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# References values for Left Atrial Volumes, Emptying Fractions, Strains, and Strain Rates and Their Determinants by Age, Gender, and Ethnicity: the Multi-Ethnic Study of Atherosclerosis (MESA)

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## Abstract

**BACKGROUND:** Left Atrial (LA) adverse remodeling is an important predictor of morbidity and mortality in several cardiovascular (CV) diseases. Our goals were to quantify and provide reference ranges for LA structure and function using feature tracking cine cardiac magnetic resonance (FT-CMR).

**METHODS:** 2,526 participants of the Multi-Ethnic Study of Atherosclerosis (MESA) study who had FT-CMR derived LA data and were free of atrial fibrillation/flutter and prior CV events at year five follow-up examination (2010–2012) were included in this study. LA phasic indexed volumes: maximum (LAVi max), minimum (LAVi min), and pre-atrial contraction (LAVi preA); LA empty fractions: total, passive, and active (LAtEF, LApEF, and LAaEF); LA longitudinal strain: maximum and pre-atrial contraction (S max and S preA); and LA longitudinal strain rate: systolic (SR max and early/late diastolic (SR e and SR a) were measured. Age, gender, and race/ethnicity-specific reference ranges were identified. Also, reference values in a select subgroup of healthy participants free of traditional CV risk factors at the time of exam date were reported.

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**RESULTS:** The mean ± SD for LAVi max, LAVi min, LAVi preA, S max, SR e, and SR a were in the 45–65 year-old participants: (33.8 ± 10 mL/$m^2$), (14.5 ± 6.4 mL/$m^2$), (24.8 ± 8.2 mL/$m^2$), (34.6 ± 13.8 %), (−1.4 ± 0.7 sec-1), (−2.1 ± 1 sec-1) and in the ≥ 65year-old participants: (35 ± 11.5 mL/m2), (16.6 ± 8.3 mL/m2), (27.6 ± 9.9 mL/m2), (31.2 ± 14.3 %), (−1 ± 0.6 sec-1), (−2.1 ± 1 sec-1) respectively. Younger individuals had Powered by Editorial Manager® and ProduXion Manager® from Aries Systems Corporation smaller LA volumes and better LA function compared with their older counterparts. Similar findings were observed in Chinese-Americans as compared with Whites.

**CONCLUSION:** This study provides reference values of LA structure and function parameters from a healthy multi-ethnic community-based population aged 53–94 years evaluated by FTMRI.

## Introduction

Left atrial (LA) adverse remodeling is a known predictor of cardiovascular (CV) morbidity and mortality (1, 2). LA enlargement and dysfunction are associated with the development of poor outcomes for various CV diseases, including cardiomyopathies, heart failure, valvar heart diseases, atrial fibrillation/flutter (AF), stroke, and hypertension (3–8).

Cardiac magnetic resonance (CMR) is the “gold standard” method to quantify LA volume due to its superior spatial resolution, reproducibility, and accuracy when compared with two- and three-dimension echocardiography (2D, 3D). Speckle tracking echocardiography (STE) and tagging MRI have been preferable techniques to evaluate myocardial deformation. However, tracking limitations of the thin LA walls have limited their widespread use. Myocardial feature tracking CMR (FT-CMR) is a novel method to quantify myocardial deformation that can overcome those limitations, offering an opportunity to measure LA phasic volumes, LA empty fractions, LA longitudinal strain, and LA longitudinal strain rate. These additional LA parameters allow a complete assessment of the LA function (reservoir, passive, and active phases) and have been shown superiority for phenotyping CV disease, stratifying risk in patients with CVD, and providing robust prognostic information of recurrence of atrial fibrillation, beyond the measurement of the LA size alone (9, 10).

Despite the growing use of FT-MRI and its validation against speckle tracking echocardiography (STE), reference values for comparison in a multi-ethnic population are still unknown. (11) Therefore, we aim to report reference values for LA structure and function parameters stratified by age, gender, and race/ethnicity, in a multi-ethnic population free of prior CV events at baseline examination. We also aim to provide reference ranges for those LA parameters in a select subgroup of healthy participants free of traditional CV risk factors at the time of the CMR exam date.

## Methods

### Study population

This study is part of the Multi-Ethnic Study of Atherosclerosis (MESA) protocol, which has been previously described in detail (12). Briefly, MESA is an observational cohort study initiated in 2000 that enrolled 6,814 men and women, aged 45–84 years who were free of clinically recognized CV diseases in 2000–2002 at enrollment, across six centers in the

United States (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; Northern Manhattan, NY; and St Paul, MN). All participants gave informed consent, and the institutional review board at each site approved the study protocol. Of the 3,015 participants that underwent to CMR at the follow-up examination in 2010–2012, 190 had missing LA FT-CMR assessment, 125 had missing data, 80 had clinically recognized atrial fibrillation (AF) on ECG before/during follow-up periods, and another 151 had known prior CV events, leaving 2,525 participants for analyses in the present study (Figure 1). A subgroup of 228 healthy study participants was selected after exclusion of individuals with traditional CV risk factors at the time of CMR exam date

## Cardiac Magnetic Resonance Study Protocol

Enrolled participants underwent CMR using 1.5T whole-body MRI scanners (Siemens Medical Systems, and GE Medical Systems) with a gradient strength of 45 mT/m, slew rate of 200 $Tm^{-1}/s$. The cine images included coverage of the LA using one 2-chamber slice and one 4-chamber view scanned by steady-state free precession sequences (SSFP) with the following parameters: slice thickness: 8 mm; gap: 2 mm; temporal resolution: 30–35 ms (reconstructed to 40 frames); matrix: 256×256, and field of view: 360 × 360 mm. The detailed CMR protocol has been previously published (13).

