Tissue Doppler imaging and strain rate of the left atrial lateral wall: age related variations and comparison with parameters of diastolic function

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Abstract

Background: Strain rate (SR) is one of the most used techniques to study left atrial (LA) although it requires post processing of the images, a learning curve and additional software, Tissue Doppler Imaging (TDI) is widely available and easy to use, TDI could detect changes in LA function associated with age similar to other parameters. The aim of this to evaluate lateral LA wall by DTI and SR, according to different age decades and compare them and with other parameters of diastolic function in a population of adults without cardiovascular disease.

Materials and Methods: 91 healthy adults were prospectively evaluated. In apical 4-chambers view the LA lateral wall was divided into three portions. Peak velocities of basal and mid portions were measured with pulsed-wave TDI color on line and SRI by speckle tracking. A first positive wave (S'la and SRS) and two negative waves (E'la and SRE, and A'la and SRA respectively) were obtained. E'la/A'la ratio and SRE/SRA ratio were analyzed. The distribution of the variables by age subgroups was described and analyzed. Correlation analyses were performed.

Results: The median age was 42 years and 54.9% were female. E'la/A'la show a positive good correlation with age. E'la/A'la and SRE/SRA ratios changed from > 1 to < 1 in the age group of 41-50 years, while this occurred in the group of 51-60 years for the E/A ratio. Lateral and septal mitral annulus E´ show decrease with age and prolongation of E -wave deceleration time was observed in the age group over 61 years.

Conclusion Normal values according to age group of TDI of the LA lateral wall were obtained. Age-related changes in LA function could be detected as early with TDI as with SRI. Future studies are required to explore if TDI could be used as an alternative to SRI in other populations.

Background

At present, 12% of the world population is older than 60 years of age, and by the year 2050 it is estimated that this percentage will double (1). If we consider that the main cause of morbidity and mortality in the world are cardiovascular diseases (2), and that the main risk factor for their development is aging (3, 4), the need to deepen the knowledge about the pathophysiology of cardiovascular diseases, and its relationship with aging, is clear.

With senescence, a series of changes occurs at the myocyte level, which results in a reduction of left ventricular (LV) distensibility and, consencuentially, at the atrial level, a decrease in the conduit phase and a compensatory increase of LV filling during atrial systole (5–8).

Several studies have shown an association between atrial dysfunction and the development of cardiovascular events during follow up, particularly atrial fibrillation (AF) (9–12) and heart failure in patients with preserved LV systolic function (13–15).

The assessment of the left atrium by echocardiography is in expansion; different new techniques have been used in these years, including Strain and Strain Rate Imaging (SRI).Alteration in left atrial (LA) function evaluated by these techniques has been associated with adverse cardiovascular events in patients with reduced and preserved systolic function, ischemic heart disease and the development of AF (16, 17).

The evaluation of the LA function by SRI can be a challenge in low resources countries or centers since it requires to use an additional expensive software, among other limitations. On the other hand, Tissue Doppler Imaging (TDI) is a simple technique and is actually widely available. Previously, we have reported the associations observed between the velocity profile of the lateral wall of the LA measured by pulsed wave color TDI online with atrial SRI by speckle tracking and other parameters of atrial and diastolic function in a population of adults without known cardiovascular disease (18). This report consists of a sub-analysis of that study and seeks to describe the age-related variations observed in the parameters analyzed in a normal population, in order to establish an initial reference value necessary, as a previous instance, for the study of atrial function through this method in other populations with established cardiovascular pathology or at risk of presenting it.

Materials And Methods

The aim of this study is to evaluate the effects of age on LA function assessed by TDI, and to compare them with age-related variations of LA SRI and parameters of diastolic function in a population of healthy adults.

As previously reported 91 healthy adults, aged between 18 and 74 years, were prospectively evaluated in two health centers between April 2016 and March 2018. None of the subjects had a known history of cardiovascular disease, high blood pressure, dyslipidemia, diabetes, electrocardiographic alterations or was under cardiovascular medical treatment. A complete color Doppler echocardiogram was performed.

