Left atrial aging: a cardiac magnetic resonance feature-tracking study

Morgane Evin, Alban Redheuil, Gilles Soulat, Ludivine Perdrix, Golmehr Ashrafpoor, Alain Giron, Jérôme Lamy, Carine Defrance, Charles Roux, Stéphane N. Hatem, et al.

▶ To cite this version:

Morgane Evin, Alban Redheuil, Gilles Soulat, Ludivine Perdrix, Golmehr Ashrafpoor, et al.. Left atrial aging: a cardiac magnetic resonance feature-tracking study. AJP - Heart and Circulatory Physiology, 2016, 310 (5), pp.H542-H549. 10.1152/ajpheart.00504.2015 . hal-01303940

HAL Id: hal-01303940
https://hal.sorbonne-universite.fr/hal-01303940

Left atrial aging: a cardiac magnetic resonance feature tracking study

Left atrial aging: a cardiac magnetic resonance feature tracking study

Morgane Evin, PhD [1,2], Alban Redheuil, MD, PhD [1,2,3,7], Gilles Soulat, MD [4,6], Ludivine Perdrix, MD [6], Golmehr Ashrafpoor, MD [1, 6], Alain Giron, PhD [1], Jérôme Lamy, MS [1,2], Carine Defrance, MD [8], Charles Roux, MD [1,2,3], Stéphane N. Hatem, MD, PhD [2,5,8], Benoit Diebold, MD, PhD [1,6], Elie Mousseaux, MD, PhD[4,6], Nadjia Kachenoura, PhD[1,2]

[1] Sorbonne Universités, UPMC Univ Paris 06, INSERM UMRS 1146, CNRS UMR 7371, Laboratoire d'Imagerie Biomédicale, F-75013, Paris, France

[2] ICAN Institute of Cardiometabolism and Nutrition, Paris, France

[3] Department of Cardiovascular Radiology, Institut of Cardiologie, Hôpital Pitié-Salpêtrière, Paris, France

[4] Paris-Centre de recherche Cardiovasculaire, INSERM, HEGP, Paris, France

[5] Université Pierre et Marie Curie-Paris 6, INSERM UMR_S956, Paris, France

[6] Department of Cardiology, European Hospital Georges Pompidou, Paris, France

[7] ICAN Imaging Core Lab, Paris, France;

[8] Department of Cardiology, Institute of Cardiologie, Hôpital Pitié-Salpêtrière, Paris, France

Address for correspondence:

Morgane Evin

Left atrial aging: a cardiac magnetic resonance feature tracking study

Sorbonne Universités, UPMC Univ Paris 06, UMR 7371, UMR_S 1146, Laboratoire d'Imagerie Biomédicale, F-75013

Institute of Cardiometabolism and Nutrition,

91 Bvd de l'Hôpital, 75013, Paris, FRANCE

Fax: (+33) 153 82 84 48

Phone: (+33) 153 82 84 35

Email: evinmorgane@gmail.com

Word count including abstract, text, references, tables and figure legends: 5633

Left atrial aging: a cardiac magnetic resonance feature tracking study

Abstract

Aims

Importance of left atrial (LA) phasic function evaluation is increasingly recognized for its incremental value in terms of prognosis and risk stratification. LA phasic deformation in the pathway of normal aging have been characterized using echocardiographic speckle tracking. However no data are available regarding age-related variations using feature tracking (FT) techniques from standard cine magnetic resonance imaging (MRI).

Methods and Results

We studied 94 healthy adults (41±14 years, 47 females.) who underwent MRI and Doppler echocardiography on the same day for left ventricular diastolic function evaluation. From cine MRI, longitudinal strain and strain rate, radial motion fraction and radial relative velocity, respectively corresponding to the reservoir, conduit and LA contraction phases were measured using dedicated FT software.

Longitudinal strain and radial motion fraction decreased gradually and significantly with aging for both reservoir ($r>0.31$, $p<0.003$) and conduit ($r>0.54$, $p<0.001$) phases whereas they remained unchanged during the LA contraction phase. Subsequently, the LA contraction to reservoir ratio increased significantly with age ($r>0.44$, $p<0.001$). Longitudinal strain rate and radial relative velocity significantly decreased with age (reservoir: $r=0.39$, $p<0.001$, conduit: $r>0.54$, $p<0.001$) and these associations tended to be stronger in females than in males. Finally, associations of LA functional indices with age were stronger in individuals with lower E/A ratio and E’ as well as higher E/E’ ratio, highlighting the LV-LA interplay.

Left atrial aging: a cardiac magnetic resonance feature tracking study

Conclusions

Age-related changes in LA phasic function indices were quantified by cine MRI images using a FT technique and were significantly related to age and LV diastolic function.

New & Noteworthy

Knowledge of the complex age-related changes in left atrial (LA) function made possible on routine cine MRI using a new feature tracking methods is a necessary prerequisite to characterize physiological age-related LA changes.

Keywords

Left atrial function; aging; feature tracking; magnetic resonance imaging.

Introduction

Left atrial (LA) evaluation has been shown to be useful in various conditions such as valvular diseases, cardiomyopathies and heart failure (1). In addition, LA dysfunction has been reported to be an important correlate of atrial fibrillation in the elderly and subsequently to stroke and poor outcome (7, 12). Accordingly, better characterization of LA function and geometry and their evolution with aging could be of major usefulness in predicting atrial fibrillation but also in differentiating physiological from pathological changes. Although age-specific changes in LA geometry and function have been described in echocardiography using speckle tracking or tissue Doppler techniques (21), only LA geometry and ejection fraction indices have been described in cardiovascular magnetic resonance imaging (MRI) in the setting of aging (9). However, the characterization of LA function in addition to its geometry and ejection fraction could be of interest since it enables a more comprehensive evaluation of the complex LA phasic behavior. Indeed, the assessment of the reservoir, conduit and LA contraction phases could enable a better evaluation of LA function as well as its coupling with the left ventricle (LV).

