

Changes of Cardiac Magnetic Resonance T1 and ECV Values in Healthy Adults of Different Gender and Age

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Abstract

Background

The correlation between T1 and ECV value and myocardial fibrosis has been confirmed. In healthy adult, many disease may change T1 and ECV value. The purpose of this reseach is to clarify the T1 mapping and extracellular volume (ECV) value of healthy adults in 3 Tesla (T) magnetic resonance imaging (MRI), and to study the relationship between the values with age and gender.

Methods

We recruited 87 healthy adult subjects (mean age 38 ± 11 years; 61% were females) for cardiac magnetic resonance examination at 3T MRI. The left ventricular function parameters were obtained from functional imaging. T1 mapping was performed using an improved Look-Locker reversal recovery sequence after motion correction.

Results

Under 3T field strength, T1 value of the myocardium of healthy adults was $1,261 \pm 52$, and the ECV value was $28.3\% \pm 2.9\%$. T1 value and ECV values of female myocardium were higher than those of males ($1,274 \pm 56$ vs. $1,241 \pm 40$, $P = 0.003$; $29.6\% \pm 2.6\%$ vs. $26.2\% \pm 2.1\%$, $P < 0.001$). Only gender (Beta = 0.311, $P = 0.003$) was independently related to the native T1 mapping of left ventricular myocardium, while gender (Beta = 0.572, $P < 0.001$) and age (Beta = 0.501, $P = 0.003$) were related to the ECV value of left ventricular myocardium. T1 value ($P = 0.002$) and ECV value ($P = 0.013$) increased significantly from the base to the apex. There were significant differences in the T1 and ECV value between each segment ($P < 0.001$) in the base of the left ventricle. Significant differences were observed between the middle segments of T1 value ($P = 0.001$) but not between the middle of the ECV value of each segment ($P = 0.068$). Lastly, there was no statistical difference between each segment in the apical of the T1 ($P = 0.756$) and ECV value ($P = 0.344$).

Conclusions

Under 3T MRI, the T1 value of the myocardium of healthy adults was $1,261 \pm 52$, and the ECV value was $28.3\% \pm 2.9\%$. T1 and ECV values of females were significantly higher than those of males. The ECV values of males increased with age, while T1 value in males and T1 and ECV values in females had no significant relationship with age.

Background

The number, size, and myocardial interstitium of females remain relatively constant throughout life. However, the size of cardiomyocytes of males generally increases with age through cardiomyocyte fusion, resulting in a marked reduction in the number of muscle cells^[1]. Loss of cardiomyocytes leads to proliferation of cardiac fibroblasts^[2] and interstitial fibers^[3]. And this interstitial fibrosis is generally

diffuse^[4]. These findings are mainly obtained through autopsy or animal experiments, and non-invasive imaging examinations also show significant advantages.

As a non-invasive examination, cardiac magnetic resonance (CMR) has received increasing attention in recent years. Late gadolinium enhancement (LGE) relies on a visual and semi-quantitative measurement of relative myocardial differences that usually present the characteristic pattern of LGE distribution. LGE can diagnose localized myocardial changes well^[4], but it is not suitable for detecting diffuse myocardial changes^[6]. There are many imaging methods for quantitative detecting diffuse myocardial changes. T2 mapping mainly reflects the water content of myocardial tissue; therefore, myocardial edema is the primary pathological basis for differences in T2 mapping^[7]. T2* mapping can diagnose and monitor iron overload in the heart and is also used to diagnose intramyocardial hemorrhage^[8]. T1 mapping has been suggested to detect myocardial fibrosis, edema, amyloid, iron overload, and lipid accumulation^[9], reflecting the changes in myocardial cells and interstitium. Therefore, T1 mapping has more applications. Extracellular volume (ECV) can be quantified by measuring T1 mapping before and after extracellular contrast agents based on hematocrit, providing an absolute physiological value, which is more accurate in assessing myocardial interstitial changes^[10]. The correlation between T1^[11] and ECV value^[12] and myocardial fibrosis has been confirmed. The measurement of ECV is mainly based on two assumptions: one is that the T1 relaxation time is directly proportional to the change in the concentration of the contrast agent; the other is that the contrast agent is distributed proportionally in the extracellular space^[13]. At present, the quantitative technology of T1 mapping and ECV has been used in areas including the brain, heart, liver, pancreas, kidney, tendon, cartilage, and spinal cord.