Echocardiogram and Cardiac Doppler

An ultrasound machine Vivid S5 or 7 (GE Medical System, Horten, Norway), equipped with a 3 MHz variable frequency transducer, was used for all of the echocardiographic evaluations. Cardiac diameters were measured according to the recommendations of the ASE (19). The M mode was used to measure the diameters of LA and LV. Volumes of LA were measured in a single plane apical four-chamber view, using the method of discs.

Transmitral flow velocities were obtained by pulsed wave Doppler echocardiography, in an apical four chamber view. Mitral flow parameters measured included peak velocities during early diastole (E) and late diastole (A), their ratio (E/A ratio), and E-wave deceleration time (DTE).

Pulsed wave color TDI online of the septal and lateral mitral annulus was performed, and peak of the systolic wave S' (Sma S´, Lma S´), early filling wave E' (Sma E´, Lma E´) and late filling wave A' (Sma A´, Lma A´) were measured. The E/e' average ratio was calculated.

Parameters used to define normal diastolic function were: Lma E' > 10 cm/s, Sma E' > 7 cm/s, average E/e' < 14, peak velocity of tricuspid regurgitation < 2.8 m/s, LA volume indexed < 34 ml/m2 (20).

For the analysis of LA function by TDI and SRI, lateral wall was obtained in the apical four chamber view and divided subjectively into three portions: basal segment, mid segment and atrial roof (Fig. 1A). Measures were taken in apnea, at the end of expiration, with a sample volume of 2 mm and trying to maintain an angle less than 15°; gain and filter were adjusted to avoid saturation of the image. Three consecutive measurements of basal and mid segments were performed; the atrial roof was excluded from the measurements.

The EchoPac software v 108.1.5 (GE Healthcare) was used for the analysis of two bidimensional SRI by speckle tracking. In an apical four chamber view, the endocardial surface of the LA was manually drawn, using a single cardiac cycle and the R wave as a reference point. A region of interest was automatically generated, and manually tracked, frame by frame, to maintain its position within the LA wall, to ensure that the regions of interest would follow the cardiac movement throughout cardiac cycle. The LA was divided into six segments automatically; the limits of the basal and mid segments of the lateral wall of the LA were manually adjusted, excluding the atrial roof and the remaining segments. All the images were obtained at an average frame rate of 63 +/-6.

With both techniques, TDI and SRI, three waves were obtained: a first positive wave, S'la and SRS (reservoir phase), and two negative waves, E'la and SRE (conduit phase) and A'la and SRA (atrial systole) respectively (Fig. 1B and 1C). The ratios between E'la/A'la and SRE/SRA were analyzed. Basal and mid segments, and their average were analyzed (when both curves could be measured). Segments that did not have adequate image quality were excluded from the analysis.

Statistic Analysis

Absolute frequency and percentage were used as frequency measures for qualitative variables; median (Md) and interquartile range (IQR) were used as frequency and dispersion measures for quantitative variables, given that the variables under study did not present normal distribution. We analyzed the distribution of the variables in the total population and by subgroups of age (< 30, 31–40, 41–50, 51–60 and ≥ 61 years). The comparisons between subgroups of age were performed with the Kruskal-Wallis method. Considering age as a continuous variable, correlation analyzes were performed to evaluate the existence of linear association between age and various parameters, using Spearman's correlation method with Holm's method adjustment. After log transformation of the abnormally distributed variables, univariable and multivariable linear regression analyzes were performed to assess association between TDI parameters and clinical predictors. Variables associated in univariate analyses were entered in multivariable models. In the hypothesis tests a statistical significance level of 0.05 was used, rejecting the null hypothesis if the value of p was lower than this level. All data analysis was performed using R Core Team 2018 software (R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

Results

Clinical characteristics and echocardiographic measures of the study population according to age subgroups.