Regarding LA geometry, both echocardiography and MRI agreed on subtle LA dilation and changes in diameters with aging (16). Interestingly, echocardiographic characterization of LA function showed significant changes even without significant LA enlargement (22). More specifically, functional parameters such as LA strain, strain rate and LA active or passive emptying fractions were reported to be significantly altered with aging (2, 18).

Cardiac MRI has been reported as a reference modality for LA volumetric quantification (16) and more recently, few studies revealed the ability of MRI to characterize LA wall deformation using endocardial feature tracking (8, 10, 14), in patients. Nevertheless, to the best of our knowledge, age-related variations in LA myocardial strain and strain rate values have never been described in MRI literature.

Accordingly, our main objective was to provide normal ranges of LA strains and strain rates for the three LA phases by applying feature tracking on MRI steady state free precession (SSFP) data of 94 healthy volunteers divided into 3 age groups, with equal distribution of males and females. Furthermore, associations between such LA functional indices and state of the art echocardiographic LV diastolic function indices were studied.

Glossary

LA Left Atrium

LV Left Ventricle

EDV End-Diastolic Volume

ESV End-Systolic Volume

EF Ejection Fraction

MRI Magnetic Resonance Imaging

E Transmitral early maximal velocity

A Transmitral atrial maximal velocity

E’ Mitral annulus maximal longitudinal velocity

Sl_R Longitudinal strain of LA reservoir phase

Sl_E Longitudinal strain of LA conduit phase

Sl_A Longitudinal strain of LA contraction phase

$SRl_{S'}$ Longitudinal strain rate of LA reservoir phase

$SRl_{E'}$ Longitudinal strain rate of LA conduit phase

$SRl_{A'}$ Longitudinal strain rate of LA contraction phase

Mr_R Radial motion fraction of LA reservoir phase

Mr_E Radial motion fraction of LA conduit phase

Mr_A Radial motion fraction of LA contraction phase

$Vr_{S'}$ Relative velocity of LA reservoir phase

$Vr_{E'}$ Relative velocity of LA conduit phase

$Vr_{A'}$ Relative velocity of LA contraction phase

Methods

Study population and MRI imaging

We studied 94 healthy volunteers (41±14years, 47 females) who underwent MRI exam on GE 1.5T Magnet, including steady state free precession (SSFP) acquisitions in short-axis views and in three long axis views (2, 3, and 4 chamber), during breathholding. All subjects were asymptomatic and had no history of cardiovascular diseases. They all had normal electrocardiogram and a body mass index (BMI) <30kg/m². SSFP acquisitions were performed with the following average scan parameters: acquisition matrix of 260×192, TR of 3.7 ms, TE of 1.5 ms, flip angle of 50°, pixel size of 0.74 mm×0.74 mm, slice thickness of 8 mm, views per segment of 12 and a temporal resolution ranging between 20 and 30ms. The study protocol was approved by the institutional review board and informed consent was obtained from all participants.

LV volumes and ejection fraction as well as LV mass and LV myocardial wall thickness were computed after manual tracing of myocardial borders on MRI images using the Qmass software (Medis, v7.6, Leiden, the Netherlands). Blinded to strain analysis, the Qmass software was also used for LA volumes and ejection fraction evaluation using the biplane method (Simpson's method).

Doppler Echocardiography Diastolic Function

Standard diastolic function assessment was performed by Doppler echocardiography as described in the guidelines (17) on the same day as MRI and included the estimation of : transmitral early (E, cm/s) and atrial (A, cm/s) maximal velocities, deceleration time (DT, ms) and mitral annulus maximal longitudinal velocity measured on the lateral wall (E', cm/s). The ratios conventionally used for diastolic function evaluation (E/E' and E/A) were calculated (Figure 1).

Cardiac MRI evaluation of LA functional indices

The LA endocardial feature tracking software used in this study was previously described in (8). Briefly, it uses block matching which is based on spatial correlation constrained by active contours and edge detection, and enables to track over the cardiac cycle the endocardial contour drawn manually on a single phase corresponding to maximal LA dilation. After tracking, LA endocardial contours were used to estimate: 1) longitudinal strain, defined as the relative temporal change in LA border length, 2) radial motion fraction, defined as the relative radial displacement of the LA endocardial border towards LA center of mass (Figure 1). Then, quantitative indices corresponding to the three LA phases were estimated from both longitudinal strain (Sl_R, Sl_E, Sl_A) and radial motion fraction (Mr_R, Mr_E, Mr_A) curves and for each LA phase, respectively: reservoir phase longitudinal strain (Sl_R) and radial motion fraction (Mr_R), corresponding to the first maximum; LA contraction phase indices, longitudinal strain (Sl_A) and radial motion fraction (Mr_A), corresponding to the second maximum; and conduit phase indices, longitudinal strain (Sl_E) and radial motion fraction (Mr_E), corresponding to the difference between the first and the second maximum. Ratios between reservoir and LA contraction indices were then calculated for both longitudinal strain (Sl_A/Sl_R) and radial motion fraction (Mr_A/ Mr_R). Afterwards, longitudinal strain rate and relative radial velocity curves were, respectively, calculated as the time derivatives of the aforementioned longitudinal strain and radial motion fraction curves (Figure 1). Then, both longitudinal strain rates and radial relative velocity indices were estimated for each LA phase: reservoir phase indices, $SRl_{S'}$ and $Vr_{S'}$, corresponding to the positive maximum; conduit phase indices, $SRl_{E'}$ and $Vr_{E'}$, corresponding to the first negative maximum; and LA contraction phase indices, $SRl_{A'}$ and $Vr_{A'}$, corresponding to the second negative maximum. Finally, ratios between conduit and LA contraction indices were provided for both longitudinal strain rate ($SRl_{E'}/SRl_{A'}$) and relative radial velocity ($Vr_{E'}/Vr_{A'}$). Of note, functional LA indices were calculated as the average of values obtained on the three long axis views (2, 3, and 4 chamber).

