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Normal Ranges of Left Atrial Strain and 3D Echocardiographic Volume Measurements in Türkiye

Türkiye'de Sol Atriyal Strain ve 3D Ekokardiyografik Hacim Ölçümlerinin Normal Değer Aralıkları

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ABSTRACT

Objective: The clinical importance of left atrial (LA) remodeling and function have been shown in various cardiovascular diseases, such as heart failure and atrial fibrillation. The LA dimension and volume index are the currently recommended parameters for evaluation of LA. Speckle tracking echocardiography makes it possible to evaluate the physio-mechanics of the LA method and threedimensional echocardiography have been shown to provide robust calculations of LA volume. However, there is still a lack of reference values regarding the LA longitudinal strain (LS) and three-dimensional (3D) volumetric measurements in Türkiye. Thus, we sought to investigate and determine normal references for mentioned echocardiographic methodologies by examining healthy individuals.

Methods: The echocardiographic data of one-hundred and forty-six volunteers without known cardiovascular pathologies were analyzed. 3D volume measurements and LA longitidinal strain in the reservoir, conduit, and contraction phase were investigated. Trigger points were placed on the R-waves on the electrocrocardiogram, as suggested by recent recommendations.

Results: Our study revealed a normal reference range for LA reservoir LS [40% (95% confidence interval (CI): 38-43%)], LA conduit LS [24% (95% CI: 22-26%)], LA contraction phase LS [16% (95% CI: 13-18%)] and for 3D maximal LA volume of 28 mL/m^2 (95% CI: 25-32).

Conclusion: We have provided normal reference ranges for phasic LA LS and 3D volume measurements. Having normal reference ranges for Turkish population carries importance as regional difference can occur.

Keywords: Adult echocardiography, left atrial function, left atrial volume, deformation imaging, 3D echocardiography, reference values

ÖZ

Amaç: Sol atriyum (SA) yeniden şekillenmesinin ve işlevinin klinik önemi, kalp yetmezliği ve atriyal fibrilasyon gibi çeşitli kardiyovasküler hastalıklarda gösterilmiştir. SA boyutu ve hacim indeksi, SA'nın değerlendirilmesi için halen önerilen parametrelerdir. Speckle tracking ekokardiyografi, SA'nın fizyomekanik özelliklerinin değerlendirilmesine olanak tanırken, üç boyutlu (3D) ekokardiyografinin SA hacminin sağlam bir şekilde hesaplanmasını sağladığı gösterilmiştir. Ancak, Türkiye'de SA longitudinal strain (LS) ve 3D hacim ölçümleri ile ilgili referans değerler konusunda hala bir eksiklik vardır. Bu nedenle, sağlıklı bireyleri inceleyerek, bahsedilen ekokardiyografik metodolojiler için normal referans değerlerini araştırmayı ve belirlemeyi amaçladık.

Yöntemler: Bilinen kardiyovasküler patolojisi olmayan yüz kırk altı gönüllünün ekokardiyografik verileri analiz edildi. Rezervuar, iletken ve kasılma fazlarında 3D hacim ölçümleri ve SA LS incelendi. Tetikleme noktaları, güncel öneriler doğrultusunda elektrokardiyogramdaki R dalgaları üzerine yerleştirildi.

Bulgular: Çalışmamız, SA rezervuar LS için normal referans aralığını [%40 (%95 güven aralığı (GA): %38-43)], SA iletken LS [%24 (%95 GA: %22-26)], SA kasılma fazı LS [%16 (%95 GA: %13-18)] ve 3D maksimum SA hacmi için 28 mL/m^2 (%95 GA: 25-32) olarak ortaya koymuştur.

Sonuç: Fazik SA LS ve 3D hacim ölçümleri için normal referans aralıkları sağladık. Türk popülasyonu için normal referans aralıklarının belirlenmesi, bölgesel farklılıklar olabileceğinden önem taşımaktadır.

Anahtar Sözcükler: Yetişkin ekokardiyografi, sol atriyal işlev, sol atriyal hacim, deformasyon görüntüleme, 3D ekokardiyografi, referans değerler