The Md age was 42 years (IQR 18) and 54.9% of the subjects were female. An adequate spectral signal was obtained in 99% and 92% of the basal and mid segments with TDI and in 90% and 84% with SRI, respectively. Table 1show the global values and the distribution of the variables according to age subgroups (data of TDI and SRI correspond to the basal segments; the values of mid segments and average, values of basal and mid segments, are presented in Supplemental Table 1). The older age subgroups presented higher values of systolic and diastolic blood pressure (SBP and DBP).No differences were observed between the subgroups in other clinical variables evaluated. Of the diastolic function parameters evaluated, progressive reduction of E wave values and parallel increase in A wave values were observed at increasing age, with reversal of the E/A ratio in the subgroups older than 50 years. Age related DTE prolongation > 240 ms, reduction of Sma E´ and Lma E´ waves, and increase of Sma A´ and Lma A´ waves were also observed. Sma E´ and Lma E´ presented values below 10 cm/s and 7 cm/s, respectively, in the subgroups over 60 years. The E/e´ ratio increased with age, with the median in all groups being less than 10.No age related changes were observed in S'la wave at the basal segments, unlike that observed with SRS, which presented lower values at increasing age. Both E'la and SRE presented progressive variations with age, with a reduction in E'la values and an increase in SRE values in the older age subgroups. A'la wave values presented significant differences between the age subgroups, and no significant differences were observed between the groups in the distribution of SRA. E'la/A'la and SRE/SRA ratios < 1 were found in age subgroups over 40 years (Table 1, Graph 1). Similar findings were observed when analyzing mid and average segments (Supplemental Table 1).

Associations observed between age, clinical characteristics and echocardiographic measures

Table 2 and Graph 2 present the results of the age correlations analyzed. SBP, A wave, E/e' ratio and SRE basal presented a positive correlation with age, while Sma E´, Lma E´, E/A, E'la, SRS (mid and average), E'la/A'la and SRE/SRA at basal segments were negatively correlated; similar correlations with age were found at mid and average segments (Supplemental Table 2).

Associations observed between TDI measures and clinical characteristics

Univariable and multivariable linear regression models for clinical predictors of LA TDI are summarized in Table 3. Age was the most important independent predictor of E´la basal, A´la basal y E´la/A´la basal.

Discussion

During the cardiac cycle the LA plays the functions of reservoir, conduit and atrial pump; the different phases are influenced by changes at the atrial chamber and the left ventricular chamber (6,21).

With normal aging cell remodeling occurs, with loss of cardiomyocytes and compensatory development of hypertrophy; changes in the extracellular matrix were also described, with greater presence of fibrosis and deposits of amyloid protein (22). At the molecular level, mitochondrial dysfunction and oxidative stress occur, as well as alterations in the entrance of calcium to the sarcoplasmic reticulum, which determine changes in cell elasticity with decreased relaxation and lower suction force by the LV, decrease in passive ventricular filling, and compensatory increase of the contribution of the atrial systole to LV filling to maintain an adequate stroke volume (23–25). These events were associated with greater predisposition to suffer AF, and heart failure with preserved systolic function (26), entities that are becoming more prevalent in Argentina and the rest of the world (27–31), given the increase in longevity that the world population is experiencing (14,22).

Different authors found an association between cardiovascular events and alteration in LA function evaluated by Strain and SRI. Inaba et al. found that SRS, SRE and SRA were lower in AF patients than in age-matched controls (32).Wang et al. found that LA SRE and LA dimension were independent predictors of CV failure (33).Mondillo et al.found that reservoir and conduit phaseswere lower in patients with hypertension or diabetes than in controls (34).

New technologies in medicine are important components of health care, which have the potential to save lives and improve quality of life and well-being. However, too many people around the world do not have access to affordable and high-quality health technology, and the problem is more serious in low and middle-income countries (35).

Many echo laboratories do not have the possibility of assessing LA by strain since it is necessary to incorporate additional and expensive software, a wide learning curve, also post-processing of the images is required to interpret them, and a high quality of images. Unlike the DTI, is a simple method, widely available, that allows analyzing the information at the time of the study and does not require an extensive learning curve, this leaded us to think it could be an alternative to LA SRI in low resource centers. As a previous instance for the study of LA function through this method in individuals with established cardiovascular pathology or at higher risk of presenting it, we need to understand how these parameters behave in normal population and stablish initial reference values according to age groups, which is the reason why we perform this sub-analysis.

In this study we described the age related changes observed in a population of adults without cardiovascular disease with TDI online, SRI and other diastolic function parameters. The variations in E'la and SRE waves, and E'la/A'la and SRE/SRA ratios identified earlier the increase in the atrial systole contribution to LV filling than others diastolic function parameter.