## LA CMR data acquisition and analysis by feature-tracking

LA structure and function were analyzed using a frame-by-frame template matching software (multimodality feature tracking (MTT) version 6.0, Toshiba, Japan) in untagged long-axis 2- and 4–chamber cine CMR images. LA endocardial and epicardial borders were traced at the reference frame (end-systole, just before mitral valve opening) in a counterclockwise direction, from the medial to the lateral mitral annulus, and excluding the LA appendage and the ostium of the pulmonary veins. The software automatically propagated these borders across the cardiac cycle recording characteristic pixel patterns of each 10 × 10 mm square area in the reference frame and recognizing similar pixel pattern area in the next frame. This process was repeated for all pixels in each frame in the whole cardiac cycle. The quality of the generated tracking was verified, with manual adjustments made when necessary (Figure 2) (14). Images with poor tracking and/or foreshortened images were excluded. The LA FT-MRI reproducibility has been previously described for multiple parameters with good-to-excellent intra-and inter-reader reproducibility (interclass correlation coefficient 0.88–0.92 for all parameters) (15). The left atrial volumes were calculated by bi-plane area-length method based on the formula: LA volume = (0.848 * area $_{4\ chambers}$ * area $_{2\ chambers}$) / ((length $_{4\ chambers}$ + length $_{2\ chambers}$) / 2) (10, 15). Maximum LAV ($LAV_{max}$) was defined as LAV at end-systole just before mitral valve opening. Minimum LAV ($LAV_{min}$) was defined as LAV at end-diastole right after closure of the mitral valve. Pre-atrial contraction volume ($LAV_{preA}$) was defined as LAV at onset of the P-wave on EKG. All LAV were indexed to body surface area ($LAVi_{max}$, $LAVi_{min}$, and $LAVi_{preA}$). Three LA emptying fractions were calculated based on the volumes: total emptying fraction (LAtEF) = ($LAV_{max}$−$LAV_{min}$) / $LAV_{max}$*100, passive emptying fraction (LApEF) = ($LAV_{max}$–$LAV_{preA}$) / $LAV_{max}$*100, and active emptying fraction (LAaEF) = ($LAV_{preA}$−$LAV_{min}$) / $LAV_{preA}$*100. LA longitudinal strain, and LA longitudinal strain rates were reported as the average from 2- and 4-chamber views. Maximum longitudinal strain ($S_{max}$)

was defined as global strain peak at end-systole. Pre-atrial contraction longitudinal strain ($S_{prea}$) was defined as global strain peak at the onset of the p-wave on EKG. Maximum longitudinal strain rate ($SR_{max}$) was defined as strain rate peak at the end-systole. Early and late diastolic strain rates ($SR_e$ and $SR_a$) were defined as first diastolic strain rate peak and late diastolic strain peak at atrial contraction, respectively (Figure 2).

### Cardiovascular Risk Factors Definition

The participants were divided into two subgroups based on the presence of CV risk factors: no known CV risk factors (NRF) and CV risk factors (RF) at the CMR exam date. CV risk factors were defined as hypertension, diabetes, obesity, dyslipidemia, and smoking (former and current) at the time of the CMR exam date. Standard definitions were used for hypertension (on antihypertensive medicine, or with blood pressure ≥ 140/90 mmHg); diabetes (on anti-diabetes medicine/insulin); obesity (body mass index (BMI) >30); and dyslipidemia (total cholesterol ≥ 240, triglycerides ≥ 200 mg/dl, or HDL < 35 mg/dl for males or HDL < 40 mg/dl for females, LDL ≥ 160mg/dl or those taking statins). LV hypertrophy and low LVEF < 52 % (man) and < 54 % (woman) at the time of exam date were also excluded criteria for the NRF group.

### Statistical Analysis

Continuous variables are present as mean ± SD and compared using Student t-test. Categorical variables are present as absolute values (percentage) and compared using chi-square statistics. Specific Age, gender, and race/ethnicity categories reference values were obtained for the entire study group, NRF, and RF groups. Also, multivariate linear regression models adjusted for demographic characteristics were performed to evaluate differences in LA indices by age, gender, and race/ethnicity and CV risk factors components. All analyses were conducted using STATA 14.2 version for Windows (StataCorp LP, College Station, TX). All tests were two-tailed and considered statistically significant when p-value ≤ 0.05.

## Results

### Clinical and Demographic Characteristics of the study participants

The characteristics of the study participants are given in Table 1. The mean age was 68.4 ± 9.1 years, 46.1 % were men, 41.7 % were white, 54 % had systemic hypertension, 16 % had diabetes mellitus, and 53 % were current smokers. 228 (about 9 %) of the total participants were characterized as the NRF population. NRF population was younger (64.7 ± 8.1 vs. 68.7 ± 9.1years) and included a larger proportion of Chinese-Americans (27 vs. 12 %) but a smaller proportion of African-Americans (12 vs. 26 %) and Hispanics (18 vs. 20 %) compared with the RF group. The proportion of participants in the NRF group that had normal BMI was higher than that in the RF group, where a greater proportion was overweight (24.3 vs. 28.3 $kg/m^2$). The NRF group also had lower systolic (110.7 ± 13.5 vs. 123.5 ± 20mmHg) and diastolic (65.9 ± 8.5 vs. 68.6 ± 9.8mmHg) blood pressure, lower coronary calcium scores (67.5 ± 169.9 vs. 213.7 ± 459.6 HU), lower triglyceride levels (88.5 ± 34.7 vs. 112 ±61.6 mg/dL), higher HDL levels (61.1 ± 16.1 vs. 55.7 ± 17.1 mg/dL), and better renal function (85.4 ± 18.1 vs. 80 ± 20.1 $mL/min/1.73m^2$) when compared to the RF participants.