The inter-observer variability analysis for this method resulted in coefficients of variation of 4.3%, 7%, and 10.2% for the three phases for longitudinal strains, of 15.1%, 12.2%, and 9.8% for longitudinal strain rate parameters, of 2.9%, 8.3%, and 9% for the three phases of radial motion fraction and of 7.4%, 8.6%, and 10.2% for radial relative velocities (8).

Statistical analysis

To assess gradual variations of LA functional indices with age, subjects were divided into 3 subgroups according to age and with equal distribution of males and females in each sub-group: age group 1 (between 20 and 29 years), age group 2 (between 30 and 49 years), age group 3 (over 50 years). All continuous variables are given as means ± standard deviations. Differences across age groups were tested using one-way Anova test. Associations between continuous variables were studied using linear regression and Pearson correlation coefficients were provided for the whole group and separately for males and females. To study the association of LA functional indices with LV diastolic function indices, distributions of LA indices according to age groups and to diastolic LV function indices (E/A, E/E’, E’) were represented while stratifying LV diastolic function indices according to their median values. For this latter analysis, the non-parametric Wilcoxon test was used to assess the significance of differences between the elderly subjects group and the remaining groups. Statistical analysis was performed using the R software and statistical significance was indicated by p-value< 0.05.

Results

Patient characteristics and LV function

Table 1 shows subjects description by age groups including basic characteristics, brachial pressures, MRI indices of LV systolic function and echocardiographic indices of LV diastolic function. Moreover, correlation coefficients corresponding to the linear regressions of the described indices with age are summarized in table 1. There was a significant increase in BMI and a gradual and significant increase in systolic and diastolic blood pressures ($p<0.001$) with age. Regarding MRI LV systolic function indices, no significant changes were observed between age groups in terms of LV mass, ejection fraction and volumes, although these measures followed the expected trends such as an increase in LV mass along with a decrease in LV volumes in the elderly. Finally, there was a slight and significant increase in LV wall thickness with age.

All diastolic function parameters varied significantly across age groups. Furthermore, all diastolic variables followed the expected trend with age. Indeed, there was a decrease in E wave ($p<0.001$) along with an increase in A wave ($p<0.001$) resulting in a decrease in E/A ratio ($p<0.001$). Moreover, deceleration time increased with age ($p=0.01$) while E’ decreased with age ($p<0.001$) resulting in a gradual increase in E/E’ ratio ($p<0.001$).

Effect of aging on LA parameters

Table 2 summarizes LA volumetric indices as well as mean values of LA functional parameters across age groups. Similar to table 1, correlation coefficients corresponding to the linear regression between LA indices and age are provided.

Regarding LA volumes, whether indexed or not to BSA, they increased slightly across age groups while EF remained stable. Linear associations of LA volumes with age were significant ($p<0.01$) although not as strong as those obtained for LV diastolic function indices.

While indices of longitudinal strain (Sl_R, Sl_E) and strain rate ($SRl_{S'}$, $SRl_{E'}$), as well as radial motion fraction (Mr_R, Mr_E) and relative velocity ($Vr_{S'}$, $Vr_{E'}$) associated with LA reservoir and conduit phases significantly decreased in terms of magnitude across age groups ($p<0.01$), those corresponding to LA contraction remained unchanged across age groups.

The strongest associations with age (Table 2) were found for indices characterizing LA conduit phase (Sl_E, $SRl_{E'}$, Mr_E, $Vr_{E'}$). Such associations were nearly as strong as those found for LV diastolic function indices.

Strain (Sl_A/Sl_R) and radial motion fraction (Mr_A/Mr_R) ratios combining LA reservoir and contraction phases increased significantly with age. Additionally, a significant decreasing trend was observed for strain rate ($SRl_{E'}/SRl_{A'}$) and relative velocity ($Vr_{E'}/Vr_{A'}$) ratios combining LA conduit and contraction phases.

Regarding gender differences, the strongest associations between LA functional indices and age were found in women group, regardless of the LA phase (Figure 2, supplementary table). LA volumes indexed to BSA were equivalent between males and females except for individuals ≥ 50 years old, where LA volumes were higher in males (supplementary table). Concerning LA functional parameters, magnitudes of longitudinal strain and strain rate as well as radial motion fraction and relative velocity, were higher in females <30 years old, regardless of the LA phase (supplementary table). Conversely, such magnitudes were slightly higher in males ≥ 50 years old.

Association between atrial and LV diastolic functions indices

Distributions of LA conduit phase longitudinal strain and radial motion fraction indices according to age groups and to diastolic LV function indices (E/A, E/E', E') are shown in Figure 3. Independent of diastolic function indices, a decreasing trend with aging was observed for LA strain and motion fraction values corresponding to conduit phases. However, such decrease in longitudinal strain and radial motion fraction with age was statistically significant only for low values of E/A ($p<0.014$), of E' ($p<0.004$) and high values of E/E' ($p<0.031$).

Discussion

Changes in LA function and dimensions have been mostly studied as a reflection of LV diastolic dysfunction. Although a part of LA functional alterations could be attributed to LA/LV coupling which are intimately related to variations in pressure gradients between the two chambers, another part could be associated to intrinsic LA tissue alterations which may increase LA stiffness and alter its contraction and relaxation, as a result of electrophysiological alterations (3). Indeed, associations between LA tissue and its functional alteration are supported by recent studies which indicated significant relation between LA function evaluated by echocardiographic speckle tracking and the amount and myocardial fibrosis provided by histological analysis (4).

