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LEFT ATRIAL VOLUME INDEX IN HEALTHY SUBJECTS: CLINICAL AND ECHOCARDIOGRAPHIC CORRELATES.

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Contribution

SS conceived, designed and did statistical analysis. SI and AM did data collection and manuscript writing. MA did review. All authors contributed equally.

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ABSTRACT

Objective: To evaluate normal reference ranges for LAVi in Pakistani population with 2D echocardiography (2DE).

Methodology: This cross sectional study was conducted at Cardiology Department of Doctors Hospital and Medical Center, Lahore from 1st February 2014 to 31st April 2016. Healthy subjects of either gender, free from cardiovascular and renal disease were included. Normal reference ranges were established using non parametric approach, which involves establishing the values falling at the 2.5 and 97.5 percentiles of the population as the lower and upper reference limits.

Results: Total of 103 subjects were included. Mean age of subjects was 30.81 ± 8.77 years. Mean LAVi was 21.96 ± 4.189 ml/m^2 with minimum of 10 ml/m^2 and maximum of 30 ml/m^2. Normal reference range estimated by non-parametric method (2.5 and 97.5 percentiles) in our population was 13-28 ml/m^2. Mean value of LAVi in females was 21.00 ml/m^2 (range 13-30) and in males it was 22.33 ml/m^2 (range 10-28). In the age group less than 40 years, mean LAVi was 21.7 ml/m^2 (range 10-30). In more than 40 years of age it was 23.14 ml/m^2 (range 15-28).

Conclusion: The present study established normal ranges for left atrial volume index (LAVi) in our population for both the genders and shows that normality in our population is different from that of other ethnicities.

Key Words: Left Atrial volume index, Echocardiography, Reference range.

INTRODUCTION

Left atrial (LA) size is part of cardiac remodelling in a variety of cardiovascular diseases and a predictor of cardiovascular morbidity and mortality.[1-4] LA dilatation is a powerful predictor of heart failure, stroke, and mortality.[5-9] Left atrium can be involved in a number of disease processes. It is commonly dilated in association with left ventricular, aortic and mitral valve diseases such as senile left ventricular diastolic dysfunction, hypertrophic, dilated or restrictive cardiomyopathy, chronic atrial fibrillation, mitral stenosis and mitral regurgitation. Imaging left atrium and its appendages can provide important diagnostic and prognostic information. The left atrium can be easily imaged in a number of views by transthoracic (surface) or transesophageal echocardiography. The most widely applied technique for measuring atrial size is two-dimensional echocardiography (2DE).[10-12] The method of assessing maximal end-systolic anteroposterior dimension of LA from the parasternal long-axis view in M-mode echocardiography is simple and convenient but its accuracy is rather limited by the anatomical confinement afforded by the spine and sternum and the resulting asymmetrical or pillow-shaped enlargement of the left atrium.[13] For these reasons, multiple linear dimensions or measurement of left atrial volume (LAV) especially when corrected for body surface area i.e. left atrial volume index (LAVi) is a more accurate representation of true LA size.[14] The normal range for LA differs between studies and guidelines and are below those obtained with MRI.[11,12,15,16] The American Society of Echocardiography in 2005 recommended a value of 28 ml/m^2 as the upper limit for normal LAVi and a value of > 40 ml/m^2 for severe dilatation.[17] But now in updates from the American Society of Echocardiography and the European Association of Cardiovascular Imaging the upper normal value of LAVi on 2DE has been increased to 34 ml/m^2.[18] However, in our routine clinical practice the LAVi values between 29 ml/m^2 to 34 ml/m^2 are observed in those having hypertension and diastolic dysfunction. Moreover the data to define normal parameters for echocardiographic measurements are scarce in Pakistan and none of the studies have used LAVi as a parameter. Therefore, we aimed at defining the normal values of LAVi for Pakistani population assuming that these may be lower than those recommended by the American Society of Echocardiography and the European Association of Cardiovascular Imaging.

The objective of the study was to evaluate normal reference ranges for LAVi in Pakistani population with 2D echocardiography (2DE).