### LA structure and functions differences between NRF and RF study subgroups

As shown in Table 2, in the overall study cohort participants, the mean ± SD for $LAVi_{max}$, $LAVi_{min}$, $LAVi_{preA}$, $S_{max}$, $SR_{max}$, $SR_e$, and $SR_a$ were 34.5 ± 11 mL/$m^2$, 15.7 ± 7.7 cmL/$m^2$, 26.5 ± 9.4mL/$m^2$, 32.6 ± 14.2 %, 1.5 ± 0.9 $sec^{-1}$, −1.2 ± 0.7 $sec^{-1}$, and −2.0 ± 1.0$sec^{-1}$, respectively.

There were statistically significant differences in LA structure and function parameters between NRF and RF groups. The NRF group demonstrated smaller LA volumes: $LAVi_{min}$ (14.2 ± 8.2 vs. 15.9 ± 7.6 mL/$m^2$) and $LAVi_{preA}$ (24.3 ± 10 vs. 26.7 ± 9.3 mL/$m^2$); higher LA emptying fractions: LAtEF (59.5 ± 10.5 vs. 55.6 ± 10.9 %) and LApEF (28.2 ± 8.7 vs 23.3 ± 7.6%); higher LA longitudinal strain: $S_{max}$ (37.5 ± 16.2 vs. 32.0 ± 13.9 %) and $S_{prea}$ (19.2 ± 9.1 vs. 17.7 ± 8.6 %); and higher absolute strain rates: $SR_{max}$ (1.6 ± 0.8 vs. 1.4 ± 0.9 $sec^{-1}$) and $SR_e$: (−1.6 ± 0.9 vs. −1.2 ± 0.6 $sec^{-1}$) as compared to the NRF group.

### LA Structure and Function Parameter Stratified by age, gender and ethnicity

Compared with older individuals (> 65 years old), younger participants had lower LA volumes ($LAVi_{max}$: 33.8 ± 10.1 vs. 35.2 ± 11.5 mL/$m^2$, p=.007; $LAVi_{min}$: 14.5 ± 6.4 vs. 16.6 ± 8.3 mL/$m^2$, p<.001; $LAVi_{preA}$: 24.8 ± 8.2 vs. 27.6 ± 9.3 mL/$m^2$, p<.001) and higher LA functional parameters (LAtEF: 58.3 ± 10 vs. 54.4 ± 14.3 %, p<.001; LApEF: 26.9 ± 7.6 vs. 21.8 ± 7.6 %, p<.001; $S_{max}$: 34.6 ± 13.8 vs. 31.2 ± 14.3 %, p<.001; $SR_{max}$: 1.5 ± 0.7 vs. 1.4 ± 1 $sec^{-1}$, p=.001; $SR_e$: −1.4 ± 0.7 vs. −1 ± 0.6 $sec^{-1}$, p<.001). (Table 3).

Compared with men, women had higher LA functional parameters (LAtEF: 57.3 ± 11 vs 54.4 ± 0.6 %, p<.001; LApEF: 25.3 ± 8.2 vs. 22 ± 7.4 %, p<.001; LAaEF: 43.2 ± 11.7 vs. 41.9 ± 11 %, p<.001; $S_{max}$: 34.6 ± 14.6 vs. 30.2 ± 13.4 %, p<.001; $SR_{max}$: 1.5 ± 0.8 vs. 1.4 ± 0.3 $sec^{-1}$, p=.004; $SR_e$: −1.3 ± 0.7 vs. −1.1 ± 0.6 $sec^{-1}$, p<.001), although men had slightly smaller indexed LA maximum volume ($LAV_{imax}$: 33.9 ± 11.1 vs 36.1 ± 10.8 mL/$m^2$, p=.006). (Table 3).

In the linear regression model adjusted for age, gender, and race/ethnicity, compared with Whites, Chinese-Americans participants were associated with lower LA phasic volumes ($LAV_{imax}$: diff.= −2.4 mL/$m^2$; LAVimin: diff.= −3.4mL/$m^2$, LAVipreA: diff= 3.2 mL/$m^2$, p<.001) and higher LA function (LAtEF: diff.= 7.6 %; LApEF: diff.= 6.9 %; LAaEF: diff.=4.6 %; $S_{max}$: diff.=11.6 %; SR : diff.= 0.5 $sec^{-1}$ max; $SR_e$: diff.= −0.4 $sec^{-1}$; $SR_a$: diff.= −0.5 $sec^{-1}$). (Supplemental data online S1- Table 1 – Results). Furthermore, compared with Whites, African-Americans participants were associated with higher LA minimum volume ($LAV_{imin}$: diff =1.2 mL/$m^2$, p=.001) and lower LA function (LAtEF: diff. = −3.1 %; LApEF: diff.= −3.2 %; LAaEF: diff.= −1.2 %; $S_{max}$: diff.= −2.3 %; $SR_e$: diff.= 0.1 $sec^{-1}$; $SR_a$: diff.= 0.2 $sec^{-1}$).

