Echocardiographic reference ranges for normal cardiac Doppler data in healthy Turkish population : ECHO-DOP-TR Trial

Özgen Şafak[1], Mustafa Gürsoy[2], Sadik Emren[2], Emre Demir[3], Tarik Yildirim[1], Onur Argan[1], Ersin Simsek[4], Fatih Aytemiz[5], Emre Özdemir[2], Nermin Bayar[6], Zehra Erkal[7], Oguzhan Celik[8], Onur Akhan[9], Cevdet Dönmez[10], Tugba Kemaloglu Oz[11], Serdar Akyel[12], Oktay Ergene[13], and Mehmet Ozkan[14]

[1]Balikesir University Faculty of Medicine
[2]Izmir Katip Celebi University Faculty of Medicine
[3]Ege University Faculty of Medicine
[4]Balıkesir State Hospital
[5]Manisa State Hospital
[6]Antalya Education and Research Hospital
[7]Antalya Training and Research Hospital
[8]Hitit University Faculty of Medicine
[9]Bilecik State Hospital
[10]Dr Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital
[11]Liv Hospital
[12]Kastamonu University Faculty of Medicine
[13]Dokuz Eylül University
[14]Kosuyolu Kartal Heart Education and Research Hospital

June 1, 2020

Abstract

Aim Doppler echocardiography has become the standard imaging modality for diastolic function and provide pathophysiological insight into systolic and diastolic heart failure. In this study we aimed to obtain normal echocardiographic Doppler parameters of healthy Turkish population. Methods Among 31 collaborating institutions from all regions of Turkey, 1154 healthy volunteers were enrolled in this study. Predefined protocols were used for all participants during echocardiographic examination and The American Society of Echocardiography and European Association of Cardiovascular Imaging recommendations were used for echocardiographic Doppler measurements. Results A total of 967 healthy participants were enrolled in this study after applying exclusion criteria. Echocardiographic examination was obtained from all subjects following predefined protocols. Mitral E wave velocity and E/A ratio were higher in females and decreased progressively in advancing ages. E wave deceleration time and A wave velocity were increased with aging. Assessment of tissue Doppler velocities showed that left ventricular lateral e', septal e' and septal s' were higher in younger subjects and in females. E/e' ratio was increased progressively with advancing decades. Right ventricular e'and s' were decreased but a' was increased with increasing age. Septal e' lower than 8 cm/s was 1.9% in the fifth decade and 13.7% in ages older than 50-years. The E/e' ratio greater than 15 (and also 13) was not found. Conclusion This study, for the first time, provides echocardiographic reference ranges for normal cardiac Doppler data in healthy Turkish population which will be useful in routine clinical practice as well as in future clinical trials.

Echocardiographic reference ranges for normal cardiac Doppler data in healthy Turkish pop-

ulation : ECHO-DOP-TR Trial

Aim

Doppler echocardiography has become the standard imaging modality for diastolic function and provide pathophysiological insight into systolic and diastolic heart failure. In this study we aimed to obtain normal echocardiographic Doppler parameters of healthy Turkish population.

Methods

Among 31 collaborating institutions from all regions of Turkey, 1154 healthy volunteers were enrolled in this study. Predefined protocols were used for all participants during echocardiographic examination and The American Society of Echocardiography and European Association of Cardiovascular Imaging recommendations were used for echocardiographic Doppler measurements.

Results

A total of 967 healthy participants were enrolled in this study after applying exclusion criteria. Echocardiographic examination was obtained from all subjects following predefined protocols. Mitral E wave velocity and E/A ratio were higher in females and decreased progressively in advancing ages. E wave deceleration time and A wave velocity were increased with aging. Assessment of tissue Doppler velocities showed that left ventricular lateral e', septal e' and septal s' were higher in younger subjects and in females. E/e' ratio was increased progressively with advancing decades. Right ventricular e'and s' were decreased but a' was increased with increasing age. Septal e' lower than 8 cm/s was 1.9% in the fifth decade and 13.7% in ages older than 50-years. The E/e' ratio greater than 15 (and also 13) was not found.

Conclusion

This study, for the first time, provides echocardiographic reference ranges for normal cardiac Doppler data in healthy Turkish population which will be useful in routine clinical practice as well as in future clinical trials.

Introduction

Echocardiography is widely used as a noninvasive cardiac imaging technique in the clinical setting for the evaluation of heart structure and functions. Doppler echocardiography is a method used to identify the direction and velocity of blood flow and therefore, it is an integral part of the cardiovascular echocardiographic examination, providing a precise hemodyanamic evaluation of the heart (1).