Comparison with previous studies

Similar to our work, Pérez Paredes et al. (36) studied the lateral wall of the LA, in that case with spectral pulsed TDI in mid segments, finding a decrease in the early diastole wave and an increase in late diastole wave in the age group over 45 years; no changes in the reservoir phase were reported. Similar results were obtained by Thomas et al. (37) with TDI color off line, when evaluating late diastole of lateral wall of the LA at the annular level and mid segments level. When comparing the results obtained in this study by TDI at the annular and auricular levels, we observed that the lateral wall of the LA has a speed profile different from the mitral annulus as shown in Fig. 2, which suggests that by directly assessing the atrial myocardium we can detect changes that are not evident at the level of the annulus.

Inaba et al. evaluated the LA by SRI in a subgroup of healthy patients; they could not find a significant correlation of late diastole with age, which according to the author could be due to the need of a high quality of images and to have analyzed only one of the walls (32). Boyd et al. also evaluated a population of healthy adults with atrial SRI and reported significant correlation of SRI with age at the different phases: reservoir, conduit and atrial systole (5). Similar findings reported by Sun et al.; this author analyzed the ratio between early and late diastole (SRe/a) finding a negative correlation with age. These authors also demonstrated changes in atrial SRI that would allow an earlier detection of altered diastolic function than with the parameters usually used (38).In a recent work Yoshida et al. evaluated the impact of age on cardiac function by speckle tracking echocardiography and serum B type natriuretic peptide and concluded that the decrease in the reservoir and conduit phase are the earliest markers of cardiac remodeling (39). Regarding the atrial contraction function and its changes with age, the information is still controversial; there are studies that show an increase in this function (22, 37) while others did not show significant changes (30, 37, 40).

In this study both TDI and SRI showed a decrease in the conduit phase in the age subgroups over 40 years old, at least a decade before the other methods analyzed.

Limitations

The main disadvantage of the pulsed TDI on line is that it is dependent on the insonation angle and the measurements can be influenced by the movement of adjacent tissues (41–44). To overcome these limitations, in this study the measurements were made trying to maintain the narrowest possible angle of the segments to be measured, with a small sample volume and in expiratory apnea. We also evaluated and compared the results obtained at the basal and mid segments and their average (when both segments were satisfactorily measured), observing similar results in the measurements, which we believe would minimize the measurement error determined by the cardiac movement. In our experience, the basal segment of the lateral wall of the LA can be correctly aligned in almost all of the studied subjects, while the mid segments presented in some cases a difficult alignment to generate an adequate curve.

The size of the sample was limited and the population sample used for this study has not been selected by random methods, so the informed results must be confirmed with other studies.

Conclusions

The effects of age on TDI on line of the LA lateral wall were assessed and normal values according to age group were reported. Age correlated with numerous parameters analyzed. Age-related changes in LA function could be detected as early with this technique as with SRI. Future studies are required to explore if this method could be used as an alternative to SRI in low-resources places to address LA function abnormalities in other populations with established cardiovascular disease or at risk of presenting it.

Abbreviations

AF: atrial fibrillation, Av.: average, BSA: body surface area, DBP: diastolic blood pressure, EF: ejection fraction, HR: heart rate, DTE: deceleration time to peak E LA: left atrial, LA Vol Ind: left atrial volume index, IQR: interquartile range, Lma: lateral mitral annulus, LV: left ventricular, Md: median, SBP: systolic blood pressure, Sma: septal mitral annulus, TDI: Tissue Doppler Imaging, SRI: Strain Rate Imaging, Y: years.

Declarations

Ethics approval and consent to participate: The study was approved by an Institutional Review Board and all subjects gave informed consent.

Consent for publication: Not applicable.

Availability of data and materials: The data and materials used in this study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors contribution: LA and CT: Concept/design, data analysis/interpretation, drafting article, data collection, statistics, critical revision and approval of article; MC, GM, SG: data collection, critical revision of article, approval of article; AS, JL, TC: analysis and interpretation of data, critical revision of article, approval of article.

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Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section.