Many heart diseases can cause increases in T1 and ECV value, including but not limited to acute chest pain syndrome, acute myocarditis, acute and chronic myocardial infarction, myocardial amyloidosis, hypertrophic cardiomyopathy, and dilated cardiomyopathy^[14]. At the same time, iron^[15] and lipid^[16] deposition diseases cause T1 value to reduce. Therefore, it is imperative to define the expected normal range of T1 and ECV values. However, as far as previous studies are concerned, the expected normal values of T1 and ECV values have not yet been fully determined. There are still controversies regarding the relationship between T1 and ECV values with age and gender. Previous studies were mostly conducted on 1.5T magnetic resonance, 3T data are limited, and most of the studies have relatively small sample sizes. Therefore, this study has two primary purposes: (1) to clarify the T1 and ECV values of normal healthy adults on 3T magnetic resonance, (2) to study the relationship between T1 and ECV values of healthy adults relative to age and gender.

Methods

The research protocol has been approved by the Ethics Committee of Guangdong Second Provincial General Hospital, and all methods were performed in accordance with the 'Sex and Gender Equity in Research – SAGER – guidelines'. All participants provided written informed consent.

Object

Ninety healthy subjects participated in the study. Among these, one male volunteer had left ventricular myocardial thickening, and one female volunteer had donated blood the day before the examination. One female volunteer had claustrophobia and did not complete the examination. The final data were collected from 87 of the 90 healthy volunteers. A low-dose chest computed tomography (CT) examination was performed 24 hours before the CMR examination to rule out chest lesions and coronary artery calcification, and blood routine examinations were also performed. The inclusion criteria included no history of cardiovascular disease, hypertension, diabetes, or chronic lung disease, but normal cardiac morphology, function, and tissue characteristics (no LGE). The exclusion criteria for all subjects included hypersensitivity to contrast agents and contraindications to CMR, such as severe claustrophobia and a history of implantation of pacemakers or other metal objects in the body.

Image acquisition

Each participant underwent a magnetic resonance imaging (MRI) examination in the 3.0-T MR imager (Ingenia; Philips, Best, The Netherlands) of the Medical Imaging Department of Guangdong Second Provincial General Hospital, using the DS Anterior coil. Retrospective electrocardiogram (ECG) gating was used to acquire images during breath-holding. Steady-state free precession film images were acquired in continuous, short-axis views (from the base to the apex of the left ventricular (LV)) and three long-axis views (two-chamber, three-chamber, and four-chamber). The imaging parameters were as follows: repetition time (TR): 3.0 ms; echo time (TE): 1.48 ms; flip angle (FA): 45°; field of view (FOV): 353 x 353 x 89 mm³; matrix size: 176 x 167, Voxel size: 2 x 2 x 8 mm³; slice thickness was 6 mm, no gap. Before the contrast agent was injected, the native T1 measurement was obtained through the single breath-hold Modified Look-Locker Inversion Recovery (MOLLI) sequence. Measurements were made on the basal, middle, and apical slices of the short axis by ECG gating. The parameters for MOLLI were as follows: TR: 2.4 ms; TE: 1.08 ms; FA: 20°; FOV: 300 x 300 x 42 mm³; Matrix size: 152 x 149; Voxel: 2 x 2 x 10 mm³. After injection of the contrast agent Gadodiamide Injection (OMNISCAN, GE Healthcare Ireland Limited, Shanghai, China) 15 minutes later, the T1 measurement was repeated in the same short-axis section (MOLLI protocol: 5 (3) 3 (3) 3).

Image and data post-processing

The post-processing of CMR was performed by two diagnostic doctors with more than 2 years of experience in CMR image analysis using the special post-processing software cvi42 (Circle Cardiovascular Imaging Inc., Calgary, Canada). The left ventricle size, including the end-diastolic volume and the end-systolic volume, was measured by automatically delineating the end-diastolic and end-systolic endocardial and epicardial boundaries on the continuous short-axis movie images, and was then correlated with the body surface area to measure the left ventricular mass, which includes left ventricular myocardium and papillary muscle. The T1 value calculation was based on MOLLI images in the three LV short-axis slices. The contours of the endocardium and epicardium were animated onto the T1 image before and after the injection of the contrast agent. After fitting the T1 curve, the average myocardial T1

value was obtained. By locating the region of interest in the blood pool in the left ventricular cavity (while avoiding the papillary muscle) in the T1 image before and after the contrast agent injection, the blood T1 value was obtained. Finally, the ECV value was calculated according to the individual's hematocrit. Hematocrit can be obtained through a blood routine. Figure 1 shows the T1 mapping and ECV map before and after the contrast agent injection. We performed segment analysis based on the American Heart Association (AHA) 16-segment model. The final calculation of ECV was performed based on the following formula:

$$ECV = (1 - \text{hematocrit}) * \frac{\left(\frac{1}{T1 \text{ myocardium post contrast}} \right) - \left(\frac{1}{T1 \text{ myocardium pre contrast}} \right)}{\left(\frac{1}{T1 \text{ blood post contrast}} \right) - \left(\frac{1}{T1 \text{ blood pre contrast}} \right)}$$

Data analysis

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA, version 25.0). The normality of the distribution was tested with Kolmogorov–Smirnov statistics. An appropriate *t*-test and a one-way analysis of variance (using Bonferroni post-hoc test) were performed to compare two or more normally distributed variables. The correlation between each parameter and T1 and ECV value was determined using linear regression analysis. Images considered to be of sufficient quality and free of artifacts were deemed diagnostic and were included to analyze for native T1 and ECV values. Categorical data were expressed as percentages, continuous variables were expressed as mean ± SD or median (interquartile range), and *p*-value < 0.05 was considered statistically significant.