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INTRODUCTION

Numerous cardiovascular conditions, including heart failure and atrial fibrillation, induce alterations in the morphology and function of the left atrium. Left atrial (LA) remodeling, characterized by structural and functional changes, holds diagnostic and prognostic significance in various critical diseases (1). Presently, LA assessment primarily relies on two-dimensional (2D) echocardiography for measuring LA size and volume index (2). Nevertheless, 2D measurements have limitations, such as susceptibility to foreshortening and dependence on geometric assumptions. In contrast, three-dimensional (3D) echocardiography, owing to its increasing use and demonstrated accuracy and reproducibility, provides precise measurements without the need for geometric assumptions (3). Volumetric measurements derived from 3D echocardiography exhibit strong correlations with computed tomography and cardiac magnetic resonance measurements. Assessing the functional aspect of the left atrium is as crucial as understanding its anatomy in managing various diseases. The left atrium fulfills multiple roles in cardiac function, acting as a reservoir during left ventricular systole, a conduit in early diastole, and a pump in late diastole (4). Speckle tracking echocardiography facilitates a comprehensive evaluation of LA physio-mechanics (5). Initial reservations regarding LA strain assessment due to the thin myocardial wall have been dispelled by subsequent studies, demonstrating robust correlations between LA strain and atrial fibrosis rates. LA strain has shown diagnostic value in conditions such as heart failure with preserved ejection fraction, predictive value for thromboembolic events, and prognostic value for mitral regurgitation and atrial fibrillation (6-9). Moreover, strain analysis obtained through speckle tracking echocardiography is angle-independent and minimally affected by loading conditions, rendering it a potent tool for detecting subclinical dysfunction (4).

Technical standardization: A significant challenge arises from the lack of a technical consensus on LA strain analysis, primarily due to variations in software used by different vendors. Standardization within a specific vendor’s system and conducting serial follow-ups with the same system are recommended to reduce measurement variability. Imaging from both apical four-chamber and two-chamber views is essential, and the region of interest (ROI) should be adjusted to avoid pericardial inclusion-related errors.

Reference values: The absence of established reference values for LA strain complicates its clinical application. Previously reported normal LA peak values vary significantly, partly due to differences in study populations and the definition of a “healthy subject group.” Establishing specific reference values is essential for reducing regional variations (2,3).

Left atrial cycle definition: Two different definitions for the LA cycle exist: RR gating and PP gating. PP gating initiates the cycle with atrial contraction, resulting in a biphasic strain curve. RR gating, conversely, defines the cycle from the R-wave peak to the same point in the next cycle, yielding a monophasic curve that clearly delineates the reservoir phase. Recent studies recommend RR gating because it can be employed during atrial fibrillation (10).

While LA strain assessment via speckle tracking echocardiography provides valuable insights into cardiac function and holds significant potential for clinical application, several challenges necessitate further exploration and standardization. These include technical standardization, the establishment of reference values and the choice of LA cycle definition. This study seeks to investigate normal reference values of LA strain and 3D echocardiographic volume measurements in healthy individuals in Türkiye, thereby contributing to a better understanding of this emerging tool in cardiac assessment.

MATERIALS AND METHODS

Study Participants

Patients over 18 years of age, without known cardiac disease and in sinus rhythm were included in the study. Patients with a history of heart failure, moderate or severe valvular heart disease, pericardial disease, coronary artery disease and pulmonary embolism were excluded from the study. Patients with poor image quality were also excluded. Finally, 146 patients were analyzed. The study protocol was approved by the Gazi University Clinical Research Ethics Committee (approval number: 753, date: 09.11.2020). Informed consent was obtained.

Echocardiographic evaluation: Echocardiographic evaluations of the patients at rest were performed by the same cardiologist using a General Electrics Vivid E95 device with a 2D M5Sc-D probe (GE Vingmed Ultrasound) according to the American Society of Echocardiography guidelines. For LA strain analysis, LA-focused images avoiding foreshortening were recorded.

3D imaging was performed with the GE Vivid E95 4V-D Probe (GE Vingmed Ultrasound). To obtain data sets of appropriate image quality, multi-beat images were recorded consecutively over 6 beats.

The acquired ECG-linked images were transferred to an offline EchoPac v201 (GE Vingmed Ultrasound) station for analysis.

Left atrial strain analysis with 2D STE: The LA ROI was determined in the obtained images. The full-wall ROI was manually adjusted for each image with an average thickness of 3 mm, optimally excluding the pericardium, pulmonary veins, and LA appendage. LA longitidinal strain curves were obtained from RR gating. The left atrial reservoir strain (LASr), left atrial conduit strain (LAScd), and left atrial contraction strain (LASc) were calculated from the obtained curve (11).

Reservoir strain (LASr): Describes the deformation of the left ventricle during isovolumetric contraction, ejection and isovolumetric relaxation. It is calculated as the difference in strain between the peak of the strain curve and the end of diastole. This value is always positive.

Conduit strain (LAScd): It occurs in patients in sinus rhythm from the opening of the mitral valve until the onset of LA contraction. It is calculated by subtracting the peak value of the curve from the strain value at the beginning of atrial contraction and is always negative.