Figures

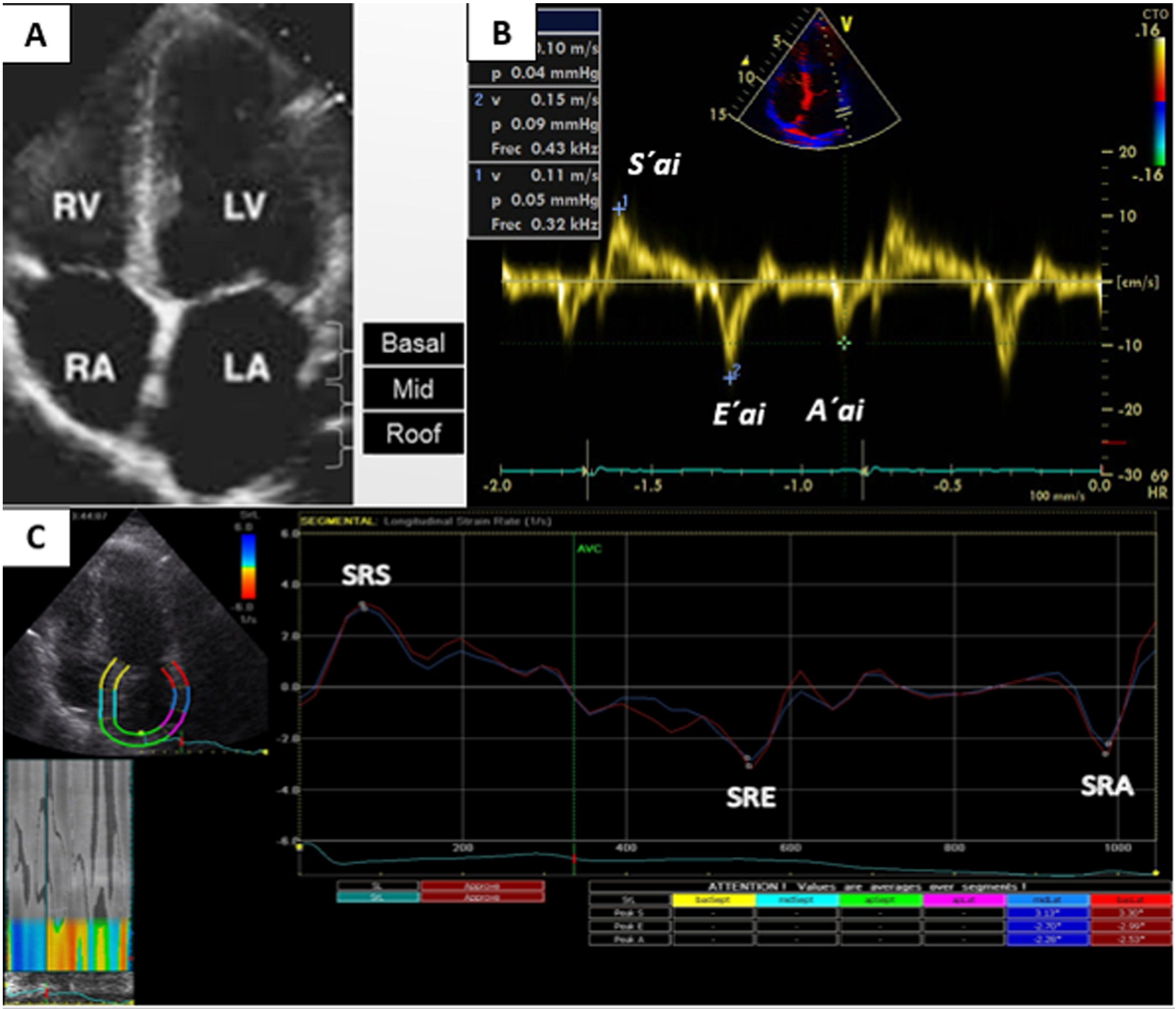

Figure 1

Methodology used for the evaluation of LA lateral wall by pulsed-wave TDI and SRI by speckle tracking. A) Subjective division of the LA lateral wall in three segments; B) Pulsed-wave color TDI at basal segment of LA lateral wall. Three waves are identified: S'la (evaluates reservoir function), E'la (evaluates conduit function), A'la (evaluates pump function). C) LA SRI by speckle tracking with the analysis of the basal and mid segments. Three waves are identified: SRS (evaluates reservoir function); SRE (evaluates conduit function) and SRA (evaluates pump function). For more information, refer to the text.