Studying LA through the sole evaluation of volumes and ejection fraction is limited since LA function is complex and comprises three main phases whose mechanisms and variations with age may be explained by both LV diastolic function alterations with aging, intrinsic LA aging and their interplay. Accordingly, in this study, an insight into LA phasic function modifications in the pathway of healthy aging was provided and its association with state of the art evaluation of LV diastolic function using Doppler echocardiography was studied.

First, the expected age-related changes in diastolic function indices were found in our population (19, 23). Indeed, there was a significant decrease in E wave, E/A and E’ as well as a significant increase in A wave, E/E’ and deceleration time with aging. Furthermore, our results regarding conventional LA volumetric indices were in line with previous MRI findings (16) despite slight discrepancies with echocardiographic results (13). LA volumes indexed to BSA increased slightly through age groups and their linear association with age resulted in significant correlations. Moreover, as previously shown (9), LA ejection fraction remained unchanged across age groups. This might be explained by the relatively parallel augmentation of both LA end-diastolic and end-systolic volumes with age.

Regarding the newly proposed MRI LA functional indices, the linear regression of their association with age resulted in higher correlation coefficient than those found for conventional LA volumetric indices although lower than those found for LV diastolic function indices. Specifically, Tables 1 and 2 indicated that the main significant variations of LA functional indices with age were: 1) a decrease in amplitude of functional indices related to reservoir and conduit phases for both longitudinal strain and radial motion fraction, 2) an increase in LA contraction over reservoir ratio for both longitudinal strain and radial motion fraction, 3) a decrease in longitudinal strain rates and radial relative velocities corresponding to LA reservoir (S') and conduit phases (E'), 4) a decrease in longitudinal strain rates and radial relative velocities ratios combining the LA conduit and contraction phases (E'/A'). Of note, the strongest associations with age were found for longitudinal strain rate and relative velocity corresponding to the conduit phase. This might be due to the LV longitudinal relaxation which affects LA wall. When studied separately in males and females, age related variations in LA function indices were found to be stronger in the females group. While, magnitudes of strain indices were higher in young females (<30 years), as compared to males, they were equivalent or even slightly inferior in elderly females (≥50 years), resulting in an accentuated decreasing trend in females. These findings are in line with those shown on the LV aging according to gender (5, 6) and might be explained by the important role played by estrogens in heart remodeling.

In addition, associations of LA function indices with LV diastolic function parameters revealed significant variations of LA longitudinal strain with age in the subgroup of individuals corresponding to higher E/E' as well as lower E/A and E', especially during the conduit phase. This finding is concomitant with the previous knowledge regarding the important role of LV-LA coupling (9) in LA aging.

Such age-related variations in LA functional parameters are in line with physiological knowledge. Briefly, during reservoir phase, the pulmonary veins inflows enter the LA cavity while the mitral valve is closed and the mitral annulus is moving towards the apex inducing LA dilation. Age-related changes in this phase can be explained by alteration in relaxation capacities of the LA associated with tissue changes (i.e. myocardial fibrosis) and the underlying electromechanical alterations (20) as well as reduced mitral valve annulus longitudinal motion. After reaching its maximal dilation, the mitral valve opens resulting in passive LA emptying due to pressure gradient between LA and LV. Such phase is named LA conduit phase and follows the significant drop in LV pressures which occurs just before opening of the mitral valve and can disappear in case of severe LV alterations, such as dilated cardiomyopathy. Effect of age on this phase combines the decrease in LA wall elastic recoil capacity with LV aging which is known to be associated with altered myocardial relaxation capacities (15). Finally, LA emptying is completed by its active contraction whose contribution to LV filling increases with age as depicted by the increase in LA contraction to reservoir strain ratio. In our data, despite a significant increase in A wave with age, LA contraction strain and radial motion fraction remain unchanged probably because of the slightly dilated LA in the elderly which might result in higher late LV filling volume without a substantial change in LA contraction. Overall changes in LA functional indices with age are concomitant with the knowledge regarding LV ageing which consists in an impaired relaxation while its contraction remains preserved. Furthermore, these findings are consistent with the known importance of a preserved LA contraction in different conditions of impaired LV relaxation such as aging and potentially other causes of LV hypertrophy (hypertension, hypertrophic cardiomyopathy) as they highlight the increased importance of atrial contraction relative to the reservoir function.

Limitations

The first limitation of our study is the low number of subjects > 70 years. However, finding healthy subjects without any cardiovascular comorbidities in such age range was difficult. The second limitation is due to the fact that feature tracking techniques might suffer from out of plane motion and the temporal resolution of our MRI data. However, feature tracking offers a good alternative to the tagging technique whose application is still restricted to LV myocardium because of the wall thickness issues. In addition, our temporal resolution was equivalent to those of previous feature tracking studies and a study performed on phantom showed that up to 30 phases per cardiac cycle the error on strain measurements remains reasonable (8). Finally, the comparison with ultrasound speckle tracking was not performed since our primary goal in the present study was to provide additional LA functional parameters to the already established reference evaluation of LA volumes by MRI and to show their variations with age. A future study, where echocardiographic acquisitions are specifically designed for LA function evaluation should be performed to enable translation of physiological knowledge between the two modalities.

Conclusions

This MRI feature tracking study on healthy volunteers highlighted a reduction of LA functional parameters associated to reservoir and conduit phases with aging along with an increase in the ratio of LA contraction to reservoir phase indices. Linear association with age resulted in higher correlation coefficients for the newly proposed indices than those obtained for conventional LA volumetric indices. The association with LV diastolic function indicated the intricate role of the LV in age-related LA dysfunction and further studies focusing on LA myocardial tissue characterization in addition to its function are needed to fully assess the possible role of intrinsic age-related alteration on LA compliance. Such studies made possible by MRI tissue mappings (11) and strain measurements could help providing a better insight into LA and LV-related functional alterations.