Results

A total of 1,392 fragments from 87 subjects were subjected to T1 and ECV value analysis.

Basic Features

Table 1.1 shows the clinical data of 87 healthy volunteers included in this study. In the clinical data, the hematocrit of males was higher than that of females (0.44 ± 0.03 vs. 0.39 ± 0.03, *P* < 0.001). There were no significant differences in age (*P* = 0.185), systolic blood pressure (*P* = 0.188), diastolic blood pressure (*P* = 0.256), body mass index (*P* = 0.119), and heart rate (*P* = 0.254) between males and females.

Table 1.1
Basic Features of a cohort of healthy adult Chinese volunteers

	Total(n = 87)	Male(n = 34)	Female(n = 53)	P-value
Age(year)	38 ± 12	36 ± 11	40 ± 12	0.185
BMI(kg/m ²)	22 ± 3	22 ± 4	21 ± 2	0.119
SBP(mmHg)	114 ± 14	117 ± 12	113 ± 14	0.188
DBP(mmHg)	69 ± 9	70 ± 7	68 ± 10	0.256
HR(bpm)	75 ± 10	73 ± 10	76 ± 10	0.254
HCT(L/L)	0.41 ± 0.04	0.44 ± 0.03	0.39 ± 0.03	< 0.001
T1(ms)	1261 ± 52	1241 ± 40	1274 ± 56	0.003
ECV(%)	28.3 ± 2.9	26.2 ± 2.1	29.6 ± 2.6	< 0.001
BMI: body mass index; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; HCT: hematocrit; continuous data are expressed as mean ± SD. P-value is male vs. Female				

The T1 and ECV values of healthy adults were 1,261 ± 52 and 28.3% ± 2.9%, respectively. The T1 and ECV values of female myocardium were higher than those of males (1,274 ± 56 vs. 1,241 ± 40, P = 0.003; 29.6% ± 2.6% vs. 26.2% ± 2.1%, P < 0.001)(Fig. 2).

Correlation analysis

We divided 87 healthy adults into four groups by the age of every 10 years. We used linear regression to analyze the relationship between clinical data, cardiac function, T1 values, ECV values, and age, and analyzed the influencing factors of T1 and ECV value. For the influencing factors of ECV value, see Tables 2.1 and 2.2 for details.

Table 2.1
Correlation between age and various parameters

	20–30 (25 ± 2)	30–40 (33 ± 3)	40–50 (46 ± 2)	50–60 (54 ± 3)	P- value	Beta
HCT(L/L)	0.40 ± 0.03	0.4 ± 0.04	0.4 ± 0.04	0.4 ± 0.03	0.641	-0.051
LVEDV(mL)	132 ± 26	123 ± 26	115 ± 20	115 ± 11	0.004	-0.305
LVESV(mL)	49 ± 11	43 ± 9	41 ± 10	40 ± 8	0.002	-0.333
LVSV(mL)	83 ± 20	80 ± 18	74 ± 15	75 ± 10	0.044	-0.217
LVEF(%)	62 ± 5	64 ± 4	64 ± 6	65 ± 6	0.147	0.157
LVM(g)	89 ± 27	85 ± 21	77 ± 15	76 ± 13	0.019	-0.250
LVEDV: left ventricular end diastolic volume; LVESV: left ventricular end systolic volume; LVSV: left ventricular stroke volume; LVEF: left ventricular ejection fraction; LVM: left ventricular mass (including left ventricular myocardium and papillary muscle); continuous The data is expressed as the mean ± SD; while we express the non-normally distributed data as the median and interquartile range.						

Table 2.2
Factors affecting T1 and ECV value

	T1(ms)		ECV(%)	
	P-value	Beta	P-value	Beta
BMI(kg/m ²)	0.425	-0.087	0.019	-0.250
HR(bpm)	0.001	0.337	0.003	0.316
HCT(L/L)	0.069	-0.196	< 0.001	-0.413
LVSV(mL)	0.029	-0.235	< 0.001	-0.434
LVM(g)	0.062	-0.201	< 0.001	-0.469

Through linear regression analysis, we found that in the cardiac function of volunteers, the left ventricular end-diastolic volume (P = 0.004, Beta = -0.305), end-systolic volume (P = 0.002, Beta = -0.333), stroke volume (P = 0.044, Beta = -0.217), left ventricular mass (P = 0.019, Beta = -0.250) all decreased with age. Left ventricular ejection fraction (P = 0.147) and hematocrit (P = 0.641) showed no correlation with age (P = 0.147) (Table 2.1).