METHODOLOGY

This cross sectional study was conducted at Cardiology Department of Doctors Hospital and Medical Center, , Lahore from 1st February 2014 to 30th April 2016. Echocardiograms were done over a period of two years. Exclusion criteria included history of congenital heart diseases, systolic or diastolic dysfunction, any cause of LA dilatation such as hypertension (on anti-hypertensive treatment), Hyper-trophic, dilated or restrictive cardiomyopathy, chronic atrial fibrillation, mitral stenosis and mitral regurgitation. These patients were further screened for major chronic and acute communicable and non-communicable diseases e.g. diabetes mellitus, hypertension, ischemic heart disease, renal dysfunction, Hepatitis B and C, thyroid or other endocrine dysfunction, anemia and liver dysfunction and were excluded if any of these were present. Patients were stratified according to gender and age i.e. more than 40 years and less than 40 years to establish a more accurate range for LAVi. An informed consent was taken and the study was approved by the ethical review board.

The study patients underwent echocardiography, using Toshiba, Aplio 300 system, Model TUS-A300. All patients were examined in the left lateral position. TTE is the recommended approach for assessing LA size and it was used in our study. TEE, is not used because the entire left atrium frequently cannot fit in the image sector. LA size is measured at the end of LV systole, when the LA chamber is at its greatest dimension. Care is taken to avoid foreshortening of the left atrium. Acquisition of the left atrium from the apical approach is done. Care is taken to have the base of the left atrium at its largest size, so that the imaging plane passes through the maximal short-axis area. LA length is also maximized to ensure alignment along the true long axis of the left atrium. The lengths of the long axes measured in the two- and four-chamber views were almost similar when tracing the borders of the left atrium, the confluences of the pulmonary veins and the LA appendage were excluded. The atrioventricular interface was represented by the mitral annulus plane and not by the tip of the mitral leaflets. LA volume is measured using the disk summation method.[19, 20] The LA endocardial borders were traced in both the apical four and two chamber views. Gender differences in LA size were accounted for by indexing to BSA.[18,21-28]

Patients' demographic features and the echocardiographic results were recorded. Data was entered in SPSS version 23 and analyzed using non-parametric analysis. Percentages and frequencies were calculated for nominal data and median and standard deviations were calculated for continuous variables.

RESULTS

Baseline characteristics of 103 healthy subjects are shown in table 1. The mean age of the participants was 30.81 $\pm$8.77 years. Majority were less than 40 years of age i.e. 89 (86.4%), while only 14 (13.6%) were more than 40 years old. Study participants were dominated by males who were 74 (71.8%) in number and 29 (28.2%) of them were females.

Mean body surface area (BSA) was 1.722 m^2 with SD of $\pm$0.209. About 63 individuals (61.00%) had normal weight, defined as having BMI <24.9 kg/m^2 and 39 (38.8%) were overweight defined as having BMI>25 kg/m^2. Risk factors for cardiovascular disease were evaluated. Patients with hypertension, diabetes mellitus, ischemic heart disease, dyslipidemia, chronic kidney disease, mitral regurgitation or diastolic dysfunction on echocardiography and previous history of coronary artery bypass grafting or hospitalization were excluded.

Mean LAVi was 21.816 ml/m^2 with SD of $\pm$ 4.2281 (minimum=10 maximum 30ml/m^2). Normal reference range estimated by non-parametric method (2.5 and 97.5 percentiles) in our population was 13-28 ml/m^2.

About 37 (35.9%) participants had LAVi between 10 to 20 ml/m^2 and majority i.e. 66 (64.1%) had a LAVi of 21 to 30 ml/m^2.

Range for LAVi was 10-30 ml/m2, for E/e′ ratio (ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity) which is a sensitive marker for the detection of left ventricular diastolic dysfunction, the range was 4-8, for pulmonary artery systolic pressure (PASP) 20-30mmHg, for glomerular filtration rate (GFR) 66-159 ml/min/1.73m^2 and the minimum ejection fraction (EF) was 55% and the maximum was 70%. (Table 2)

LAVi was studied in both genders and the age groups of less than and more than 40 years (Table 3). Values were not significantly different statistically in the age and gender groups (p=0.25 and 0.14 respectively). Normal reference range for LAVi using nonparametric approach was 13-28 ml/m^2.