Acknowledgements

We thank the ICAN Institute of Cardiometabolism and Nutrition, Paris, France for the funding of a Post-Doctoral Grant for ME on this research program.

Grants

This work was supporting by the ICAN Institute of Cardiometabolism and Nutrition, Paris.

Disclosure

None declared.

References

1. **Blume GG**, **Mcleod CJ**, **Barnes ME**, **Seward JB**, **Pellikka PA**, **Bastiansen PM**, **Tsang TSM**. Left atrial function: physiology, assessment, and clinical implications. *Eur J Echocardiogr J Work Group Echocardiogr Eur Soc Cardiol* 12: 421–430, 2011.

2. **Boyd AC**, **Richards DAB**, **Marwick T**, **Thomas L**. Atrial strain rate is a sensitive measure of alterations in atrial phasic function in healthy ageing. *Heart* 97: 1513–1519, 2011.

3. **Boyd AC**, **Schiller NB**, **Leung D**, **Ross DL**, **Thomas L**. Atrial dilation and altered function are mediated by age and diastolic function but not before the eighth decade. *JACC Cardiovasc Imaging* 4: 234–242, 2011.

4. **Cameli M**, **Lisi M**, **Righini FM**, **Massoni A**, **Natali BM**, **Focardi M**, **Tacchini D**, **Geyer A**, **Curci V**, **Di Tommaso C**, **Lisi G**, **Maccherini M**, **Chiavarelli M**, **Massetti M**, **Tanganelli P**, **Mondillo S**. Usefulness of atrial deformation analysis to predict left atrial fibrosis and endocardial thickness in patients undergoing mitral valve operations for severe mitral regurgitation secondary to mitral valve prolapse. *Am J Cardiol* 111: 595–601, 2013.

5. **Cheng S**, **Fernandes VRS**, **Bluemke DA**, **McClelland RL**, **Kronmal RA**, **Lima JAC**. Age-related left ventricular remodeling and associated risk for cardiovascular outcomes: the Multi-Ethnic Study of Atherosclerosis. *Circ Cardiovasc Imaging* 2: 191–198, 2009.

6. **Cheng S**, **Xanthakis V**, **Sullivan LM**, **Lieb W**, **Massaro J**, **Aragam J**, **Benjamin EJ**, **Vasan RS**. Correlates of echocardiographic indices of cardiac remodeling over the adult life course: longitudinal observations from the Framingham Heart Study. *Circulation* 122: 570–578, 2010.

7. **European Heart Rhythm Association**, **European Association for Cardio-Thoracic Surgery**, **Camm AJ**, **Kirchhof P**, **Lip GYH**, **Schotten U**, **Savelieva I**, **Ernst S**, **Van Gelder IC**, **Al-Attar N**, **Hindricks G**, **Prendergast B**, **Heidbuchel H**, **Alfieri O**, **Angelini A**, **Atar D**, **Colonna P**, **De Caterina R**, **De Sutter J**, **Goette A**, **Gorenek B**, **Heldal M**, **Hohloser SH**, **Kolh P**, **Le Heuzey J-Y**, **Ponikowski P**, **Rutten FH**, **ESC Committee for Practice Guidelines**. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Eur Eur Pacing Arrhythm Card Electrophysiol J Work Groups Card Pacing Arrhythm Card Cell Electrophysiol Eur Soc Cardiol* 12: 1360–1420, 2010.

8. **Evin M**, **Cluzel P**, **Lamy J**, **Rosenbaum D**, **Kusmia S**, **Defrance C**, **Soulat G**, **Mousseaux E**, **Roux C**, **Clement K**, **Hatem SN**, **Redheuil A**, **Kachenoura N**. Assessment of left atrial function by MRI myocardial feature tracking. *J. Magn. Reson. Imaging JMRI* (January 28, 2015). doi: 10.1002/jmri.24851.

9. **Germans T**, **Götte MJW**, **Nijveldt R**, **Spreeuwenberg MD**, **Beek AM**, **Bronzwaer JGF**, **Visser CA**, **Paulus WJ**, **van Rossum AC**. Effects of Aging on Left Atrioventricular Coupling and Left Ventricular Filling Assessed Using Cardiac Magnetic Resonance Imaging in Healthy Subjects. *Am J Cardiol* 100: 122–127, 2007.

10. **Habibi M**, **Venkatesh BA**, **Lima JAC**. Feature Tracking Cardiac Magnetic Resonance Imaging in the Assessment of Left Atrial Function. *J Am Coll Cardiol* 63: 2434–2435, 2014.

11. **Imai M**, **Venkatesh BA**, **Samiei S**, **Donekal S**, **Habibi M**, **Armstrong AC**, **Heckbert SR**, **Wu CO**, **Bluemke DA**, **Lima JAC**. Multi-Ethnic Study of Atherosclerosis: Association between Left Atrial Function Using Tissue Tracking from Cine MR Imaging and Myocardial Fibrosis. *Radiology* (July 14, 2014). doi: 10.1148/radiol.14131971.

12. **January CT**, **Wann LS**, **Alpert JS**, **Calkins H**, **Cigarroa JE**, **Cleveland JC**, **Conti JB**, **Ellinor PT**, **Ezekowitz MD**, **Field ME**, **Murray KT**, **Sacco RL**, **Stevenson WG**, **Tchou PJ**, **Tracy CM**, **Yancy CW**. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation* 130: e199–e267, 2014.