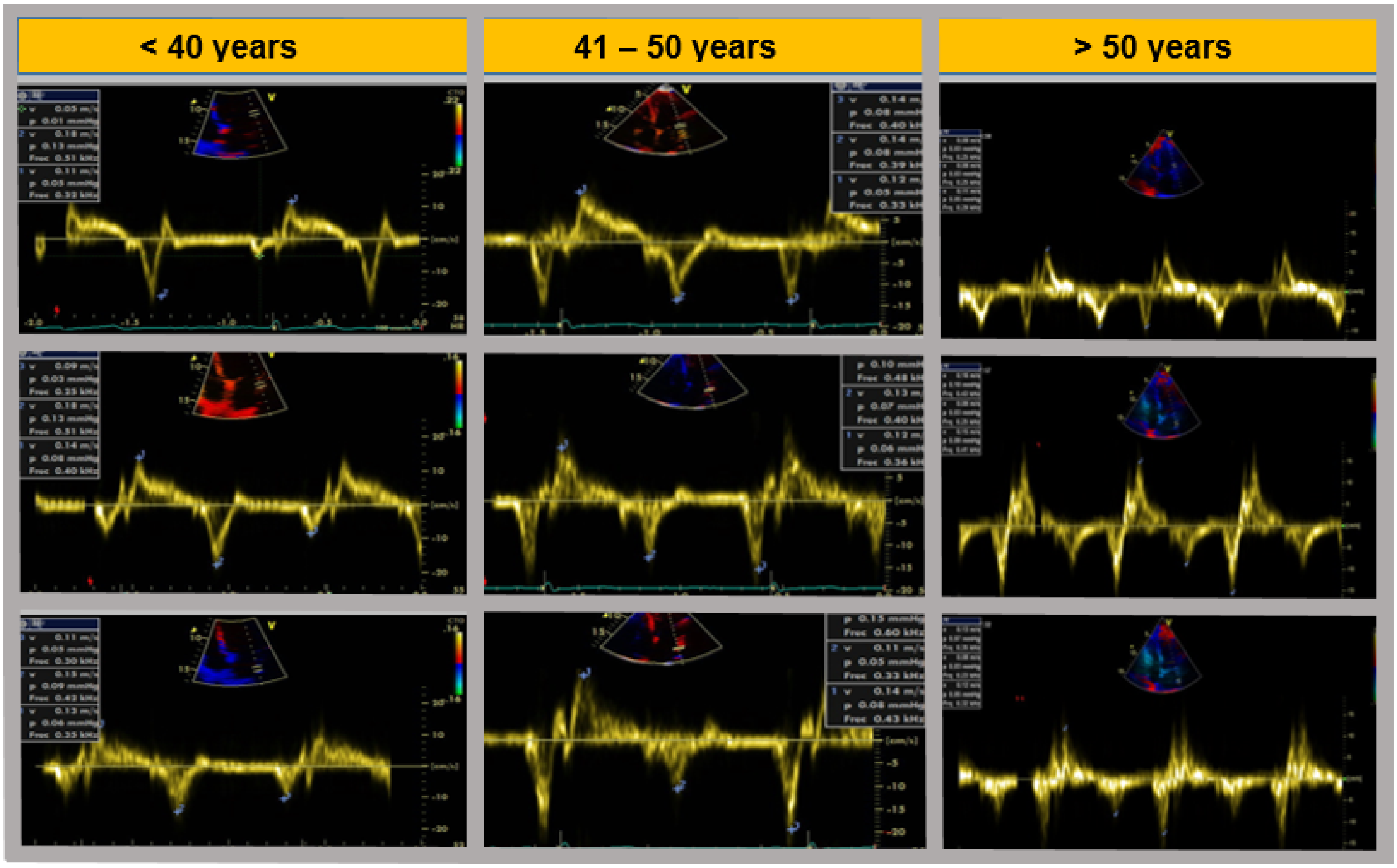

Figure 2

Pulsed TDI at the annular level (upper row), basal LA (middle row), and mid LA (lower row), according to age groups