Contraction strain (LASc): Defines the deformation from the beginning of LA contraction to the end of diastole. Therefore, it is calculated as the difference between the tension value at the end of diastole (zero by definition) and the value at the beginning of atrial contraction. LASc occurs only in sinus rhythm and always has a negative value.

3D echocardiographic left atrial volume measurement: The image was aligned to obtain an optimal border delineation of the left atrium. The 3D longitudinal axis was aligned parallel to the axis of the left atrium. The 3D transverse axis was positioned approximately at the level of the left atrium, where it intersected the 3D longitudinal axis at the geometric center point of the left atrium. For LA border tracking, 4 mitral annular points (lateral, septal, inferior, anterior) and the atrial superior dome point opposite the annulus were marked for semi-automatic LA border tracking. The LA maximum volumes were calculated automatically by the software. Maximum LA volume was measured in the frame just before mitral valve opening and manually indexed to BSA.

Statistical Analysis

Continuous variables have been conveniently summarized as mean values accompanied by their respective standard deviations, whereas categorical data are presented as percentages or frequencies. To assess the normality of the distribution of continuous variables, the Kolmogorov-Smirnov test was employed. A stringent criterion for statistical significance, denoted by a two-tailed p-value of <0.05, was uniformly adopted throughout all analyses. The statistical analysis was conducted using SPSS version 23.0, developed by IBM Corp in Armonk, NY, USA.

RESULTS

We provide normal reference ranges for phasic LA LS and 3D volume measurements. A total of 146 healthy volunteers were included in the study. The mean age of the population was 34.1±7.2 years. 48.6% were female. There were no known diseases that could affect hemodynamics. Arterial blood pressure and heart rate were within the normal range. The demographic, anthropometric, and clinical characteristics of the patients are summarized in Table 1.

Phasic LA longitidinal strain obtained from 2D speckle tracking echocardiography and 3D echocardiographic LA volume measurements are summarized in Table 2. LASr was 40% [confidence interval (CI): 95% 38-43%], conduit strain (LAScd) 24% (CI: 95% 22-26%), and contraction phase strain (LASc) 16% (CI: 95% 13-18%). 3D echocardiographic LA maximum volume was 28 mL/m^2 (25-32 mL/m^2).

Table 1. Demographic anthropometric and clinical features

Parameters	(n=146)
Age (years)	34.1±7.2
Gender (f) (n, %)	71 (48.6%)
SBP (mmHg)	115.7±8.7
DBP (mmHg)	78.1±6.9
Heart rate (bpm)	71.5±9
Weight (kg)	70.7±14.5

SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

Table 2. Comparison of conventional echocardiographic parameters among groups

Parameters	Referance value	95% CI
LASr (%)	40%	38-43%
LAScd (%)	24%	22-26%
LASc (%)	16%	13-18%
LA volume indeks (mL/m^2)	28 mL/m^2	25-32 mL/m^2

LA: Left atrium, LS: Longitudinal strain, LASr: Left atrial reservoir strain, LAScd: Left atrial conduit strain, LASc: Left atrial contraction strain, CI: Confidence interval.

DISCUSSION

In this study, a healthy population in Türkiye was analyzed. The aim was to determine LA phasic strain values and 3D echocardiographic LA volume reference values. The findings of this study can be summarized as follows: (a) LA phasic strain values were 40% for the reservoir phase, 24% for the conduit phase, and 16% for the contraction phase. (b) 3D echocardiographic volume measurements showed a maximum LA volume index of 28 mL/m^2. (c) Our measurements were correlated with other comprehensive studies.

Deformation Imaging and 2D Speckle Tracking Echocardiography for Left Atrial Remodeling

LA remodeling refers to cumulative structural and functional changes due to haemodynamic stress. Given the absence of other structural abnormalities, the main cause of LA remodeling is high LV filling pressure (5). Therefore, the presence of LA remodeling reflects the long-term progression of various cardiovascular diseases. Currently, LAVI is the main parameter of LA remodelling and has its proven clinical advantages of simple measurement and derived from various cardiovascular diseases. However, the LAVI actually represents a static volume. Therefore, LAVI has limitations in reflecting the unique LA mechanics during the cardiac cycle, including reservoir, channel, and contractile functions.

Assessment of phasic atrial function provides an understanding of the complex role of the atria and its various phasic functions (reservoir, channel, and contractile) (1). Assessment of atrial function by speckle tracking echocardiography is a reproducible and accurate method of analysis for the detection of subclinical LA dysfunction that is relatively free from loading conditions and relatively geometric assumptions. The prognostic significance has been demonstrated in many cardiovascular diseases. LA strain values of atrial fibrillation patients have been shown to be associated with increased gadolinium uptake, i.e., fibrosis, in cardiac magnetic resonance (6). Subsequently, many studies have emphasized the relationship between atrial fibrillation frequency and atrial strain (8). LA strain has been shown to be a very strong predictor of atrial fibrillation recurrence. In particular, a peak atrial strain below 23% predicted recurrence after atrial fibrillation ablation. LA strain has also been associated with survival after stroke in patients with chronic atrial fibrillation. In this study, 12% was used as the limit value (9,12,13). Another use of LA strain is in heart failure (14). It has been found to be a prognostic marker in heart failure with low ejection fraction. It has been shown that the prognosis is extremely poor when peak atrial strain is below 13 per cent.