Blood and tissue velocities measured by Doppler are widely used tools for the evaluation of cardiac systolic and diastolic functions. Blood flow causes high frequency, low amplitude signals that are obtained using Pulse Wave (PW) Doppler. Tissue Doppler Imaging (TDI) is designed to characterise low velocity, high amplitude signals from myocardial motion, and are obtained by inverting the low pass filter used in traditional Doppler to a high pass filter (2,3). Tissue Doppler imaging examines the longitudinal component of myocardial contraction throughout the cardiac cycle.

The diastolic parameters may show difference in distinct patient subgroups. Age-related changes in diastolic indices have also been found to be gender specific. In the elderly population, diastolic function deteriorates more significantly in female gender than in male. Furthermore, although standart Doppler values have been established in current guidelines, these values may also be variable according to racial and ethnical factors. Therefore, it is important to be aware of the normal reference values of cardiac Doppler data in the clinical setting according to age, gender, race and body surface area (4).

Recently, we, for the first time in Turkey, have reported two-dimensional echocardiographic normal reference ranges for cardiac chamber quantification in a large cohort of Turkish individuals (5). Besides the chamber sizes, essential data regarding the relationship between these measurements and age, gender, body surface area and geographical region-dependent differences have been provided.

In this study, we aimed to determine echocardiographic reference values for PW Doppler and TDI velocities in a healthy Turkish population to obtain normal Doppler findings and patterns according to age and gender.

Methods

Study Population

Between October 2016 and June 2019, 1046 healthy volunteers from all regions of Turkey were evaluated in the study. The exclusion criteria included the following; people under 18 years of age, patients who had history of having any cardiovascular disease, hypertension, diabetes mellitus, hyperlipidemia, systemic disease, glomerular filtration rate under 60ml/min/1.73m$^{\mathbf{2}}$, genetical disease with cardiac involvement in the first-degree relatives, electrocardiography (ECG) without sinus rhythm or with left bundle branch block, waist circumference more than 102 cm in men and 88 cm in women, high body mass index, abnormal glycaemia values, smoking and/or alcohol abus\soute, and regarding the echocardiographical examination, any regurgitation of heart valves more than mild, stenosis of any valve, left ventricular ejection fraction less than 50%, any wall motion abnormality, systolic pulmonary artery pressure more than 35mmHg and volunteers with poor image quality. Ultimately, 967 volunteers constituted the study population.

Baseline measurements included assessment of blood pressure, weight (kilograms); height (centimeters), body mass index and body surface area. Basic hematological and biochemical parameters were also recorded.

Echocardiographic examination

ECG guided, standard two-dimensional transthoracic echocardiographic studies were performed using available equipments VIVID 7 (General Electric Company) and IE33 (Philips Company) instruments, with 1.5-4.0 MHz transducer, according to a predetermined protocol recommended by American Society of Echocardiography and European Association of Cardiovascular Imaging (EACVI) (3,6,7).

All studies were done with patients lying in the left lateral decubitus position and breathing quietly. M-mode, 2D (frame rates .50–70 fps), colour Doppler, PW Doppler, pulsed-wave tissue Doppler, and PW and TDI (frame rates[?]110 s-1) data were obtained in all patients. PW Doppler was obtained at the left and right ventricle outflow tract and continuous wave Doppler at the aortic and pulmonary valve. Transmitral flow pattern with E and A wave velocities was obtained with the sample volume positioned at mitral leaflet tips. PW TDI was obtained at the septal and lateral annular ring of the mitral valve, measuring s', e'and a' peak velocities . PW TDI was also obtained at the lateral tricuspid annulus in the four chamber view. Left atrium (LA) volume was measured from standard apical 4-chamber views at end-systole just before mitral valve opening. Left atrial volume index (LAVi) was calculated by dividing LA volume by body surface area of subjects.

All Doppler echocardiographic images were recorded in a digital raw-data format (native DICOM format), centralized and sent to core laboratory. The images were evaluated by three experienced echocardiographers blinded to any patient data.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 21.0. (IBM Corp. Armonk, NY: USA. Released 2012). The normality distribution patterns of variables were evaluated using histograms, probability plots, and analytical methods (Kolmogorov-Smirnov). Variables showed as mean +- standard deviation. Categorical variables were presented as percentages. Continuous data was compared in gender and age groups using independent T test and One-way ANOVA respectively. Turkey's HSD was used in post-hoc comparisons. Categorical variables were compared using the Chi-square test. Pearson correlation test was performed for bivariate correlations. All tests were 2-tailed and the p value was less than 0.05 ($p < 0.05$) was accepted as significant.