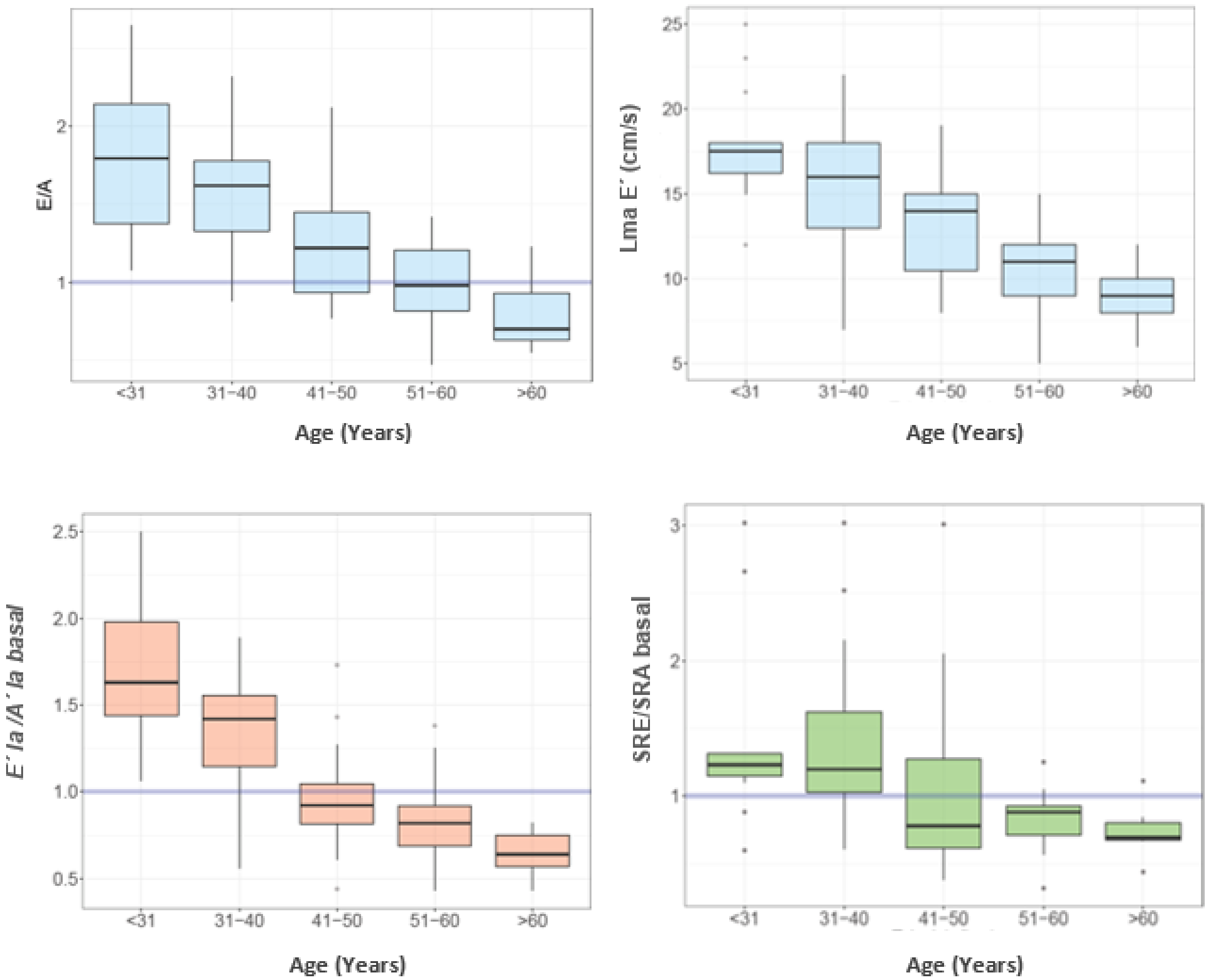

Figure 3

Graph 1: Box plot: analysis of age in relation to the variable E/A, LmaE´ basal, E'la/A'la basal, SRE/SRA.