There was a certain degree of correlation between T1 mapping and ECV values with age and gender. ECV values of males increased with age (P = 0.003, Beta = 0.501), while age and T1 values of males had no obvious correlation (P = 0.107, Beta = 0.281). T1 values (P = 0.852, Beta = 0.026) and ECV values (P =

0.753, Beta = -0.044) of females, and overall T1 values (P = 0.199, Beta = 0.139) and ECV values (P = 0.079, Beta = 0.189) had no obvious correlation with age (Fig. 3).

It can be seen from Table 2.2 that T1 and ECV values increased with the increase in heart rate (P = 0.001, Beta = 0.337; P = 0.003, Beta = 0.316), and decreased with the increase of stroke volume (P = 0.029, Beta = -0.235; P < 0.001, Beta = -0.434). ECV value decreased with increasing body mass index (P = 0.019, Beta = -0.250), hematocrit (P < 0.001, Beta = -0.413), and left ventricular mass (P < 0.001, Beta = -0.469), and those parameters have a strong relationship with T1 value.

The relationship between the layers of myocardial T1 and ECV value

We divided the heart into basal, middle, and apical and used linear regression to analyze the changes in T1 and ECV values at each layer. The specific analysis is shown in Table 3.1.

Table 3.1
T1 and ECV values at all slices

		basal	mid	apical	P-value	Beta
T1 (ms)	total	1247 ± 65	1259 ± 65	1286 ± 82	< 0.001	0.209
	male	1230 ± 53	1242 ± 53	1257 ± 69	< 0.001	0.179
	female	1258 ± 70	1270 ± 69	1305 ± 84	< 0.001	0.234
ECV(%)	total	27.6 ± 3.6	28.1 ± 3.4	29.6 ± 4.0	< 0.001	0.205
	male	25.7 ± 3.0	26.2 ± 2.7	27.3 ± 2.7	< 0.001	0.214
	female	28.8 ± 3.4	29.4 ± 3.2	31.1 ± 4.0	< 0.001	0.237

The linear regression analysis of T1 and ECV values of each layer showed that, from basal to apical, T1 and ECV values of males and females gradually increased (P < 0.001).

The relationship between the segments of myocardial T1 and ECV value

All segments of T1 and ECV values are displayed in the bull's eye diagram. According to the AHA 16 segment model (Fig. 4) and box plot analysis (Fig. 5), for the basal, there were significant differences in T1 and ECV value between each segment (all P < 0.001). There were also significant differences between the segments in the middle of T1 value (P = 0.001), but there was no statistical difference in the middle of ECV values between the segments (P = 0.068). T1 (P = 0.756) and ECV value (P = 0.344) of apical of the heart had no statistically significant differences among the segments.

Discussion

Our study reported T1 and ECV values of 87 healthy volunteers aged 20–60 years old and determined their dependence on age and gender. Our data showed that the T1 value of healthy adults was $1,261 \pm 52$, ECV value was $28.3\% \pm 2.9\%$. T1 and ECV value of females were higher than males, while ECV value of males increased with age. The T1 values of males and females and the ECV values of females were not related to age. Both the T1 and ECV values gradually increased from the basal to the apical of the heart. For the basal, T1 and ECV values between each segment showed significant differences. There were also significant differences for T1 value for different segments of the middle part. However, there was no differences for ECV value for different segments of the middle part. and for the apical, no differences for T1 and ECV value between different segments.

The T1 value of healthy adults calculated in our study was $1,261 \pm 52$, which was similar to the result reported by Kawel et al. ($1,286 \pm 59$)^[17]. Data from previous studies were highly inconsistent. For example, the T1 mapping reported by Jason J Lee et al. (1315 ± 39) was higher than found in our research^[18]. Most reports showed lower values than ours, such as the results from Yang Dong ($1,202 \pm 45$)^[19] and Stefania Rosmini (1025 ± 38)^[20]. These differences may come from different scanner fitting algorithms, pulse types, race, sample size, age group, and other unknown factors. Since the measured value of myocardial T1 value under 3T field strength is about 30–40% higher than that measured at 1.5T field strength^[21, 22], T1 mapping under different field strengths should be discussed separately.

Contrary to changes in myocardial T1 values, ECV values measured by various studies are similar. Even with different magnetic field strengths in healthy adults, the reported ECV values did not change markedly^[23]. This finding was confirmed by a previous study, which showed that the ECV measured at 1.5T or 3.0T was very similar, ranging from 25–28%^[18]. Therefore, relative to T1 values, it is more meaningful to compare ECV values between different centers.