13. **Kou S**, **Caballero L**, **Dulgheru R**, **Voilliot D**, **Sousa CD**, **Kacharava G**, **Athanassopoulos GD**, **Barone D**, **Baroni M**, **Cardim N**, **Diego JJGD**, **Hagendorff A**, **Henri C**, **Hristova K**, **Lopez T**, **Magne J**, **Morena GDL**, **Popescu BA**, **Penicka M**, **Ozyigit T**, **Carbonero JDR**, **Salustri A**, **Veire NVD**, **Bardeleben RSV**, **Vinereanu D**, **Voigt J-U**, **Zamorano JL**, **Donal E**, **Lang RM**, **Badano LP**, **Lancellotti P**. Echocardiographic reference ranges for normal cardiac chamber size: results from the NORRE study. *Eur. Heart J. - Cardiovasc. Imaging* (January 22, 2014). doi: 10.1093/ehjci/jet284.

14. **Kowallick JT**, **Kutty S**, **Edelmann F**, **Chiribiri A**, **Villa A**, **Steinmetz M**, **Sohns JM**, **Staab W**, **Bettencourt N**, **Unterberg-Buchwald C**, **Hasenfuß G**, **Lotz J**, **Schuster A**. Quantification of left atrial strain and strain rate using Cardiovascular Magnetic Resonance myocardial feature tracking: a feasibility study. *J Cardiovasc Magn Reson* 16: 60, 2014.

15. **Lakatta EG**, **Levy D**. Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: Part II: the aging heart in health: links to heart disease. *Circulation* 107: 346–354, 2003.

16. **Maceira AM**, **Cosin-Sales J**, **Roughton M**, **Prasad SK**, **Pennell DJ**. Reference left atrial dimensions and volumes by steady state free precession cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 12: 65, 2010.

17. **Nagueh SF**, **Appleton CP**, **Gillebert TC**, **Marino PN**, **Oh JK**, **Smiseth OA**, **Waggoner AD**, **Flachskampf FA**, **Pellikka PA**, **Evangelista A**. Recommendations for the evaluation of left ventricular diastolic function by

echocardiography. *J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr* 22: 107–133, 2009.

18. **Okamatsu K**, **Takeuchi M**, **Nakai H**, **Nishikage T**, **Salgo IS**, **Husson S**, **Otsuji Y**, **Lang RM**. Effects of aging on left atrial function assessed by two-dimensional speckle tracking echocardiography. *J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr* 22: 70–75, 2009.

19. **Okura H**, **Takada Y**, **Yamabe A**, **Kubo T**, **Asawa K**, **Ozaki T**, **Yamagishi H**, **Toda I**, **Yoshiyama M**, **Yoshikawa J**, **Yoshida K**. Age- and gender-specific changes in the left ventricular relaxation: a Doppler echocardiographic study in healthy individuals. *Circ Cardiovasc Imaging* 2: 41–46, 2009.

20. **Spadaccio C**, **Rainer A**, **Mozetic P**, **Trombetta M**, **Dion RA**, **Barbato R**, **Nappi F**, **Chello M**. The role of extracellular matrix in age-related conduction disorders: a forgotten player? *J Geriatr Cardiol JGC* 12: 76–82, 2015.

21. **Sun JP**, **Yang Y**, **Guo R**, **Wang D**, **Lee AP-W**, **Wang XY**, **Lam Y-Y**, **Fang F**, **Yang XS**, **Yu C-M**. Left atrial regional phasic strain, strain rate and velocity by speckle-tracking echocardiography: normal values and effects of aging in a large group of normal subjects. *Int J Cardiol* 168: 3473–3479, 2013.

22. **Thomas L**, **Levett K**, **Boyd A**, **Leung DYC**, **Schiller NB**, **Ross DL**. Compensatory changes in atrial volumes with normal aging: is atrial enlargement inevitable? *J Am Coll Cardiol* 40: 1630–1635, 2002.

23. **Yamada H**, **Oki T**, **Mishiro Y**, **Tabata T**, **Abe M**, **Onose Y**, **Wakatsuki T**, **Ito S**. Effect of aging on diastolic left ventricular myocardial velocities measured by pulsed tissue Doppler imaging in healthy subjects. *J Am Soc Echocardiogr Off Publ Am Soc Echocardiogr* 12: 574–581, 1999.

Figure captions

Figure 1 – Example of echocardiographic diastolic function graphs, and MRI frames along with LA functional parameters for a young female (31 years old) and an elderly female (78 years old).

1-A and 2-A. Echocardiographic parameters: transmitral velocity curves (top panel) and myocardial mitral annulus maximal velocity curves (lower panel).

1-B and 2-B. The calculated longitudinal strain and radial motion fraction curves (top panel) and the derived longitudinal strain rate and radial velocity curves (median panel) along with the MRI frames corresponding to a 2 chamber view (lower panel).

Figure 2 – Linear regressions between LA functional parameters and age in males and females.

Reservoir longitudinal strain for males (A) and females (B), conduit longitudinal strain for males (C) and females (D) and longitudinal strain rate E' for males (E) and females (F).

Figure 3 – Distribution of LA functional parameters according to age groups and to diastolic function parameters-based sub-groups.

Sub-groups according to diastolic function indices were defined according to the median value of the considered parameter. Statistical significance for comparisons against the elderly was noted: * for $p<0.05$, ** for $p<0.01$, *** for $p< 0.001$.

Text tables

Table-1. Basic characteristics and MRI indices of LV systolic function, across age groups and echocardiographic diastolic function parameters.

LV for left ventricular, EDV for end diastolic volume, ESV for end systolic volume, EF for ejection fraction, SBP and DBP: systolic and diastolic blood pressures. Differences across age groups are tested using one-way Anova test and the p values are provided for significant differences, while the non-significant ones are noted “ns”. Correlation coefficients and levels of significance r (p) are provided for linear regressions between LV indices with age. Non-significant correlations were noted “ns”.