Intra-observer and inter-observer variability was evaluated in 50 randomly selected subjects. Intraclass correlation coefficient with 95% confidence interval and the relative differences (means+-SD) were reported overall. The Bland-Altman plot was drawn to obtain better insights into the data quality between two echocardiographers.

Ethics committee

The Healthy Heart ECHO-TR Trial respect the ethical principles for conducting research on human subjects. The study protocol was approved by 9 Eylul University Ethics Committee and written informed consent was given by all subjects.

Results

Demographic data

A total of 454 female (46.9%) and 513 male (53.1%) were included in the study. The mean age of the study population (n= 967) was 33.6+-12. The patients were grouped by age according to decades (4 groups). The number of the healthy participants above 50 years of age was lower compared to 3 other groups; therefore it was classified as a single group.

The age of the study population was most commonly distributed between 18-29 (35.2%) and 30-39 (32.4%) years. With increasing decades, the mean height of the volunteers was progressively decreased whereas weight, body mass index (BMI), systolic and diastolic blood pressures, serum creatinine levels, total cholesterol and low-density lipoprotein (LDL) levels demonstrated a highly significant rise. Table 1 summarizes the demographic data of each group.

Left ventricular parameters

E and A wave velocities were higher in women than in men and E wave tended to decrease with advancing age ($p<0.05$). E wave deceleration time was increased in older ages and men had higher values than women, showing a significant positive correlation with age and gender ($p<0.001$ for both). The mean E/A ratios were 1.63+-0.49 (18-29 years), 1.43+-0.42 (30-39 years), 1.4+-0.4 (40-49 years), 1.25+-0.44 ([?]50 years) (with <0.001 p value for decades) (Figure-1). Table-2 summarizes data regarding the PW Doppler velocities and LAVI according to age and gender.

Septal e' and lateral e' waves were higher in the first decades and women had higher levels than men, whereas septal a' and lateral a' waves were higher in men and showed a negative correlation with advancing age (all these parameters were statistically significant ($p<0.001$). Septal s' and lateral s' waves tended to decrease with advancing age, showing a negative correlation. Lateral and septal s' waves were decreased progressively with advancing age. Lateral s' wave was higher in men whereas septal s' wave was higher in women.

In four-chamber view, septal and lateral E/e' ratios were getting higher with increasing age and women had a little bit higher value than men. The average of septal and lateral E/e' ratio was 6.7+-1.3 (18-29 years), 7.6+-1.7 (30-39 years), 8.4+-2 (40-49 years), 8.9+-2.1 ([?]50 years) (statistically not significant between decades) (Figure-2).

The intraclass correlation coefficient was obtained and the Bland-Altman plot test was performed to gain better insights into the data quality between two echocardiographers. In our study, the intraclass correlation coefficient value was 0.965 (95% CI: 0.975–0.992; $p<0.001$) (Figure-3).

Right ventricular parameters

Right ventricular s' and e' waves were decreased and a' wave tended to increase with advancing age (13.1+-2.3, 12.7+-2.3, 12.4+-2.5, 12+-2.4 cm/s for average s' waves, 14.5+-3.4, 13.9+-3.2, 13.2+-3.1, 11.7+-3.2 cm/s for average e' waves, 11.6+-3, 12.6+-3.2, 13.7+-3.5, 14.9+-3.5 cm/s for average a' waves with advancing ages). Besides, a' and e' waves were higher in women than in men. Table-4 shows data about right ventricular TDI.

Discussion

This study provides normal reference ranges for cardiac Doppler parameters of healthy Turkish population according to age and gender using conventional recommended echocardiographic approaches including PW

Doppler and TDI.

E wave and also E/A ratio were slightly higher in women than in men, and tended to decrease with advancing ages, which were statistically significant. On the other hand A wave and E wave deceleration time (Edt) were increased with advancing decades. These results were similar to data reported in European and American echocardiographic studies (2,3,6,7).

Most diastolic parameters varied and changed according to age similarly for both genders. Lateral and septal e' were lower in men and in older population, whereas lateral a' and septal a' had a positive correlation with age and were slightly higher in men. These parameters were found to be prominently higher in a study authored by Nagueh et al. (8) when compared with our study . For example, the septal e' wave velocities they obtained were 14.9+-2.4 cm/s (16-20 years), 15.5+-2.7 cm/s (21-40 years), 12.2+-2.3 cm/s (41-60 years) and 10.4+-2.1 cm/s ([?]61 years) according to ages. On the other hand, Chahal et al. (9) obtained similar results when compared with our study and, reported the septal e'wave 8.6+-1.9 cm/s as an average value.