Our results showed that both T1 and ECV value in females are higher than in males. This result is consistent with the results obtained by most researchers^[19, 20, 24, 25]. The possible reasons for this phenomenon may include blood pool pollution, which is a relatively large influencing factor because females' hearts are thinner (on average), and some volume effects are more pronounced than males^[26]. Longer blood T1 value in the capillaries in the myocardium is also a reasonable explanation^[26]. The higher ECV value found in females than in males is also related to the lower hematocrit found in females. Our data showed that the ECV value was negatively correlated with hematocrit. Therefore, it is necessary to take gender into account when discussing T1 and ECV values of normal myocardium.

However, there is no consensus on the correlation between age and T1 and ECV value. We found that ECV value increased with age in males but not in females, which is consistent with the results shown by Liu et al.^[27]. The T1 value of males and females had no correlation with age, which is similar to the data from Joseph J Pagano et al.^[28], and Piechnik et al.^[29] showed that there is no correlation between T1 and age in men, and there is a negative correlation between T1 and age in women. Ito et al. through histopathological studies, found that male interstitial myocardial fibrosis increased with age, but females

did not show this change^[30]. Therefore, when interpreting the results of T1 and ECV values in the heart, age and gender must be considered.

Our research found that T1 mapping and ECV values gradually increased from basal to apical, consistent with the results reported by von Knobelsdorff-Brenkenhoff et al^[31]. This phenomenon can be explained by the partial volume effect of image acquisition at apical^[32]. The influence of MRI artifacts on the left ventricular apical is generally more significant^[33].

Our research found that T1 and ECV values between each segment showed significant differences for the basal. There were also significant differences for T1 value for different segments of the middle part. However, there was no differences for ECV value for different segments of the middle part. and for the apical, no differences for T1 and ECV value between different segments. In their study, Messroghli et al. also did not find segmental changes in T1 values^[34]. However, studies by Kawel et al.^[35], von Knobelsdorff-Brenkenhoff et al.^[31], and Yang Dong^[31] showed that the T1 and ECV values of the septal wall were the highest. Their findings are consistent with the histological data of healthy myocardium. Studies have shown that the ventricular septal collagen content is higher compared with other regions^[36]. The mechanism of T1 or ECV values heterogeneity in different segments is still unclear. Rogers et al. believe that these differences are unlikely to represent actual regional differences in longitudinal relaxation. They may be related to many confounding factors, including susceptibility artifacts, issues related to receiver coil sensitivity, and the large distance between receiver coil components—the resulting signal gradient between the interval and the lateral myocardium^[32].

Limitation

This study was single-center, single-supplier with a medium sample size. We ruled out lung disease and coronary artery calcification through low-dose chest CT examination. However, we did not perform coronary computed tomography angiography examination, and coronary artery problems were not completely ruled out. Although all controls with normal blood pressure and normal heart structure had no cardiovascular disease in the medical history, we did not perform a 12-lead ECG to supplement this assessment further. We did not perform echocardiography on healthy volunteers to investigate whether there was a correlation between diastolic function and myocardial ECV value. The relationship between the T1 and ECV values and the gender hormones was not analyzed.

Conclusion

In healthy adults, T1 mapping of healthy adults was $1,261 \pm 52$, ECV value was $28.3\% \pm 2.9\%$. Gender affects myocardial T1 and ECV values. Females have higher T1 and ECV values than males. With increasing age, males' ECV values gradually increase, but males' T1 values and females' T1 and ECV values are not affected by age.

Declarations

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors read, critically edited the initial manuscript, added intellectual content, and approved the final version. HS and YK designed, coordinated and conducted the study, HS and ZM acquired all data, LZ, LC, FY and LS Obtained informed consent and related basic information.

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No.

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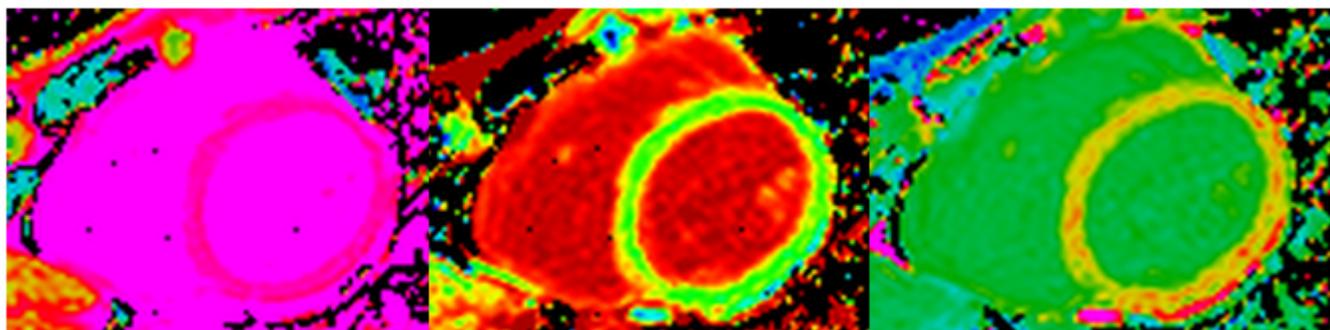
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Figures



a

b

c

Figure 1

a: Pre-contrast T1 mapping, refers to the longitudinal relaxation time value of the myocardial tissue without contrast agent; b: Post-contrast T1 mapping, refers to the longitudinal relaxation time value of the myocardial tissue after the contrast agent is injected; c: ECV, reflects the volume fraction of myocardial tissue do not occupied by cardiomyocytes.