### Association of CV risk factors and LA structure/function

In multivariate regression analysis after adjusting for age, gender, and race/ethnicity, as shown in Table 4, BMI, smoking, systolic and diastolic blood pressure, LV mass index, diabetes, and hypertension were statistically associated with adverse LA remodeling. Every 10 kg/$m^2$ increase in BMI was associated with 2.9 % decrease in total, 3.1 % in passive, and

1.6 % in LA emptying fraction, as well as in 5 % decrease in LA longitudinal strain. Also, every 10 mmHg increase in systolic blood pressure was associated with approximately 0.5 $ml/m^2$ increase in LA phasic volumes and about 0.5 % reduction in LA emptying fractions. Furthermore, every 10 $g/m^2$ increase in LV mass index was associated with around a 2–3 ml increase in LA phasic volumes, 0.8–1.1 % decrease in LA emptying fractions, and 1.5 % decrease in the longitudinal strain. Diabetes Mellitus was associated with 1.5–3.5 % decrease in the LA emptying fractions and 5 % reduction in LA longitudinal strain.

## Discussion

This study provides reference values of LA structure and function parameters from a healthy multi-ethnic community-based population aged 53–94 years evaluated by FT-MRI. Several LA function and structural parameters, stratified by age, gender, and race/ethnicity are reported, including LA phasic index volumes, LA emptying fractions, and LA longitudinal strain/strain rates. We also describe ranges and variability in the study subgroup free of CV disease and its risk factors at the time of the CMR exam.

Previous studies have focused on normal reference ranges of maximum LA volume and total LA emptying fraction (16, 17). Petersen et al. had documented LA maximum and minimum index volumes and total emptying fraction in Caucasians from the UK Biobank cohort (18). Zemrak et al. had reported determinants of maximum LA volume in relation to age, sex, and ethnicity using the MESA population (19). Also, normal values for morphologic and functional CMR parameters in adults and children have been published (20). However, unlike those prior investigations, our study extended this evaluation, providing reference ranges for LA longitudinal deformation parameters. These additional measurements allow a complete assessment of LA function (reservoir, passive, and active) and to be superior when predicting atrial fibrillation and cerebral ischemic events, and when categorizing LV diastolic dysfunction beyond the measurement of LA size alone (21, 22).

LA index volume obtained in this study was higher than previously reported values acquired by 2DE and 3DE (23–25). The discordance between echocardiographic and CMR volume measurements has been extensively documented and may partially be explained by the lower spatial resolution for detecting myocardial borders and the incomplete ability to visualize the entire LA chamber by the former method (17). However, the LA maximum volume index in this study population was at the upper normal reference values recommended by the current American Society of Echocardiography guideline (26).

The gold standard method to assess myocardial deformation is tagged CMR, which is not feasible to perform with available technology due to the LA thin wall. To date, a wide range of values of LA longitudinal strain and strain rates have been reported, depending on the imaging modality and vendor-specific post processing software utilized (27–30). Our study results provide reference values of LA longitudinal strain/strain rate parameters in the middle age-elderly population with and without CV risk factors, evaluated by FT-CMR.

NRF participants have smaller LA phasic volumes, higher LA emptying fraction, and higher absolute longitudinal strain / strain rates compared to the RF subgroup. These results are

similar to preceding studies that showed an association of traditional CV risk factors and CV disease with LA adverse remodeling (31–34). Also, in the NRF subgroup, LA maximum index volume was similar in both genders, which was consistent with previous CMR and echocardiographic studies (35). However, both minimum and pre-atrial systolic LA volumes were slightly lower in women than in men, which is consistent with previous investigations (36).

LA phasic functional parameters have been associated with the presence of myocardial scars, incident heart failure, and risk of ischemic stroke (37). Investigators have shown an association of LA maximum strain and the invasive measurement of LV end-diastolic pressure (38, 39). Additionally, previous studies indicated that phasic atrial function, including strain and strain rate, could provide potential prognostic value in patients with CV disease (40, 41). Our study results are in line with those previous investigations and provide additional information about differences in LA function by gender and race/ethnicity. On average, LA functional parameters were significantly higher in women compared to men, and in the younger age group compared to the older age group, in both genders. Similar to previous studies, Chinese Americans had better LA function compared with other ethnicities (42). This difference was more robust in the NRF population.

## Limitations

There are several limitations to our study. Few participants with poor LA imaging quality, in which it was challenging to accurately and reproducibly assess LA structure and function by FT-CMR, were excluded from our analysis. Also, the lower temporal resolution obtained in the CMR studies could induce an underestimation of the strain and strain rate values when compared to the two-dimension speckle tracking echocardiography evaluation. Moreover, the area-length method used to calculate the LA phasic volumes might undervalue the true LA volume depending on the alignment of the collect slice with the true orientation of the LA. In spite of the use of strict inclusion criteria to select the NRF, underlying subclinical CV disease in those participants could not be ruled out, leading to several biases in the LA structure and function comparison between NRF and RF groups. Additionally, the possibility of severe mitral valve insufficiency and stenosis could not be evaluated. Finally, direct comparison with other images modalities was not feasible.