For evaluation of the left ventricular diastolic function, e', E/A and E/e' values are highly important and are known to have a positive correlation with left ventricular filling pressures. In our study we did not observe any value of septal (and also lateral) e' lower than 8 cm/s whereas in the study authored by Cabellero et al. (10) 2 out of 170 (1.2%) in 20-40 years, 38 out of 193 (19.7%) in 40-60 years, 46 out of 83 (55.4%) in [?]60 years had values lower than 8 cm/s. Indeed, LAVI of participants were lower than 34 mL/m2 in all age groups. E/A ratio was decreased with increasing age, as shown in several previous studies (10-13). E/e' tended to increase in older ages but none of the participants had a value higher than 15, although it has been reported in some European studies (11). In the present study, E/e' was found to be slightly higher in women compared to men, although it was not statistically significant. Several studies have previously showed that there is relatively a higher incidence of deteriorated diastolic functions in elderly female patients and higher cardiovascular mortality in female gender when compared to men (14-16).

s' wave velocity measures longitudinal LV contraction and is a surrogate of LV systolic function and it is also well-known that it has a good correlation with left ventricular ejection fraction (LVEF). s' wave velocity [?]7.5 cm/s has a sensitivity of 79% and a specificity of 88% in predicting LVEF [?]50% (2, 17). As summarized in Table-3, lateral s' was higher than septal s' in our study and also higher in younger volunteers. Lateral s' was higher in men whereas septal s' was higher in women, concordant with previous data (12,13).

Meluzin and co-workers (17), reported good correlation between right ventricular (RV) s' wave velocity and right ventricular ejection fraction (RVEF); RV s' wave velocity <11.5 cm/s predicted RV dysfunction (EF < 45%) with a sensitivity of 90% and specificity of 85%. In our study, none of the participants had a lower RVs wave than these established data. Ischemic heart diseases, chronic pulmonary hypertension and chronic lung diseases can cause a decrease in RV s' wave velocity which should be evaluated during echocardiographical examinations.

In the present study, right ventricular parameters also exhibited gender-related differences, e' and a' were higher in women whereas s' wave was higher in men. s' and e' wave velocities were decreased with advancing ages as demonstrated in previous studies (10,11, 13).

Systolic pulmonary artery pressure (sPAP), an important predictor of several cardiac abnormalities, was also evaluated in the current study. We did not obtain any sPAP above 36 mmHg in healthy volunteers, whereas, higher levels have been rarely detected in past studies (11). However, it should be kept in mind that echocardiography is a observer-dependent modality, and the patients with slightly elevated pulmonary artery pressure should be evaluated with further imaging modality to avoid under-diagnosis of any organic heart disease.

In conclusion, the current data obtained from healthy Turkish volunteers are comparable with most previous studies in this era (2,3,5,6,10,11,13,18). E and A waves of mitral annulus and also E/A ratios were greater compared to European registries, but these differences were not statisitically significant. Data regarding E/e' ratio especially seems interesting, as in a European study (6) that it has been found to be significantly increased in advancing ages whereas no remarkable difference has been detected in our study. But we have to emphasize that E/e' higher than 15 is correlated with diastolic dysfunction and the study above-mentioned had several participants with these values (0.05% of the population) (11).

As being the first large-scaled healthy population based Doppler study in Turkey, ECHO-DOP-TR provides essential data regarding left and right ventricular PW Doppler and TDI studies, and helps us to evaluate the systolic and diastolic functions of the heart.

Limitations

The results mainly pertain to Turkish population who live in Turkey, a bridge country between Europe and Asia. Despite the fact that all patients were considered healthy normal subjects, the possibility of subclinical coronary artery disease particularly in older subjects cannot be excluded. The study groups were not equally distributed according to age as it was not easy to find healthy patient without any chronic disease in advancing ages. The data regarding e' and a' waves in inferior, anterior, posterior segments are unavailable in most of the patients and therefore were not included in the Results section.