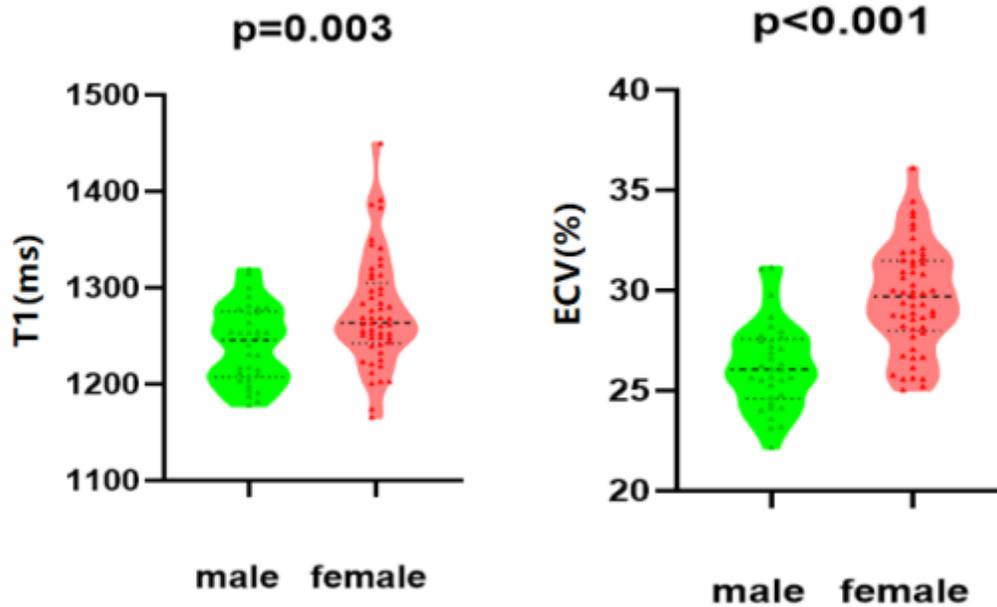


Figure 2

Violin graph of male and female overall T1 and ECV values. The scatter points in the violin represent each individual data, the thick black bar in the middle represents the median, and the thin black line extending from it represents the 95% confidence interval.

