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Original Article

T1 and T2* relaxation time in the parcellated myocardium of healthy Taiwanese participants: A single center study

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ABSTRACT

Background: Quantitative maps from cardiac MRI provide objective information for myocardial tissue. The study aimed to report the T1 and T2* relaxation time and its relationship with clinical parameters in healthy Taiwanese participants.

Methods: Ninety-three participants were enrolled between 2014 and 2016 (Males/Females: 43/50; age: 49.7 ± 11.3/49.9 ± 10.3). T1 and T2* weighted images were obtained by MOLLI recovery and 3D fully flow compensated gradient echo sequences with a 3T MR scanner, respectively. The T1 map of the myocardium was parcellated into 16 partitions from the American Heart Association. The septal part of basal, mid-cavity, and apical view was selected for the T2* map. The difference of quantitative map by sex and age groups were evaluated by Student's TTEST and ANOVA, respectively. The relationship between T1, T2* map, and clinical parameters, such as ejection fraction, pulse rate, and blood pressures, were evaluated with partial correlation by controlling BMI and age.

Results: Male participants decreased T1 relaxation time in partitions which located in the mid-cavity and apical before 55 years old compared with females (Male/Female: 1143.1.4 ± 72.0–1191.1 ± 37.0/1180.1 ± 54.5–1326.1 ± 113.3 msec, $p < 0.01$). For female

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participants, T1 relaxation time was correlated negatively with systolic pressure ($p < 0.01$) and pulse rate ($p < 0.01$) before 45 years old. Besides, T1 and T2* relaxation time were positively and negatively correlated with ejection fraction and pulse rate after 45 years old in male participants, respectively. Decreased T2* relaxation time could be noticed in participants after 45 years old compared with youngers (26.0 ± 6.5/21.9 ± 8.0 msec; 25.2 ± 5.0/21.6 ± 7.2 msec, $p < 0.05$).

Conclusion: Reference T1 and T2* relaxation time from cardiac MRI in healthy Taiwanese participants were provided with sex and age-dependent manners. The relationship between clinical parameters and T1 or T2* relaxation time was also established and could be further investigated for its potential application in healthy/sub-healthy participants.

At a glance commentary

Scientific background on the subject

MRI provided a new non-invasive technique to monitor the myocardial conditions. The quantitative measurement of the MR relaxation times can provide the baseline information within the myocardium.

What this study adds to the field

We reported both the T1 and T2* relaxation times from each cardiac partition in healthy Taiwanese. Differences in T1 and T2* relaxation times can be noticed between either sex or age. T1 relaxation time was correlated with blood pressure, pulses rate, and ejection fraction.

Patients with myocardial diseases might suffer from a serious impact on daily living activity, which could lead to increased care burden. Because of the very low capacity in myocardial regeneration, tissue damage by myocardial necrosis is usually irreversible [1,2]. Therefore, great interest has been raised to monitor the healthy myocardial conditions, to prevent the occurrence and the subsequent deterioration of the myocardial disease, preferably with non-invasive methods. Computed tomography (CT), ultrasound, and magnetic resonance image (MRI) were widely used as image-based diagnostic techniques without invasive for myocardial tissue. In this regard, although CT could provide superior spatial resolution, its performance at discriminating between soft-tissue lesions of cardiomyopathy might be less than satisfactory [3]. The limited temporal resolution, the risk from radiation, and the use of contrast agent might raise further concerns. Cardiac MRI (CMRI) might provide a choice because of the improved contrast and the non-invasive nature without the need to use a contrast agent.

The myocardial T1 and T2* relaxation time, as derived from CMRI, have been previously reported in many cardiomyopathies such as acute myocardial infarction [4], fibrosis [5], and iron deposition [6]. For diagnosis, quantitative values of relaxation time were often obtained from either healthy myocardial tissue, such as the remotely-located unaffected tissue from the same participant [7,8], or healthy volunteers [9–11]. These quantitative maps provide an objective assessment of the myocardial tissue properties in comparison to the disease-induced abnormalities or diffused changes within myocardium [12].

The Caucasian population usually has a high cardiovascular-disease-related mortality rate [11,13–15]. In contrast, the Asian population has a higher mortality rate by stroke, which was often attributed to the poor control of cardiovascular risk factors, such as high blood pressure or cholesterol level [16]. The relaxation time in the healthy myocardium was previously reported from the Caucasian population [11,13–15]. To evaluate the potential relationship between clinical parameters and quantitative mapping from CMRI, mastered the reference values of T1 and T2* relaxation time of myocardium in healthy populations were important. This study aimed to measure and report the T1 and T2* relaxation time of myocardium in healthy Taiwanese participants. We further investigated the association between T1, T2* relaxation time of myocardium, and clinical parameters, including blood pressure, pulses rate, and ejection fraction.