	Age group 1 20-29 y. (n=28)	**Age group 2 30-49 y. (n=36)**	**Age group 3 ≥50 y. (n=30)**	**p inter. age groups**	**Correlation coefficient r(p)**
Age (years)	24.9±2.8	38.8±5.8	58.9±6.5		
Male/Female	14/14	18/18	15/15		
Body Surface Area (m^2)	1.8±0.2	1.8±0.2	1.9±0.2	ns	ns
Body Mass Index (kg/m^2)	22.7±3.0	23.1±3.3	25.2±3.7	0.001	0.33(0.001)
Brachial SBP (mmHg)	105.4±5.8	109.5±11.4	118.0±14.1	<0.001	0.42(<0.001)
Brachial DBP (mmHg)	62.4±6.2	68.8±8.0	74.1±10.3	<0.001	0.52(<0.001)
MRI LV systolic function					
LV Mass /BSA (g/m^2)	64.4±10.6	60.5±11.7	66.8±12.4	ns	ns
LV EDV (mL)	140.9±28.0	135.7±28.0	137.0±38.7	ns	ns
LV ESV (mL)	53.4±12.6	49.4±12.6	48.9±14.3	ns	ns
LV EDV /BSA (mL/m^2)	79.7±13.7	75.5±14.1	71.9±17.7	ns	ns
LV ESV /BSA (mL/m^2)	30.2±6.6	27.5±6.9	25.6±6.7	ns	ns
LV EF (%)	62.2±4.7	63.8±5.4	64.0±6.1	ns	ns
Global LV thickness (mm)	7.4±1.3	7.5±1.2	8.1±1.2	0.03	0.25(0.02)
Echocardiographic diastolic function					
Ewave (cm/s)	84.1±15.8	74.6±17.5	67.0±11.0	<0.001	-0.49(<0.001)
Awave (cm/s)	54.8±9.8	56.1±13.4	74.4±16.3	<0.001	0.58(<0.001)
E/A Mitral	1.6±0.4	1.4±0.5	0.9±0.3	<0.001	-0.64(<0.001)

E' lat (cm/s)	17.2±3.7	14.6±3.3	10.5±2.6	<0.001	-0.70(<0.001)
E/E'	4.9±1.3	4.7±1.1	6.6±1.7	<0.001	0.45(<0.001)
Deceleration Time (ms)	165.7±54.9	176.8±38.3	188.2±40.7	0.02	0.26(0.01)

Table-2. Distribution of LA volumes and functional parameters across age groups.

Longitudinal strains: reservoir Sl_R, conduit Sl_E and LA contraction Sl_A; longitudinal strain rates: $SRl_{R'}$, $SRl_{E'}$, $SRl_{A'}$. Radial motion fraction: reservoir Mr_R, conduit Mr_E and LA contraction Mr_A; radial relative velocities: $Vr_{S'}$, $Vr_{E'}$, $Vr_{A'}$. The last column summarizes the correlation coefficient (r) for the linear regression between LA indices and age along with their significance. Non-significant differences across groups and non-significant correlations were noted "ns". Of Note, systolic and diastolic phases are defined according to LA rather than to LV.

	Age group 1 20-29 y. (n=28)	**Age group 2 30-49 y. (n=36)**	**Age group 3 ≥50 y. (n=30)**	**p inter. age groups**	**Correlation coefficient r(p)**
MRI LA volumetric parameters					
LA ESV / BSA (mL/m²)	11.9±2.8	14.1±4.0	14.8±4.7	0.007	0.26(0.008)
LA EDV / BSA (mL/m²)	27.9±5.6	31.9±6.1	33.4±9.6	0.006	0.25(0.01)
LA EF (%)	57.4±5.6	56.0±7.5	56.5±6.0	ns	ns
MRI LA functional indices					
Longitudinal strain (%)					
Sl_R	25.6±5.7	25.0±5.4	21.2±5.8	0.002	-0.36 (<0.001)
Sl_E	13.3±3.0	12.5±3.3	9.0±3.8	<0.001	-0.54(<0.001)
Sl_A	12.3±3.9	12.5±4.0	12.1±4.0	ns	ns
Sl_A/Sl_R	0.5±0.1	0.5±0.1	0.6±0.1	<0.001	0.44(<0.001)
Longitudinal strain rate (%/s)					
$SRl_{S'}$	1.3±0.4	1.2±0.4	0.9±0.2	<0.001	-0.39(<0.001)
$SRl_{E'}$	-1.4±0.4	-1.2±0.4	-0.8±0.3	<0.001	0.54(<0.001)
$SRl_{A'}$	-1.0±0.4	-1.0±0.4	-1.0±0.4	ns	ns
$SRl_{E'}/SRl_{A'}$	1.4±0.5	1.3±0.6	0.9±0.5	<0.001	-0.38(<0.001)
Radial motion fraction (%)					
Mr_R	27.6±5.7	27.2±5.3	23.9±5.4	0.01	-0.31(0.003)
Mr_E	15.3±3.3	13.9±3.7	10.1±3.7	<0.001	-0.55(<0.001)
Mr_A	12.3±4.4	13.2±3.5	13.8±3.9	ns	ns
Mr_A/Mr_R	0.4±0.1	0.5±0.1	0.6±0.1	<0.001	0.52(<0.001)
Radial relative velocity (%/s)					
$Vr_{S'}$	1.5±0.5	1.2±0.3	1.1±0.2	<0.001	-0.39(<0.001)
$Vr_{E'}$	-1.5±0.4	-1.4±0.4	-0.9±0.3	<0.001	0.61(<0.001)
$Vr_{A'}$	-1.3±0.6	-1.3±0.4	-1.2±0.6	ns	ns
$Vr_{E'}/Vr_{A'}$	1.3±0.5	1.2±1.1	0.8±0.5	0.001	-0.29 (<0.05)