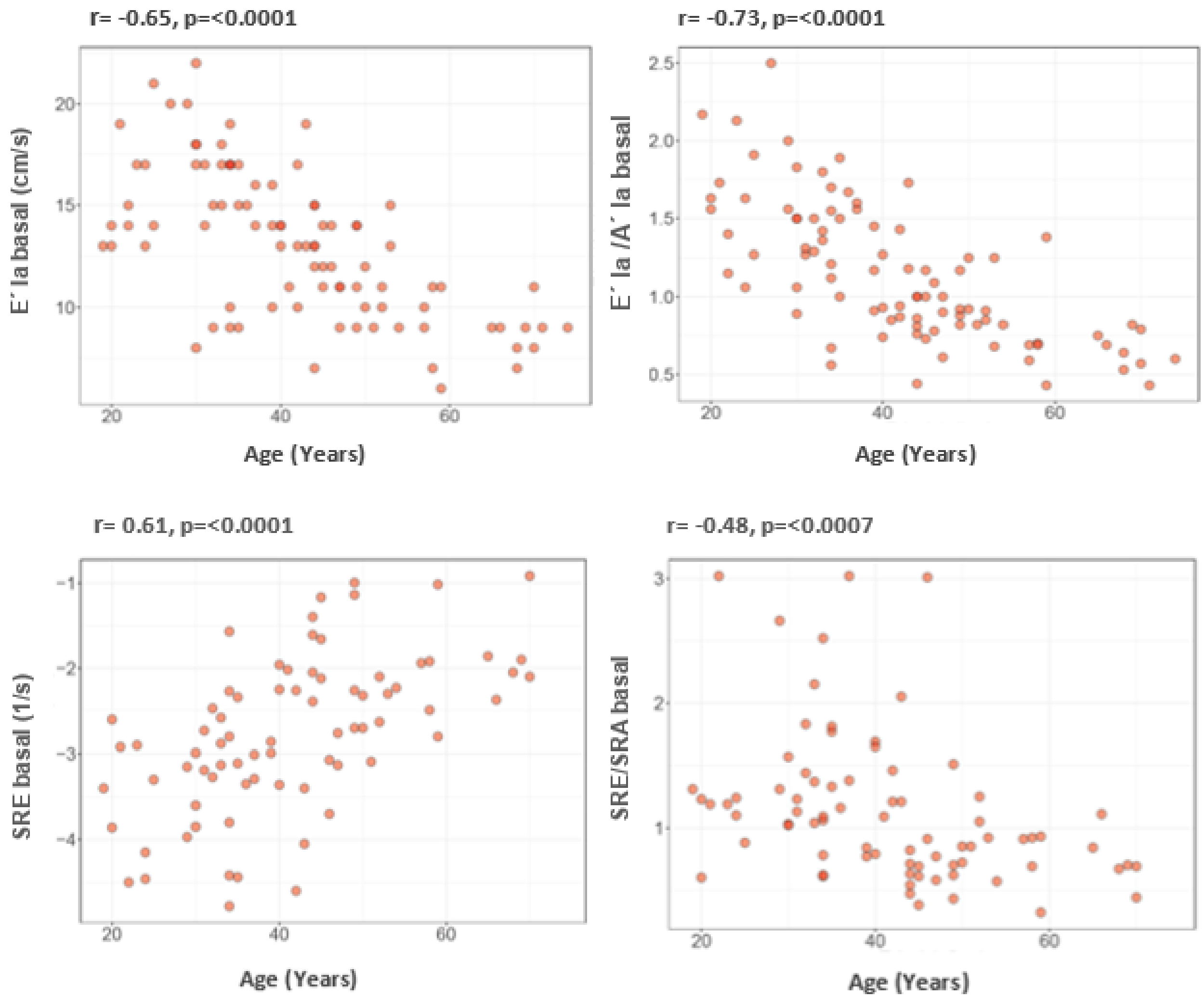

Figure 4

Graph 2: linear correlations with age obtained in the conduit phase and the ratio between the conduit phase and atrial contraction using TDI and SRI

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- *Table2.PNG*
- *SupplementalTable1.pptx*
- *Table3Univariateandmultivariateanalysis.pptx*
- *SupplementalTable2.PNG*
- *Table1Globalparameters.pptx*