## Conclusion

The present study provides reference ranges for LA phasic volumes, LA empty fractions, and LA longitudinal deformation parameters, categorized by the presence of CV risk factors, age groups, gender, and race/ethnicity categories, evaluated by FT-CMR. Given the emerging data supporting the role of LA longitudinal deformation in the risk assessment of the general population and also in patients without CV disease, references presented in this study could be helpful for comparison purposes.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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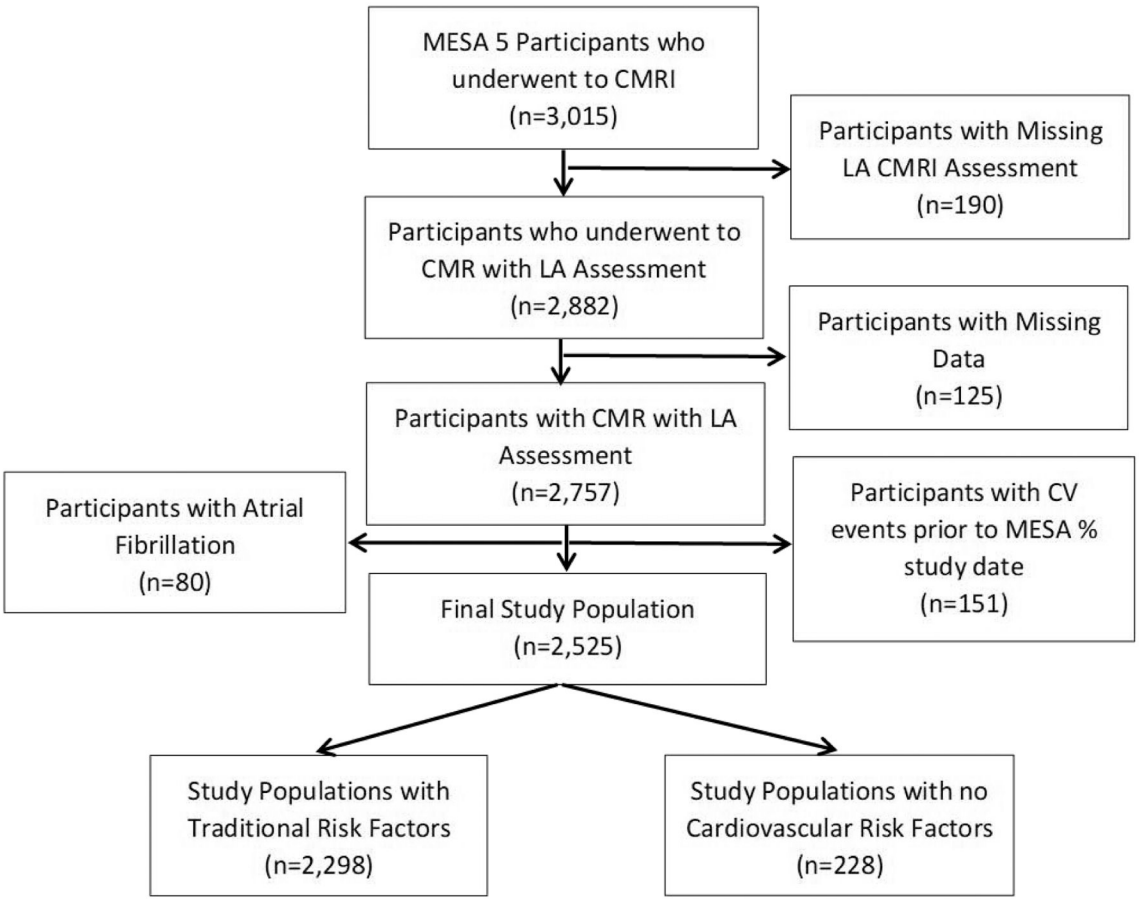