Materials and Methods

Participants

The study was approved by the Institutional Review Board (ChangGung Medical Systems). All procedures followed the tenet in the Declaration of Helsinki. After a detailed explanation of the examination process, all the participants signed and gave their consent.

From 2014 to 2016, a total of 93 healthy volunteers (mean age: 49.7 ± 11.3; 43 males, mean age: 49.8 ± 11.1 years; 50 females, mean age: 49.9 ± 10.3 years) were recruited from the local community. Potential participants were evaluated for the medical history, inclusion, and exclusion criteria. None of the participants reported any potential heart disorders or diseases bringing impact on the image such as hormone therapy, renal disease, or liver cirrhosis. The biochemistry test indicated normal functions of both the kidney (blood urea nitrogen, creatinine, estimated glomerular filtration

rate) and the liver (aspartate aminotransferase, AST; alanine aminotransferase, ALT; alkaline phosphatase, ALK-P; bilirubin, gamma-glutamyl transpeptidase, γ-GT; alpha-fetoprotein, α-FP). Also, it was noticed that the structure, regional wall motion, and contraction functions of the heart were normal, as diagnosed by cardiovascular radiologists. No hormone therapy or long-term blood transfusion for thalassemia was recorded in the medical history of our participants.

After the physical and electric cardiogram examinations, the qualified participant was subsequently arranged for the MR examination. The inclusion criteria were the following: (1). Aged between 20 and 70 years old; (2). No known cardiovascular disorder. The exclusion criteria included general MRI contraindication conditions and the following: (1). History of the heart (such as angina pectoris and cardiomyopathy) and psychiatric diseases; (2). Open heart surgery; (3). Pregnancy or women who were breastfeeding; (4) chemotherapy for malignant tumors.

Because aging could increase the risk of cardiovascular disease, the participants were further divided into the following three groups: young group (<45 years old), middle-aged group (45–55 years old), and old group (>55 years old) [17,18]. The height, weight, clinical parameters such as pulse rate, systolic, and diastolic pressures were taken immediately before the MR examination. Table 1 showed the demographic data of all participants.

Imaging

MR images were acquired from a 3T scanner (Skyra, Siemens, Erlangen Germany) equipped with an 18 channel body matrix coils and spine 32-channel coil at Keelung Chang Gung Memorial Hospital. All images were obtained during breath-holds by retrospective ECG gating. The scout images were acquired to provide localization of the heart. Both modified Look-Locker Inversion recovery (MOLLI) and 3D fully flow compensated gradient echo sequences were acquired for the quantitative mapping of native T1 and T2* relaxation times, respectively. In addition, the cine imaging sequence was acquired for the evaluation of ejection fraction by using a True Fast Imaging with Steady-state Precession (True FISP) sequence. The imaging parameters were summarized as in the following:

A Native T1 measurement was obtained using a motion-corrected (ECG triggered) MOLLI sequence, a single shot true fast imaging with steady-state precession (FISP) acquired in two Look-Locker experiments with separate 180-degree inversion recovery pulses in each prepared. Eight readouts required in 11 heartbeats using the 5 (3)3 protocol, which included 5 readouts from separate 5 heart cycles set after the first inversion time (TI), and another 3 readouts in 3 heart cycles set after the second TI [19]. Between these two readout groups, 3 heart cycles pause set to make a signal recovery. The following parameters were: Repetition Time (TR) = 324 msec, Echo Time (TE) = 1.12, flip angle = 35°, Field of View (FOV) = 306 mm × 360 mm, matrix size = 256 × 218, Number of Excitation (NEX) = 1 and slice thickness = 8 mm. Three short-axis views (basal, mid-cavity, and apical) were obtained in three inversion-recovery prepared experiments, which contained eight TI for each view.

T2* weighted images were obtained using a 3D fully flow compensated gradient echo sequence. Three short-axis views (basal, mid-cavity and apical) were obtained in three prepared experiments, which contained eight echoes (TE = 2.21; 4.18; 6.15; 8.12; 10.09; 12.06; 14.3 and 16 msec) in each view. Additional imaging parameters included TR = 844.8 msec, FOV = 332 mm × 379 mm and matrix size = 118 × 224.

