s)	-0.92 (-0.46 to -1.39)	0.001	-	0.31	-	0.44
EA ratio	-0.04 (-0.01 to -0.07)	0.02	-	0.12	-0.02 (0.01 to -0.04)	0.03
E/septal e' ratio	-	0.41	-	0.17	-	0.07
E/lateral e' ratio	0.38 (0.03 to 0.74)	0.04	-	0.24	-	0.45
TAPSE (mm)	-0.60 (-0.01 to -1.20)	0.049	-	0.09	-	0.80
Peak TR gradient (mm Hg)	4.29 (3.21 to 5.37)	<0.001	-0.86 (-0.24 to -1.47)	0.007	-	0.37
<i>Females</i>						
LV End-Diastolic Diameter/BSA (mm/m ²)	-0.66 (-0.39 to -0.94)	<0.001	0.48 (0.33 to 0.62)	<0.001	0.20 (0.06 to 0.34)	0.005
LV end-systolic Diameter/BSA (mm/m ²)	-0.62 (-0.37 to -0.87)	<0.001	-	0.07	-	0.46
Septal wall thickness/BSA (mm/m ²)	0.33 (0.25 to 0.41)	<0.001	0.09 (0.05 to 0.13)	<0.001	0.05 (0.01 to 0.09)	0.03
Posterior wall thickness/BSA (mm/m ²)	0.28 (0.20 to 0.35)	<0.001	0.06 (0.02 to 0.10)	0.02	0.04 (0.01 to 0.08)	0.04
Left atrial diameter/BSA (mm/m ²)	-	0.48	0.34 (0.19 to 0.49)	<0.001	0.30 (0.16 to 0.45)	<0.001
Left atrial volume/BSA (ml/m ²)	-	0.41	-1.27 (-0.25 to -2.28)	0.01	-	0.11
LV mass/BSA (g/m ²)	3.37 (1.83 to 4.92)	<0.001	-0.93 (-0.10 to -1.75)	0.03	-	0.28
Global longitudinal strain	-	0.10	-	0.67	-	0.81
E velocity (m/s)	-	0.74	-	0.10	-	0.60
Septal e' (cm/s)	-0.55 (-0.12 to -0.98)	0.01	-	0.58	-	0.27
Lateral e' (cm/s)	-0.91 (-0.32 to -1.50)	0.003	-	0.51	-	0.60
EA ratio	-0.05 (-0.01 to -0.09)	0.03	-	0.11	-	0.15
E/septal e' ratio	-	0.78	-	0.11	0.26 (0.01 to 0.51)	0.04
E/lateral e' ratio	-	0.18	-	0.21	-	0.47
TAPSE (mm)	-	0.23	-	0.39	-	0.83
Peak TR gradient (mm Hg)	4.96 (3.65 to 6.27)	<0.001	-0.89 (-0.17 to -1.60)	0.02	-	0.21
<i>Males</i>						
LV end-diastolic Diameter/BSA (mm/m ²)	-	0.42	-	0.31	-	0.23
LV end-systolic Diameter/BSA (mm/m ²)	-	0.31	-	0.18	-	0.90
Septal wall thickness/BSA (mm/m ²)	0.39 (0.28 to 0.50)	<0.001	0.07 (0.01 to 0.14)	0.03	-	0.07
Posterior wall thickness/BSA (mm/m ²)	0.48 (0.39 to 0.58)	<0.001	0.07 (0.01 to 0.12)	0.02	-	0.12
Left atrial diameter/BSA (mm/m ²)	-	0.99	-	0.64	0.33 (0.01 to 0.51)	0.001
Left atrial volume/BSA (ml/m ²)	-	0.26	-	0.22	-	0.66
LV mass/BSA (g/m ²)	6.22 (3.84 to 8.60)	<0.001	-2.62 (-1.25 to -3.99)	<0.001	-	0.59

(continued on next page)

Table 3 (Continued)

	Blacks		Asians		Hispanics	
	Adjusted difference (95% CI)	P	Adjusted difference (95% CI)	P	Adjusted difference (95% CI)	P
Global longitudinal strain	-	0.58	-0.97 (-0.17 to -1.77)	0.02	-	0.80
E velocity (m/s)	-	0.39	-	0.59	-	0.52
Septal e' (cm/s)	-0.81 (-0.28 to -1.35)	0.003	-	0.17	-	0.72
Lateral e' (cm/s)	-0.95 (-0.21 to -1.69)	0.01	-	0.46	-	0.62
EA ratio	-	0.38	-	0.58	-	0.09
E/septal e' ratio	-	0.08	-	0.71	-	0.75
E/lateral e' ratio	-	0.10	-	0.82	-	0.78
TAPSE (mm)	-	0.08	-	0.09	-	0.87
Peak TR gradient (mm Hg)	2.92 (1.04 to 4.80)	0.002	-	0.20	-	0.85

Variables adjusted for age, gender (when appropriate), and mean arterial pressure. BSA = body surface area; CI = confidence interval; LV = left ventricle; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

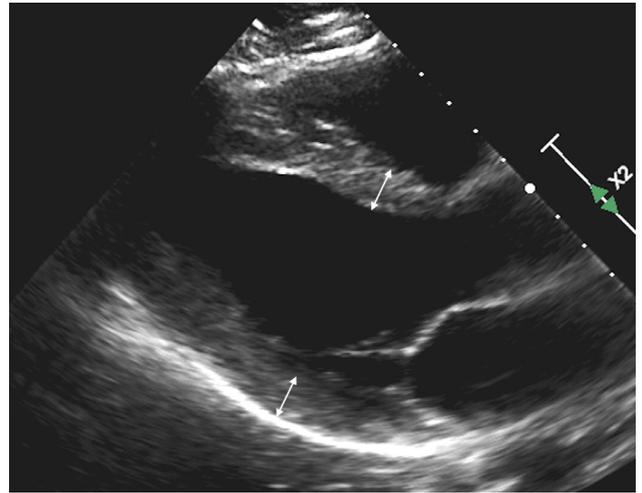


Figure 2. This 25-year-old black man has no cardiovascular risk factors and was referred for a stress echocardiogram for atypical chest pain. His septal and posterior wall thicknesses were both measured as 11 mm (arrows), which are considered increased based on current guidelines (abnormal >10 mm for men).¹ Our observation that black men have increased wall thicknesses (nearly 1 mm using a body surface area of 2 m²) suggest a potential to over-diagnose increased wall thickness in borderline cases if we use reference ranges that do not include black populations.

between race and other variables including socioeconomic status²⁵ which may influence these findings and cannot be examined in the present study.

Among patients without known cardiovascular risk factors, race is associated with small but clinically meaningful differences in LV size, left atrial size, mitral annular velocity, and peak tricuspid regurgitation. As our cohort does not represent a truly “normal” population, our findings should not be used to define normal ranges of echocardiographic variables by race; instead it should inform echocardiographers and patient providers of potential differences in echocardiography findings by race. Further, these findings highlight the need for normal reference ranges for echocardiography measurements that utilize racially diverse cohorts to prevent incorrect classification of findings based on race.

Disclosures

The authors have no conflicts of interest to disclose.

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