Table 1: Baseline Characteristics of the Participants (n=103)

Variables	Frequency (n)	Percentage (%)
Age		
< 40 years	89	86.4
> 40years	14	13.6
Gender		
Male	74	71.8
Female	29	28.2
BSA (1.722m^2 $\pm$0.209)		
BMI (21.916kg/m^2 $\pm$ 4.900)		
Normal weight (BMI < 24.9)	63	61.0
Overweight (BMI >25.0)	40	38.8
Risk Factor		
Dyslipidemia	0	0
Hospital admission	0	0
LVH		
None	103	100
Yes	0	0
MR		
None/Trace	103	100
DD		
None	103	100
LAVI GROUP (21.816 ml/m^2 $\pm$ 4.2281)		
10-20	37	35.9
21-30	66	64.1

Table 2: Ranges Observed for Echocardiographic and other Parameters in Study Population (n=103)

	LAVI (ml/m^2)	E/e RATIO	PASP (mmHg)	GFR ml/min/1.73m^2)	EF (%)
Mean	21.961	6.51	24.77	113.50	63.45
Std. Deviation	4.1890	1.047	2.291	17.091	3.211
Minimum	10.0	4	20	66	55
Maximum	30.0	8	30	159	70

LAVi= Left atrial volume index, E/e/ ratio= ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E'), PASP= Pulmonary artery systolic pressure, GFR= Glomerular filtration rate,EF= Ejection fraction

Table 3: Left atrial volume index (ml/m^2) in the Age and Gender Groups (n=103)

	Groups	Frequency (n)	Mean	SD	P value
Age					
LAVi	<40 years	89	21.775	4.2740	p= 0.258
	>40 years	14	23.143	3.5051	
Gender					
LAVi	Males	74	22.338	4.1489	p=0.146
	Females	29	21.000	4.2088	

DISCUSSION

Clinically applicable database is required for determining normal values of atrial volumes. The maximum value of LAVi in the study group was 30 which is different from the American Society of Echocardiography/European Association of Echocardiography (ASE/EAE) guidelines where the upper normal limit for max LAVI is 34 mL/m^2 (mean +2 SD).[29,30] This reference value is not only derived from population studies, but it is also based upon an estimation of risk related to chamber size, and from expert opinion. The discrepancy from our upper reference may therefore not only be related to different selection criteria of the study populations and different methodology but also to the principles for defining normality. In general, men are considered to have larger cardiac dimensions than females even after scaling for body size. Studies have shown to eliminate the gender differences when cardiac dimensions were scaled allometrically.[31] In our study, gender difference had no role in the normal reference ranges for LAVi. Therefore, gender-related reference values are not deemed necessary, provided body surface area-corrected variables are used. However the proportion of males and females was largely different in the selected volunteers (74 vs 29) which might be a hurdle to establish this reference range with certainty. Similarly, this study did not find the influence of age on LAVi. Therefore, age corrected reference ranges do not seem to be justified. Similar findings were seen by Aune et al. with newer 3D echocardiography.[32] EF range we observed was 55-70 % which matches the other studies in Pakistani population.[33] Mean PASP and E/e' ratio were consistent with American Society of Echocardiography recommendations.

At present, cardiomagnetic Resonance (CMR) is considered to be the gold standard tool for measuring cardiac dimensions. Hudsmithet al. studied 108 healthy volunteers aged (38±12) years.[16] Their results showed upper normal limit of 80 mL/m^2 for max LAVI and 37 mL/m^2 for min LAVI. The lower limit for LVEF was 30%, far below our lower limit and within the level suggested to indicate increased LV filling pressure.[34] These differences are disturbing and emphasize the need for proper reference values for the actual method applied in the clinical setting. Some of the discrepancies vs. 2DE may be related to the use of the biplane area-length method in the CMR study which incorporated inclusion of the LA appendage.2DE is very reproducible for left atrial volume measurements which is probably related to the use of three loops in both views and the availability of former loops during the second investigation. But this process is time-consuming and that is the reason most of the cardiologists do not perform it. However it gives very useful information in terms of LAVi as a prognostic tool for cardiovascular morbidity.

When 2DE is compared with newer and fast real-time three-dimensional echocardiography (RT3DE), RT3DE gives higher upper normal values which may reflect an underestimation to the 2DE-derived normal range, as presented in the guidelines. Khan Kirawatana et al. found a small underestimation in 8 mongrel dogs.[35] When these same authors compared LA size with 4 different methods of echocardiography, they found a fairly close agreement between Biplane Simpson methods and 3D reconstruction.[36] Another study by Badano et al. found close correlation of 3D and 2D left atrial volumes.[37] Hence 2DE has not been found to underestimate reference values of atrial volumes on most of the occasions.

CONCLUSION

The present study has provided normal ranges for LAVi with 2DE from a series of normal individuals aged 20-60 years. LAVi values were similar for both genders and for both age groups i.e more than and less than 40 years. According to our study, normal values for LAVi are lower in the Pakistani population than those found in western guidelines. Larger studies including individuals from all across Pakistan would have to be conducted to validate our findings.

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