**Figure 1:**
Study enrollment flow chart.

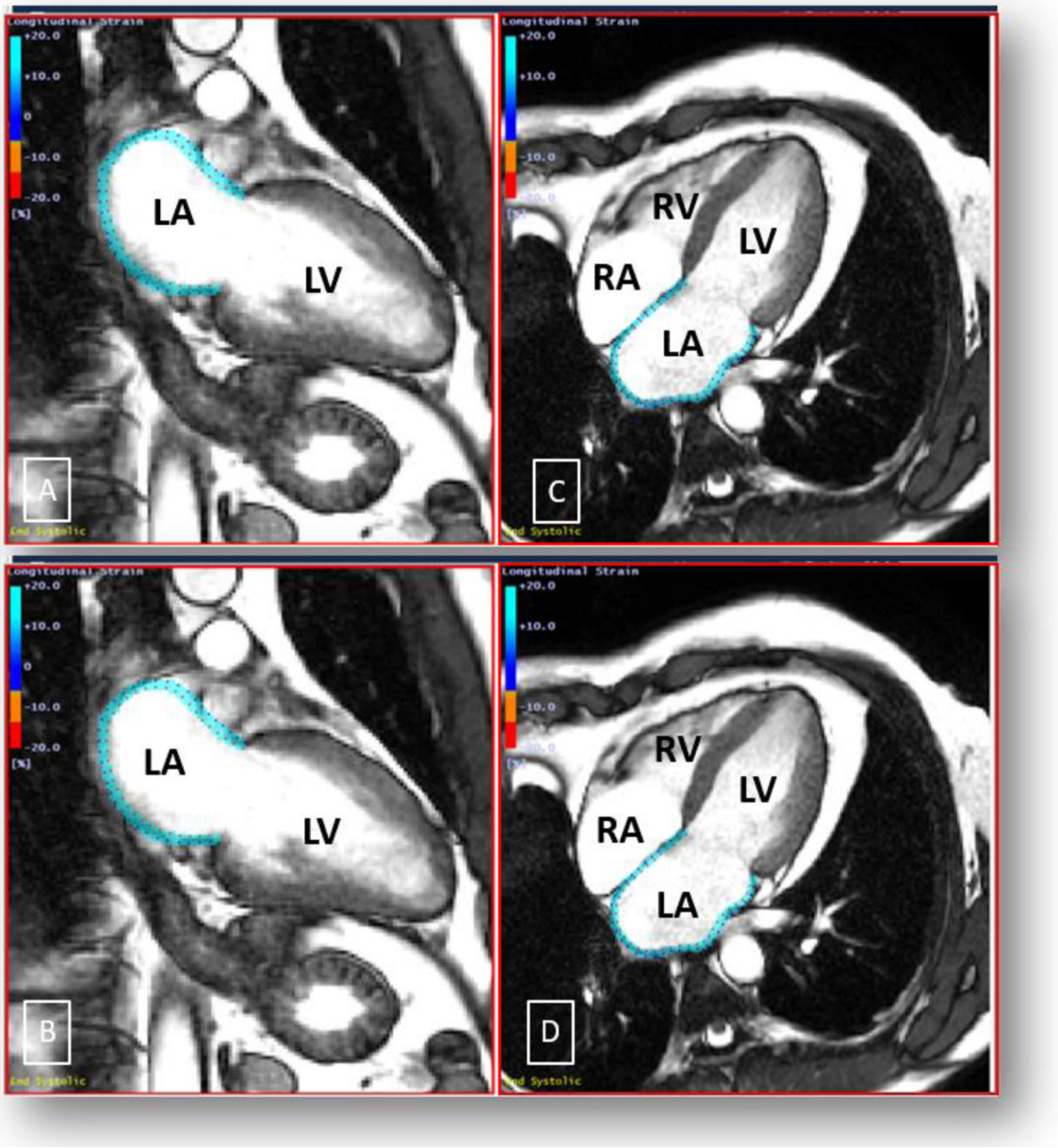


**Figure 2.**
Multimodality feature tracking cardiac magnetic resonance imaging: (A) End-systolic 2-chamber view, (B) End-diastolic 2-chamber view, (C) End-systolic 4-chamber view, and (D) End-diastolic 4-chamber view.

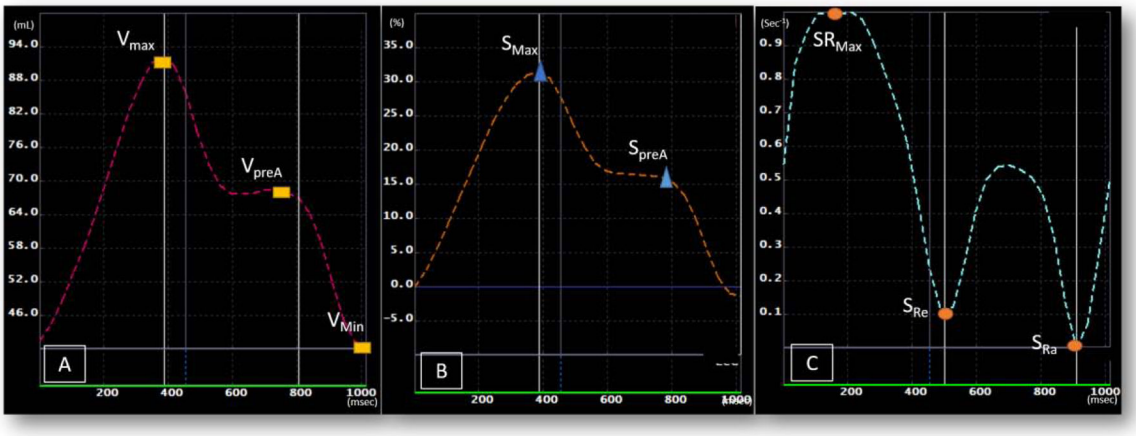


**Figure 3.**

Featuring tracking cardiac MRI volume analysis (A, red line), strain analysis (B, orange line), and strain rate analysis (C, blue line). $V_{max}$: maximum LA volume; $V_{preA}$: pre-atrial contraction LA volume; $V_{min}$: minimum LA volume; $S_{max}$: maximum LA longitudinal strain; $S_{min}$: minimum LA longitudinal strain; $S_{preA}$: pre-atrial contraction LA strain; $SR_{max}$: maximum systolic LA strain rates peak; $SR_e$: early diastole strain rate peak; and $SR_a$: late diastole strain rate peak.

**Table 1.**

Clinical characteristics of study participants by the presence of cardiovascular risk factors at the visit five follow-up examination (MESA 5).