References

1. Anavekar NS, Oh JK. Doppler echocardiography: a contemporary review. J Cardiol. 2009;54(3):347-58. doi: 10.1016/j.jjcc.2009.10.001.
2. Krishna K. Kadappu, MBBS, MD, Liza Thomas, MBBS, PhD. Tissue Doppler Imaging in Echocardiography: Value and Limitations. Heart, Lung and Circulation (2015) 24, 224–233
3. Isaaz K, Munoz del Romeral L, Lee E, Schiller NB. Quantitation of the motion of the cardiac base in normal subjects by Doppler echocardiog- raphy. Journal of the American Society of Echocardiography 1993;6: 166–76.
4. Cheng S, Fernandes VR, Bluemke DA, McClelland RL, Kronmal RA, Lima JA. Age-related left ventricular remodeling and associated risk for cardiovascular outcomes: the Multi-Ethnic Study of Atherosclerosis. Circ Cardiovasc Imaging 2009; 2: 191-8.
5. Şafak Ö, Gürsoy OM, Karakoyun S, Çağdaş M, Dinç Asarcıklı L, Avcı Demir F et al. Normal echocardiographic measurements in a Turkish population: The Healthy Heart ECHO-TR Trial. Anatol J Cardiol. 2019;22(5):262-270.
6. Lancellotti P, Badano LP, Lang RM, Akhaladze N, Athanassopoulos G, BaroneDet al. Normal reference ranges for echocardiography: Rationale, study design, and methodology (NORRE study). Eur Heart J Cardiovasc Imaging. 2013;14:303–8.
7. Cosyns B, Garbi M, Speparovic J, Pasquet A, Lancellotti P. Update of the echocardiography core syllabus of the European Association of Cardiovascular Imaging (EACVI). Eur Heart J Cardiovasc Imaging. 2013;14:837–9.
8. Nagueh S. F., Smiseth O. A., Appleton C. P. et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. (J Am Soc Echocardiogr 2016;29:277-314.
9. Chahal N. S., Lim T. K., Jain P. et al. Normative reference values for the tissue Doppler imaging parameters of left ventricular function: a population-based study. European Journal of Echocardiography, Volume 11, Issue 1, January 2010, Pages 51–56, (https://doi.org/10.1093/ejechocard/jep164)
10. Caballero L., Kou S., Dulgheru R. et al. Echocardiographic reference ranges for normal cardiac Doppler data: results from the NORRE Study. European Heart Journal – Cardiovascular Imaging (2015) 16, 1031–1041
11. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr. 2010;23:685–713.
12. Miyatake K, Okamoto M, Kinoshita N, Owa M, Nakasone I, Sakakibara H et al. Augmentation of

atrial contribution to left ventricular inflow with aging as assessed by intracardiac Doppler flowmetry. Am J Cardiol 1984;53:586–9.

13. Okura H, Takada Y, Yamabe A, Kubo T, Asawa K, Ozaki T et al. Age and gender specific changes in the left ventricular relaxation: a Doppler echocardiographic study in healthy individuals. Circ Cardiovasc Imaging 2009;2:41–6.
14. Klapholz M, Maurer M, Lowe AM, Messineo F, Meisner JS, Mitchell J, Kalman J, Phillips RA, Steingart R, Brown EJ Jr, Berkowitz R, Moskowitz R, Soni A, Mancini D, Bijou R, Sehhat K, Varshneya N, Kukin M, Katz SD, Sleeper LA, Le Jemtel TH. Hospitalization for heart failure in the presence of a normal left ventricular ejection fraction: results of the New York Heart Failure Registry. J Am Coll Cardiol. 2004;43: 1432–1438.
15. Vasan RS, Larson MG, Benjamin EJ, Evans JC, Reiss CK, Levy D. Congestive heart failure in subjects with normal versus reduced left ventricular ejection fraction: prevalence and mortality in a population-based cohort. J Am Coll Cardiol. 1999;33:1948 –1955.
16. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N et al. Heart disease and stroke statistics 2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008; 117: e25–e146
17. Meluzin J, Spinarova L, Bakala J, Toman J, Krejci J, Hude P et al. Pulsed Doppler tissue imaging of the velocity of tricuspid annular systolic motion; a new, rapid, and non-invasive method of evaluating right ventricular systolic function. European Heart Journal 2001;22: 340–8.
18. Alam M, Wardell J, Andersson E, Samad BA, Nordlander R. Effects of first myocardial infarction on left ventricular systolic and diastolic function with the use of mitral annular velocity determined by pulsed wave Doppler tissue imaging. Journal of the American Society of Echocardiography 2000;13:343–52.

Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the populat
	18-29 years (n:341) Mean±SD	30-39 years (n:314) Mean±SD	40-49 years (n:202) Mean±SD	[?]50 years (n:110) Mean±SD	p*	Female (n:454) Mean±SD	Male (n:513) Mean±SD	p**
Height, cm	170.8±8.9	169.1±8.8	167.8±9.2	167.6±8.6	<0.001	166±6.6	175±6.8	0.013
Weight, kg	69.1±11.7	71±11.2	72.4±10.2	73.2±10.4	<0.001	68.4±8.7	73.6±9.1	0.106
Body mass index, kg/m^2	23.6±2.8	25±2.8	25.4±2.7	25.9±3.2	<0.001	24.4±3.45	24.9±2.5	0.129
Body surface area, m^2	1.9±0.5	2±0.6	2.1±0.6	2.1±0.7	0.024	1.69±0.2	1.87±0.2	0.058
Systolic blood pressure, mmHg	112.3±11.4	115.9±10.7	118.9±10.4	120.3±10.1	<0.001	113.9±11.7	116.8±11.1	0.089

Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the population	Table-1 Demographic data of the populat
Diastolic blood pressure, mmHg	69.9±9	73.2±8.3	73.8±8.4	75.5±8.1	<0.001	71.4±8.7	72.6±8.5	0.183
Glycaemia, mg/dL	90.4±9	94.1±9.1	95.6±9.5	97.9±8	<0.001	92±10	93±11	0.396
Serum creatinine, mg/dL	0.71±0.11	0.81±0.15	0.83±0.17	0.85±0.18	0.521	0.76±0.13	0.84±0.14	0.198
Hemoglobin, g/dL	14.9±1.3	14.8±1.3	14.5±1.4	14.3±1.3	0.763	13.5±1.4	15.1±1.4	0.349
Total cholesterol, mg/dL	151.2±18.3	158.2±19	164.5±22.3	173.4±24.3	<0.001	163±27	165±26	0.037
Low-density lipoprotein (LDL)	92.1±21.4	105.7±24.6	111.8±26.7	114.5±27.9	<0.001	105.3±24	106.6±25.4	0.049
High-density lipoprotein, mg/dL	49.4±11.5	48.5±11.2	47.9±10.5	47.4±10.1	0.693	47.9±11.2	44.3±10.3	0.003
Triglyceride, mg/dL	104.5±32	112.2±33	118.1±34	120.4±31	0.031	107.4±32.7	114.8±35.7	0.009

Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	T 2 M t v P D v l t a l a v u i d (
	18-29 years (n:341) Mean±SD Female	18-29 years (n:341) Mean±SD Male	18-29 years (n:341) Mean±SD p**	30-39 years (n:314) Mean±SD Female	30-39 years (n:314) Mean±SD Male	30-39 years (n:314) Mean±SD p**	40-49 years (n:202) Mean±SD Female	40-49 years (n:202) Mean±SD Male	40-49 years (n:202) Mean±SD p**	[?]50 years (n:110) Mean±SD Female	[?]50 years (n:110) Mean±SD Male	[y (M p
E wave velocity, cm/s	0.88±0.14	0.84±0.13	0.024	0.86±0.15	0.82±0.13	0.036	0.80±0.11	0.78±0.1	0.042	0.78±0.1	0.76±0.11	0
A wave velocity, cm/s	0.58±0.1	0.57±0.1	0.031	0.6±0.11	0.58±0.1	0.029	0.62±0.1	0.59±0.11	0.049	0.64±0.11	0.59±0.1	0
E wave deceleration time, ms	178±48	181±51	<0.001	184±45	186±43	<0.001	188±44	190±43	<0.001	201±47	209±46	<
E/A ratio	1.65±0.49	1.61±0.49	0.038	1.45±0.4	1.42±0.41	0.03	1.41±0.44	1.4±0.45	0.041	1.26±0.46	1.24±0.43	0

Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	Table-2 Mitral valve Pulse Doppler velocities and left atrial volume index (LAVI)	T 2 M t v P D v l t a l a v u i d (
Left atrial volume index, mL/m²	18.7±2.8	19.2±2.7	0.048	19.9±2.9	20.9±2.8	0.018	21.7±3	22.6±2.8	0.027	23.4±2.7	24.7±2.4	0

Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	T 3 D a l v t u t s D
	18-29 years (n:341) Mean±SD Female	18-29 years (n:341) Mean±SD Male	18-29 years (n:341) Mean±SD p**	30-39 years (n:314) Mean±SD Female	30-39 years (n:314) Mean±SD Male	30-39 years (n:314) Mean±SD p**	40-49 years (n:202) Mean±SD Female	40-49 years (n:202) Mean±SD Male	40-49 years (n:202) Mean±SD p**	[?]50 years (n:110) Mean±SD Female	[?]50 years (n:110) Mean±SD Male	[y (M p
Septal e' wave, cm/s	11.9±2.3	11.7±2	<0.001	11.1±2.1	10.7±1.9	<0.001	8.9±1.7	8.4±1.5	<0.001	8±1.4	7.7±1.5	<
Septal a' wave, cm/s	8.6±1.5	8.9±1.8	<0.001	9.1±1.6	9.4±1.8	<0.001	9.5±1.4	9.9±1.6	<0.001	10.1±1.5	10.5±1.4	<

Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	Table-3 Data about left ventricular tissue Doppler	T 3 I a l v t u t s I
Septal s' wave, cm/s	8.9±1.3	8.6±1.2	<0.001	8.4±1.2	8±1.3	<0.001	7.8±1.4	7.7±1.3	0.671	7.4±1.3	7.3±1.4	0
Lateral e' wave, cm/s	13.1±3.1	12.7±3	<0.001	11.9±2.9	10.6±2.7	<0.001	10.4±2.6	9.7±2.4	<0.001	9.6±2.1	9.3±2	<
Lateral a' wave, cm/s	8.6±1.9	8.9±2.1	<0.001	8.9±2	9.5±2.2	<0.001	9.4±1.8	9.9±1.9	<0.001	9.7±1.6	10.4±1.7	<
Lateral s' wave, cm/s	10.7±2.1	10.9±2.4	0.067	10.2±2.1	10.5±2.3	0.054	9.9±1.9	10.2±2	0.098	9.7±1.8	9.9±1.9	0
Lateral E/e'	5.7±1.5	5.6±1.5	0.029	6.6±1.7	6.3±1.6	0.014	7.4±1.7	7±1.7	0.016	7.9±2	7.7±1.9	0
Septal E/e'	6.6±1.5	6.3±1.6	0.028	7.1±1.7	6.9±1.6	0.032	8.6±2	8.3±2.1	0.019	9.6±2.2	9.3±2.2	0

Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	T 4 R v t u T s I d
	18-29 years (n:341) Mean±SD Female	18-29 years (n:341) Mean±SD Male	18-29 years (n:341) Mean±SD p**	30-39 years (n:314) Mean±SD Female	30-39 years (n:314) Mean±SD Male	30-39 years (n:314) Mean±SD p**	40-49 years (n:202) Mean±SD Female	40-49 years (n:202) Mean±SD Male	40-49 years (n:202) Mean±SD p**	[?]50 years (n:110) Mean±SD Female	[?]50 years (n:110) Mean±SD Male	[y (M p
s' wave, cm/s	12.9±2.1	13.2±2.5	0.198	12.6±2.2	12.9±2.4	0.234	12.1±2.5	12.5±2.6	0.224	11.8±2.5	12.2±2.3	0

Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	Table-4 Right ventricular Tissue Doppler datas	T 4 R v t u T s D d
e' wave, cm/s	14.8±3.4	14.1±3.1	0.072	14.2±3.3	13.7±3.1	0.198	13.5±3.1	12.9±3.2	0.091	11.7±3.3	11.6±3.2	0
a' wave, cm/s	11.7±3.1	11.5±3	0.481	12.7±3.2	12.5±3.3	0.201	13.8±3.4	13.5±3.5	0.187	15±3.5	14.7±3.6	0