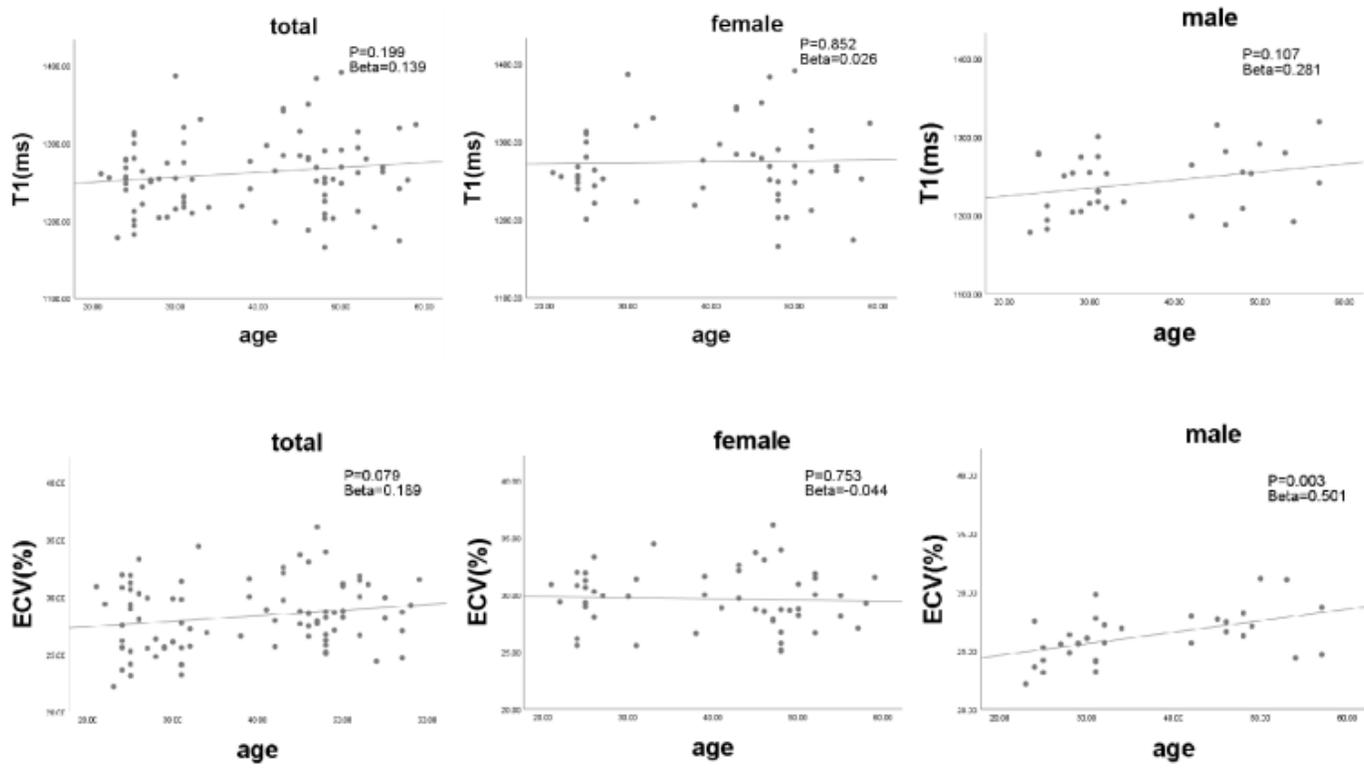


Figure 3

T1 and ECV values changes with age and gender.