| Covariates[a] | Study Cohort (n = 2,526) | Cohort with No CV Risk Factors (n = 228) | Cohort with CV Risk Factors (n = 2,298) | p-value[b] |
|---|---|---|---|---|
| Age (years) | 68.4 ± 9.0 | 64.7 ±8.1 | 68.7 ±9.1 | **<0.001** |
| Men, n (%) | 1165 (46) | 91 (40) | 1074 (47) | 0.05 |
| White, n (%) | 1054 (42) | 98 (43) | 956 (42) | **<0.001** |
| African-American, n (%) | 615 (24) | 28 (12) | 587 (26) | **<0.001** |
| Hispanic, n (%) | 518 (21) | 38 (18) | 480 (20) | **<0.001** |
| Chinese-American, n (%) | 339 (13) | 65 (27) | 274 (12) | **<0.001** |
| Body mass index (kg/m$^2$) | 28.0 ±5.2 | 24.3 ±3.1 | 28.3 ±5.2 | **<0.001** |
| Hypertension, n (%) | 1370 (54) | | 1370 (60) | |
| Diabetes, n (%) | 396 (16) | | 396 (17) | |
| Current or former smoker, n (%) | 1331 (53) | | 1331 (58) | |
| Former smoker, n (%)XXCurrent smoker, n (%) | 955 (42.16) | | 1140 (50) | |
| | 175 (7.73) | | 191 (8) | |
| Previous history of myocardial infarction, n (%) | 2(0.2) | | 5(0.2) | |
| Previous history of heart failure, n (%) | 4(0.2) | | 4(0.2) | |
| Previous history of revascularization, n (%) | 19 (0.8) | | 19 (0.8) | |
| Previous history of stroke, n (%) | 15 (0.6) | | 15 (0.6) | |
| Total cholesterol (mg/dL) | 186.5 ±35.9 | 193.6 ±26.0 | 185.4 ±36.7 | **<0.001** |
| High-density lipoprotein (mg/dL) | 56.2 ±17.1 | 61.1 ±16.1 | 55.7 ±17.1 | **<0.001** |
| Triglyceride (mg/dL) | 109.9 ± 60.0 | 88.5 ± 34.7 | 112.0 ±61.6 | **<0.001** |
| Agatston Coronary Calcium Score | 200.7 ± 443.5 | 67.5 ± 169.9 | 213.7 ±459.6 | **<0.001** |
| Heart Rate (bpm) | 60.8 ±9.0 | 60.6 ± 8.8 | 60.8 ±9.0 | **0.94** |
| Systolic blood pressure (mmHg) | 122.4 ±19.7 | 110.7 ±13.5 | 123.5 ± 20.0 | **<0.001** |
| Diastolic blood pressure (mmHg) | 68.4 ±9.7 | 65.9 ±8.5 | 68.6 ±9.8 | **0.001** |
| Estimated glomerular filtration rate (ml/min/ 1.73m$^2$) | 81.1 ±20.0 | 85.4 ±18.1 | 80.7 ±20.1 | **0.001** |
| Statins, n (%) | 843 (33) | | 843 (37) | |
| Beta-blockers, n (%) | 358 (14) | | 358 (16) | |
| Ca-channel blockers, n (%) | 395 (16) | | 395 (17) | |

[a] Data are expressed as mean ± SD or as number (percentage).

[b] P-values were calculated using Student t-test and chi-square test for continuous and categorical variables, respectively

**Table 2.**

Left atrial structure and parameters of study participants stratified by the presence or absence of cardiovascular risk factors at the visit five follow-up examination (MESA 5).

| **Covariates**[a,c] | **Study Cohort (n = 2,526)** | **Cohort with No CV Risk Factors (n = 228)** | **Cohort with CV Risk Factors (n = 2,298)** | **p-value**[b] |
|---|---|---|---|---|
| $LAVi_{max}(mL/m^2)$ | 34.5 ± 11 | 33.5 ±11.7 | 34.7 ± 10.9 | 0.06 |
| $LAVi_{min}$ $(mL/m^2)$ | 15.7 ±7.7 | 14.2 ±8.2 | 15.9 ±7.6 | **<0.001** |
| $LAVi_{preA}$ (mL/m') | 26.5 ±9.4 | 24.3 ± 10 | 26.7 ±9.3 | **<0.001** |
| LAtEF (%) | 56.1 ±11 | 59.5 ±10.5 | 55.6 ±10.9 | **<0.001** |
| LApEF (%) | 23.8 ±8 | 28.2 ±8.7 | 23.3 ±7.6 | **<0.001** |
| LAaEF (%) | 42.6 ±11.4 | 44 ±11.3 | 42.5 ±11.4 | 0.09 |
| Smax (%) | 32.6 ± 14.2 | 37.5 ±16.2 | 32 ±13.9 | **<0.001** |
| $S_{prea}$ (%) | 17.8 ±8.6 | 19.2 ±9.1 | 17.7 ±8.6 | 0.008 |
| $SR_{max}$ $(sec^{-1})$ | 1.5 ±0.9 | 1.6 ±0.8 | 1.4 ±0.9 | **<0.001** |
| $SR_e$ $(sec^{-1})$ | −1.2 ±0.7 | −1.6 ±0.9 | −1.2 ±0.6 | **<0.001** |
| $SR_a$ $(sec^{-1})$ | −2.1 ±1.0 | −2.1 ±1.0 | −2.1 ± 1.0 | 0.06 |

[a] Data are expressed as mean ± SD.

[b] P-value was calculated by Student t-test.

[c] Abbreviations. $LAVi_{max}$ = left atrial maximum volume indexed to body surface area, $LAVi_{min}$ = left atrial minimum volume indexed to body surface area, $LAVi_{preA}$ = left atrial pre-atrial contraction volume indexed to body surface area, LAtEF = left atrial total emptying function, LAaEF = left atrial active empting fraction, LApEF = left atrial passive empting fraction, $S_{max}$ = left atrial maximum strain, $S_{prea}$ = left atrial strain at atrial contraction, $SR_{max}$ = left atrial strain rate peak at end systole, $SR_e$ = left atrial first diastolic strain rate peak, $SR_a$ = left atrial late diastolic peak measured at atrial contraction.