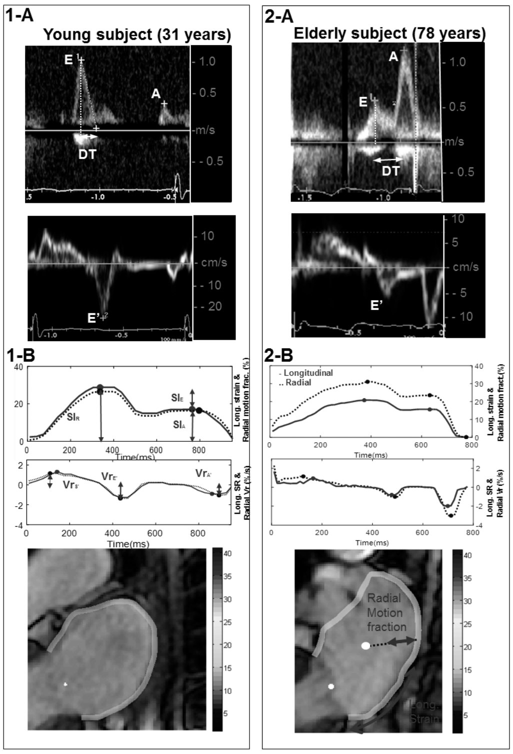
1-A
Young subject (31 years)
E
A
DT
m/s
1.0
0.5
- 0.5
E'
cm/s
10
- 10
- 20
1-B
SlR
SlE
SlA
Time(ms)
Long. strain & Radial motion frac. (%)
VrS'
VrE'
VrA'
Long. SR & Radial Vr (%/s)
2-A
Elderly subject (78 years)
E
A
DT
m/s
1.0
0.5
- 0.5
E'
cm/s
5
- 5
- 10
2-B
- Longitudinal
.. Radial
Long. strain & Radial motion fract.(%)
Long. SR & Radial Vr (%/s)
Time(ms)
Radial Motion fraction
Long. Strain

Figure 1

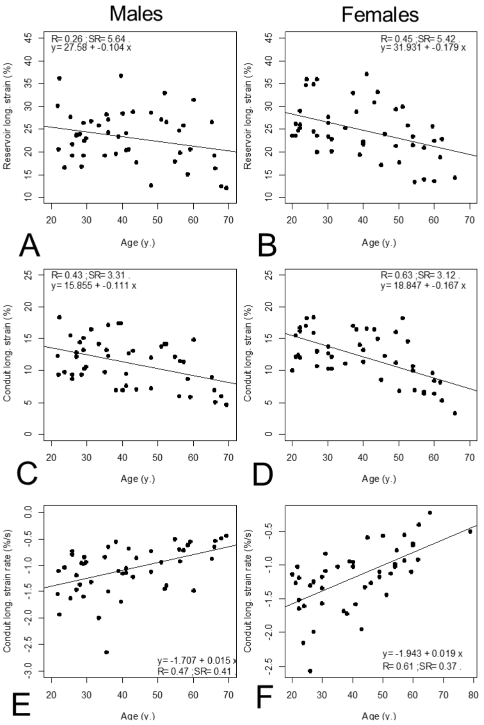
Males
Females
R= 0.26 ;SR= 5.64 .
y= 27.58 + -0.104 x
Reservoir long. strain (%)
10
15
20
25
30
35
40
45
20
30
40
50
60
70
Age (y.)
A
R= 0.45 ;SR= 5.42 .
y= 31.931 + -0.179 x
Reservoir long. strain (%)
Age (y.)
B
R= 0.43 ;SR= 3.31 .
y= 15.855 + -0.111 x
Conduit long. strain (%)
0
5
10
15
20
25
Age (y.)
C
R= 0.63 ;SR= 3.12 .
y= 18.847 + -0.167 x
Conduit long. strain (%)
Age (y.)
D
Conduit long. strain rate (%/s)
0.0
-0.5
-1.0
-1.5
-2.0
-2.5
-3.0
y= -1.707 + 0.015 x
R= 0.47 ;SR= 0.41 .
Age (y.)
E
Conduit long. strain rate (%/s)
-0.5
-1.0
-1.5
-2.0
-2.5
y= -1.943 + 0.019 x
R= 0.61 ;SR= 0.37 .
20
30
40
50
60
70
80
Age (y.)
F

Figure 2

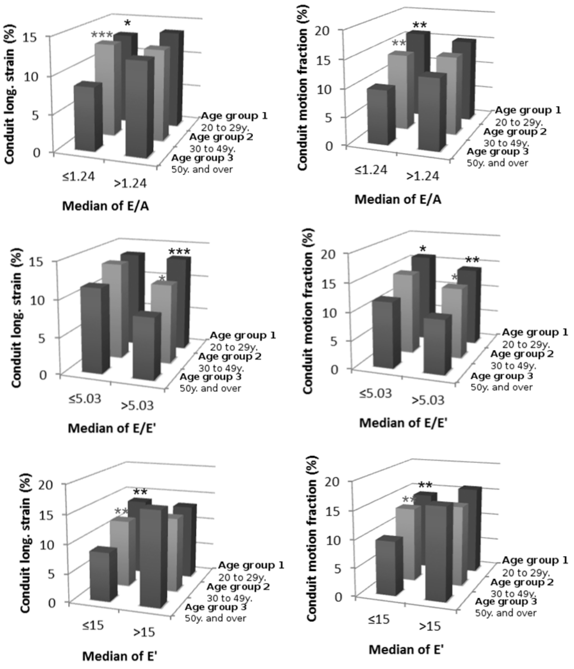
Conduit long. strain (%)
Conduit motion fraction (%)
Median of E/A
≤1.24
>1.24
Median of E/E'
≤5.03
>5.03
Median of E'
≤15
>15
Age group 1
20 to 29y.
Age group 2
30 to 49y.
Age group 3
50y. and over
0
5
10
15
20
*
**
***

Figure 3