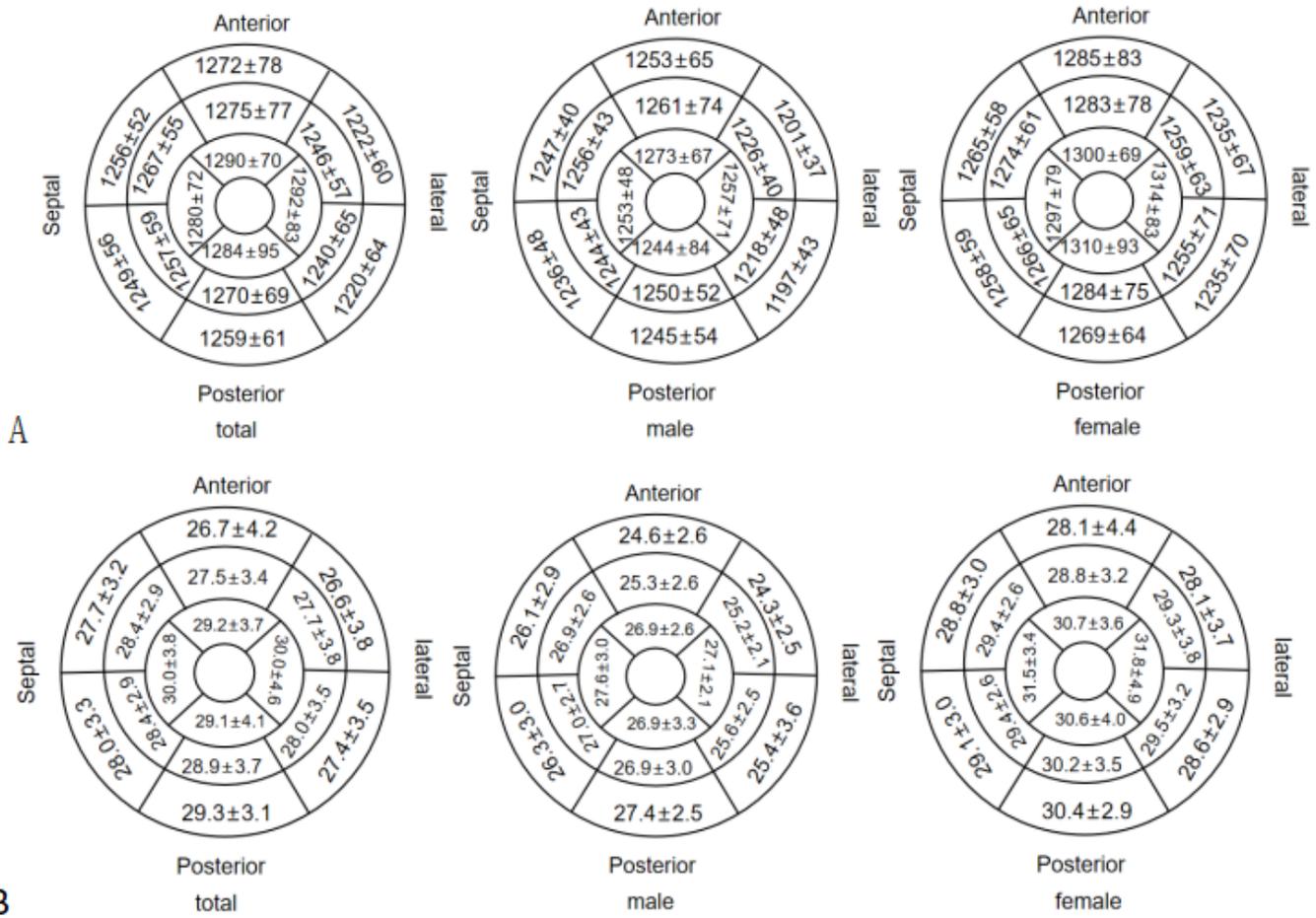


Figure 4

Bulls'eye model shows the T1 value and ECV (median and interquartile range) in the 16 segments of AHA by gender. T1 value (A) and ECV (%) value (B) in the 16th segment of AHA.

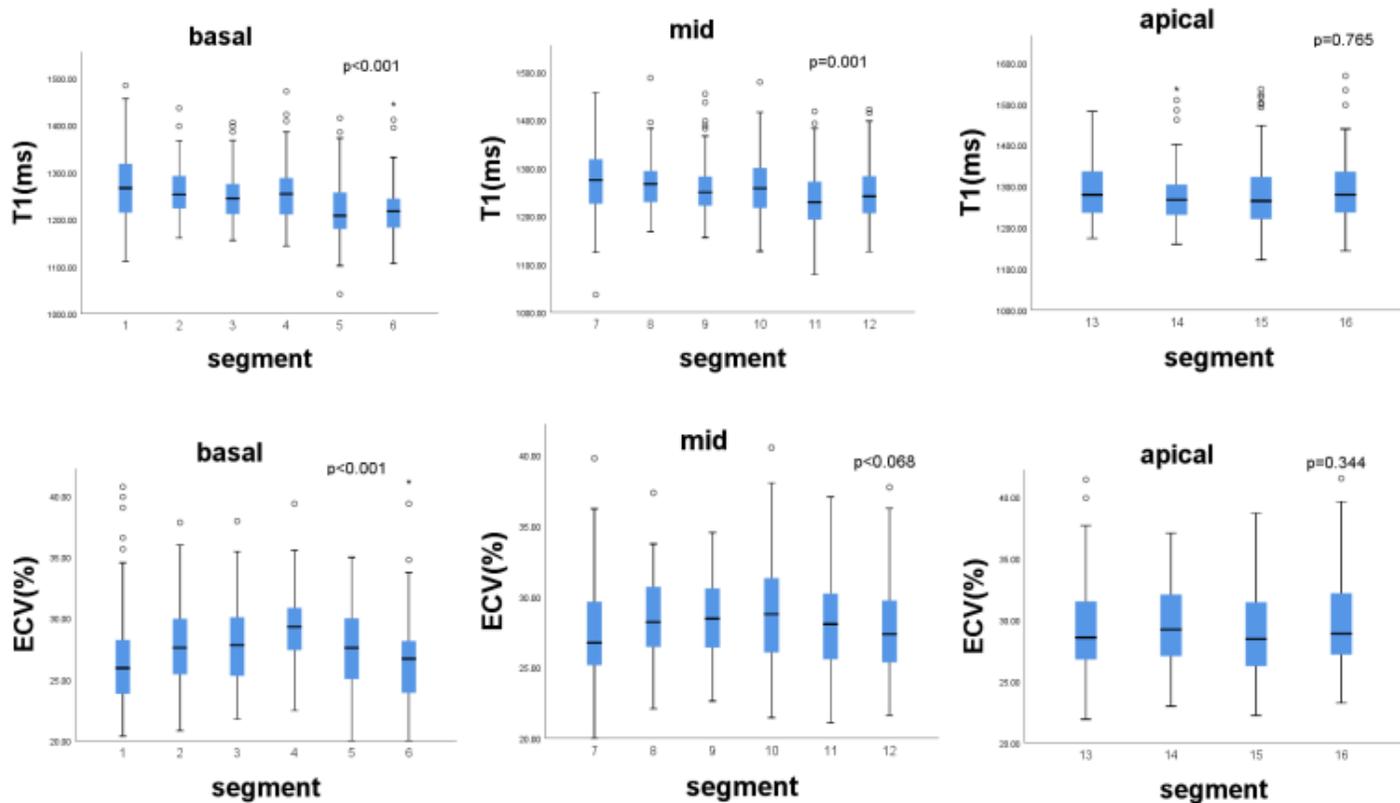


Figure 5

Box plot of segmental changes (by slice position) of T1 mapping and ECV. The central box represents the values from the lower quartile to the upper quartile. The median line shows the median. The range is from the minimum to the maximum (excluding outliers, expressed in points). A one-way analysis of variance (ANOVA) test was used to analyze the differences in T1 and ECV values between the fragments.