**Table 3.**

Left atrial structure and function parameters of the study participants stratified by age and gender at the visit five follow-up examination (MESA 5)[a].

| Covariates | Women (n = 1,361) | | Men (n = 1,165) | |
|---|---|---|---|---|
| | 45–65 years (n = 529) | ≥ 65 years (n = 832) | 45–65 years (n=472) | ≥ 65 years (n = 693) |
| $LAVi_{max}(mL/m^2)$ | 34.4 ± 9.5 | 35.5±11.6 | 33.1 ±10.6 | 34.4 ±11.4 |
| $LAVi_{min}$ $(mL/m^2)$ | 14.3 ± 6.3 | 16.4 ±8.6 | 14.7 ±6.5 | 16.717.9 |
| $LAVi_{preA}$ $(mL/m^2)$ | 24.7 ±7.9 | 27.5 ±10 | 25.0 ±8.5 | 27.619.9 |
| LAtEF (%) | 59.7 ± 10 | 55.8±11.3 | 56.7 ±9.8 | 52.8110.7 |
| LApEF(%) | 28.8 ±7.8 | 23.1 ±7.7 | 24.6 ±6.9 | 20.117.1 |
| LAaEF(%) | 43.8 ±11 | 42.9 ± 12 | 42.7 ± 10.9 | 41.3 ± 10.9 |
| $S_{max}$ (%) | 36.9 ±13.8 | 33.1 ±14.8 | 32 ±13.2 | 29 ± 13.4 |
| $S_{prea}$ (%) | 18.5 ±8.1 | 18.7 ±9.1 | 17.1 ±8.6 | 16.9 ±8.3 |
| $SR_{max}$ $(sec^{-1})$ | 1.6 ±0.7 | 1.5 ±0.8 | 1.5 ±0.8 | 1.4 ±1.1 |
| $SR_e$ $(sec^{-1})$ | −1.6 ±0.7 | −1.1 ±0.6 | −1.3 ±0.6 | −0.9 ±0.5 |
| $SR_a$ $(sec^{-1})$ | −2.2 ±1 | −2.1 ±1 | −2.1 ±1.1 | −1.9 ±1 |

[a]Data are expressed as mean ± SD.

[b]Abbreviations. LAVimax = left atrial maximum volume indexed to body surface area, LAVimin = left atrial minimum volume indexed to body surface area, LAVipreA = left atrial pre-atrial contraction volume indexed to body surface area, LAtEF = left atrial total emptying function, LAaEF = left atrial active empting fraction, LApEF = left atrial passive empting fraction, Smax = left atrial maximum strain, Sprea = left atrial strain at atrial contraction, SRmax = left atrial strain rate peak at end systole, SRe = left atrial first diastolic strain rate peak, SRa = left atrial late diastolic peak measured at atrial contraction.

**Table 4.**

Association between cardiovascular risk factors and LA structure /function parameters at the visit five follow-up examination (MESA 5)[a]

| **Covariates**[b] | **$LAVi_{max}$ ($mL/m^2$)** | **$LAVi_{min}$ ($mL/m^2$)** | **$LAVi_{preA}$ ($mL/m^2$)** | **LAtEF (%)** | **LApEF (%)** | **LAaEF (%)** | **$S_{max}$ (%)** | **$SR_{max}$ ($sec^{-1}$)** | **$SR_e$ ($sec^{-1}$)** | **$SR_a$ ($sec^{-1}$)** |
|---|---|---|---|---|---|---|---|---|---|---|
| BMI(per 10 $kg/m^2$) | 0.2 | **0.9**¥ | **1.1**¥ | **−2.9**¥ | **−3.1**¥ | **−1.6**¥ | **−5.1**¥ | **−0.2**¥ | **0.3**¥ | **0.1**¥ |
| SBP(per 10mmHg) | **0.5**¥ | **0.4**¥ | **0.5**¥ | **−0.5**¥ | **−0.3**¥ | **−0.4**¥ | **−0.3**¥ | −0.01 | **0.03**¥ | **0.01**¥ |
| Hypertension | **1.0**¥ | **1.0**¥ | **1.2**¥ | **−1.5**¥ | **−1.4**¥ | **−0.9**¥ | **−1.5**¥ | **−0.1**¥ | **0.1**¥ | 0.001 |
| LVMi (per 10$g/m^2$) | **3.0**¥ | **2.1**¥ | **2.6**¥ | **−1.1**¥ | **−1.0**¥ | **−0.8**¥ | **−1.5**¥ | **−0.08**¥ | **0.09**¥ | **0.1**¥ |
| Current smoker | −0.2 | 0.2 | 0.1 | **−1.1**¥ | **−1.0**¥ | **−0.63**¥ | **−1.7**¥ | −0.03 | **0.08**¥ | 0.02 |
| Diabetes | −1.1 | −0.3 | −0.4 | −0.6 | **−1.2**¥ | 0.1 | **−1.9**¥ | −0.04 | **0.1**¥ | −0.1 |

[a]Multivariable linear regression analysis, adjusted for age, gender, and race/ethnicity.

[b]Abbreviations. Abbreviations. LAVimax = left atrial maximum volume indexed to body surface area, LAVimin = left atrial minimum volume indexed to body surface area, LAVipreA = left atrial pre-atrial contraction volume indexed to body surface area, LAtEF = left atrial total emptying function, LAaEF = left atrial active empting fraction, LApEF = left atrial passive empting fraction, Smax = left atrial maximum strain, Sprea = left atrial strain at atrial contraction, SRmax = left atrial strain rate peak at end systole, SRe = left atrial first diastolic strain rate peak, SRa = left atrial late diastolic peak measured at atrial contraction.

¥$p < 0.05$.