LA strain was also found to be a prognostic parameter in heart failure with preserved ejection fraction with low ejection fraction. The limit values are 31% for patients with sinus rhythm and 35% for patients with atrial fibrillation. In the staging of diastolic dysfunction, LA peak strain was found to be an important marker of diastolic dysfunction in all diastolic dysfunction groups and subgroups, while other echocardiographic parameters did not show continuity between groups (7). However, despite these strong studies, LA strain could not be included as a basic parameter because a specific reference value could not be determined. Moderately comprehensive studies in different patient groups and lack of technical standardization are the most important obstacles to establishing a clear reference value (11). In addition, there is a high heterogeneity between groups in studies conducted to determine reference values. Regional differences are also one of the biggest obstacles in the clarification of the reference value. Therefore, there is still a need for studies to determine reference values in healthy participant groups. In response to this practical need, this study presents reference values for LA stain obtained from a group of healthy subjects in Türkiye.

The mean LASr in our study was 40% (95% CI: 37-43%). Several previous studies have reported LASr values (also defined as peak LA trains) in healthy groups. Pathan et al. (15) conducted a meta-analysis on 2,542 healthy subjects and found that the mean LASr was 39.4% (95% CI: 38.0%-40.8%). D'Ascenzi et al. (16) performed a meta-analysis on 2,087 subjects and reported a mean LASr of 38±3% (95% CI: 32%-43%). Although these studies reported LASr values similar to our results, Sun et al. (17) reported a mean LAS RES of 35.7±5.8% in a study of 54 healthy Korean subjects. This is substantially different from our results. The main difference in these results seems to be related to regional variation. However, there are few original studies analysing LAScd and LASc. This study additionally provides a reference value for LAScd and LASc.

3D Echocardiographic Volume Assessment for Left Atrium

The prognostic value of LAV as a predictor of morbidity and mortality is well recognized in many cardiovascular disease states and is particularly important for the assessment of LV diastolic function. However, 2DE techniques routinely used to measure LAV in clinical practice are prone to errors due to their 2D nature. Extensive studies have shown a significant underestimation of 2D LAV measurements compared with computed tomography and cardiac magnetic resonance results. Traditional assessment of LA volumes by 2DE is limited by prior abbreviation and reliance on incorrect geometric assumptions for volumetric estimation, leading to underestimation of true LA volumes (18). There are several publications showing that this underestimation is significantly reduced by the use of 3DE imaging. However, there are very few studies on reference values. Determination of reference values with 3D echocardiography, which is a more accessible and inexpensive method compared to cardiac MR, is important for clinical practice (19). In our study, we determined the reference value for the indexed 3D LAV as 28 mL/m^2. Our reference value seems to be more compatible with cardiac MR results obtained in previous comprehensive studies compared to 2D echocardiography (18,19).

Study Limitations

It is important to recognize the limitations of our study. Perhaps the most important limitation was the relatively small sample size and the recruitment of participants from a single center. Although our findings provide valuable information, future research with larger and more diverse cohorts will allow for the clarification and establishment of reference values in clinical practice.

CONCLUSION

In conclusion, we proposed reference values for strain analysis and 3D echocardiographic indexed volume assessment of the LA reservoir, duct, and contractile components in a large group of healthy subjects living in Türkiye. New developments in echocardiography allow non-invasive elucidation of LA physiomechanics. However, more comprehensive studies on reference values are needed to incorporate these parameters in clinical practice.

Ethics

Ethics Committee Approval: The study protocol was approved by the Gazi University Clinical Research Ethics Committee (approval number: 753, date: 09.11.2020).

Informed Consent: It was obtained.

Authorship Contributions

Surgical and Medical Practices: Ö.S.G., S.Ü., B.C.T., Concept: Ö.S.G., S.Ü., B.C.T., Design: Ö.S.G., S.Ü., B.C.T., Data Collection or Processing: Ö.S.G., S.Ü., B.C.T., Analysis or Interpretation: Ö.S.G., S.Ü., B.C.T., Literature Search: Ö.S.G., S.Ü., B.C.T., Writing: Ö.S.G., S.Ü., B.C.T.

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