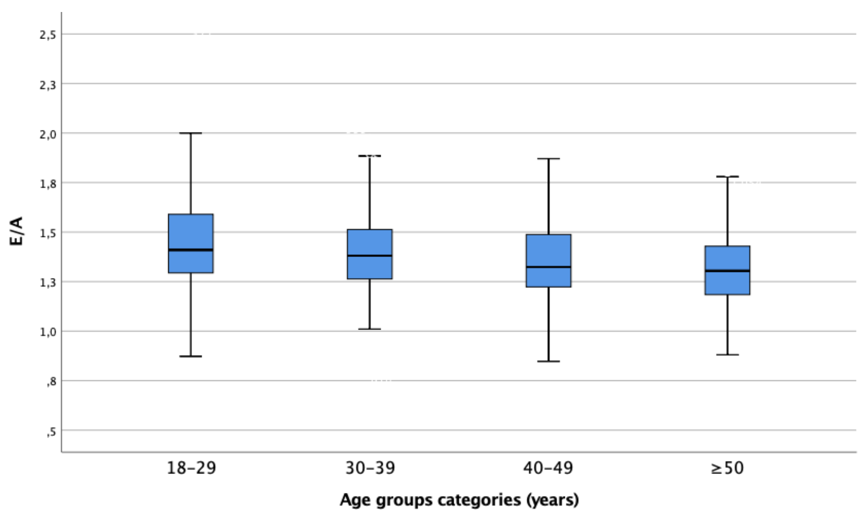


Figure-1 ; Mean E/A ratios according to ages

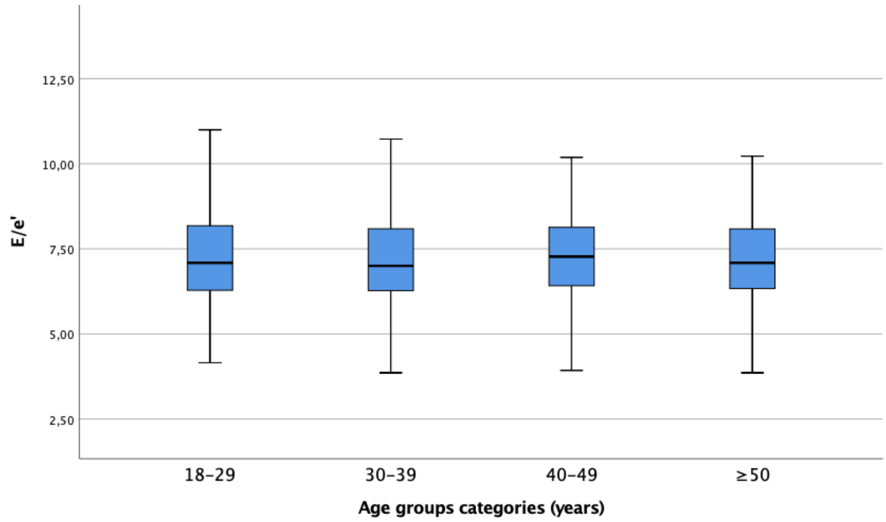
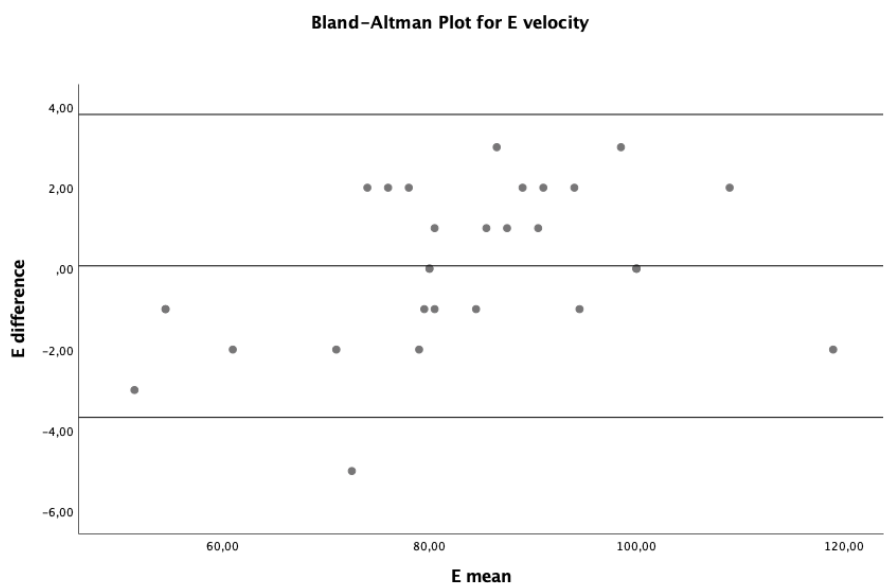


Figure-2 ; Average of septal and lateral E/e' ratio according to ages



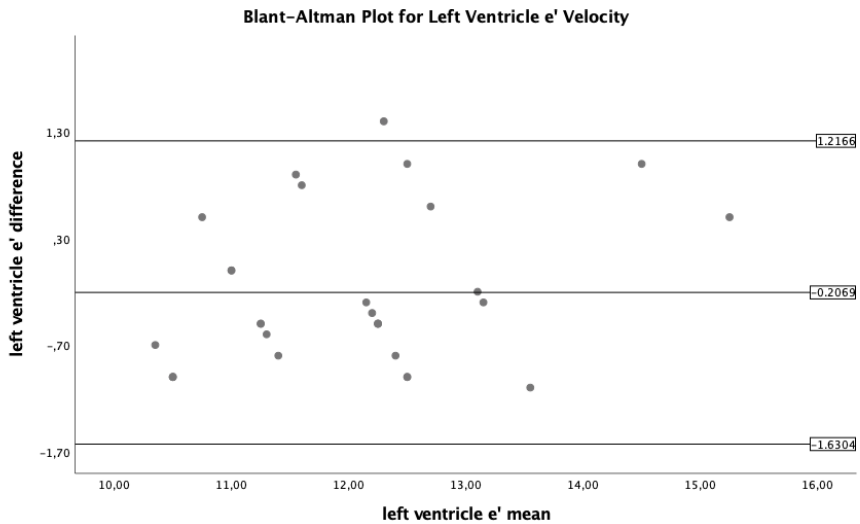


Figure-3 ; Intraclass correlation coefficient value was 0.965 (95% CI: 0.975–0.992; P<0.001)