Cine image for ejection fraction was obtain by breath-hold, ECG gated segmented TrueFISP. Additional imaging parameters included TR/TE = 36.9 msec/1.35 msec, slice thickness = 6 mm, FOV = 434 × 430 mm, matrix size 208 × 210, 12 segments, and 25 phases.

Image processing

The ejection fraction, as one of the clinical parameters, was calculated from cine protocol MRI by the following formula [(EDV-ESV)/EDV*100] (EDV, end-diastolic volume; ESV, end-systolic volume).

The T1 and T2* maps were calculated by using QMASS (Version 7.6, Medis Suite 2.1.12.2, Leiden, The Netherlands) following the recommended procedure. The acquired inversion recovery images were first registered using a novel motion correction algorithm which is based on estimating

Table 1 General characteristics of participants.

	Young			Middle-aged			Old		
	All	Male	Female	All	Male	Female	All	Male	Female
Subjects	30	14	16	30	13	17	33	16	17
Age (years)	37.4 (5.5)	36.7 (6.6)	37.9 (4.5)	49.9 (3.2)	49.8 (3.6)	50.0 (2.9)	61.0 (4.3)	60.8 (4.6)	61.2 (4.2)
Height (cm)	166.2 (7.9)	172.4 (5.2)	160.8 (5.4)***	162.3 (7.9)	168.8 (7.1)	157.4 (4.1)***	159.8 (7.6)	164.7 (5.1)	155.2 (6.7)***
Weight (kg)	68.2 (13.4)	76.8 (7.5)	60.6 (13.0)***	67.3 (15.3)	77.3 (16.4)	59.6 (8.7)**	65.1 (10.4)	71.8 (8.0)	58.9 (8.5)***
BMI (kg/m^2)	24.5 (3.7)	25.8 (2.5)	23.4 (4.3)	25.3 (4.1)	27.0 (4.6)	24.0 (3.3)*	25.4 (3.2)	26.4 (2.8)	24.5 (3.3)
BP_S (mmHg)	129.2 (12.9)	136.1 (11.6)	123.2 (11.2)**	129.2 (19.0)	134.5 (20.5)	125.1 (17.3)	134.2 (22.7)	133.9 (19.7)	134.5 (25.8)
BP_D (mmHg)	73.9 (8.9)	76.6 (10.1)	71.4 (7.0)	76.6 (13.6)	81.9 (13.9)	72.5 (12.2)	76.3 (12.0)	79.6 (11.6)	73.2 (11.9)
EF (%)	67.0 (9.9)	68.3 (9.6)	67.2 (8.3)	70.7 (10.9)	72.7 (6.2)	69.2 (13.5)	72.7 (8.9)	72.3 (10.3)	73.1 (7.7)
Pulse rate (bpm)	81.3 (14.7)	83.6 (17.3)	79.3 (12.1)	77.4 (10.0)	72 (6.7)	81.6 (10.3)**	77.0 (10.7)	78.6 (10.5)	75.6 (11.0)

Data are presented as means (standard deviations in parentheses). * Male versus female in same age group, $p < 0.05$; ** Male versus female in same age group, $p < 0.01$; *** Male versus female in same age group, $p < 0.001$. BMI, body mass index; BP_S, systolic blood pressure; BP_D, diastolic blood pressure; EF, ejection fraction; bpm beats per minute.

synthetic images presenting contrast changes similar to the acquired images by solving a variational energy minimization problem. Thereafter, the T1 estimate is computed on a per-pixel basis by performing a non-linear curve fitting using the three-parameter signal model.

The T1 map of myocardial ROI was segmented according to the American Heart Association segment model [Supplementary Fig. 1], including 6 basal (basal anterior, basal anteroseptal, basal inferoseptal, basal inferior, basal inferolateral, basal anterolateral), 6 mid-cavity (mid anterior, mid anteroseptal, mid inferoseptal, mid inferior, mid inferolateral, mid anterolateral) and 5 apical (apical anterior, apical septal, apical inferior, apical lateral and apical cap) partitions [20]. The apical cap was excluded from the final analysis because of insufficient acquisition coverage. Each partition was further classified according to the territories of left anterior descending (LAD, including basal anterior, basal anteroseptal, mid anterior, mid anteroseptal, apical anterior, and apical septal), the right coronary artery (RCA, including basal inferoseptal, basal inferior, mid inferoseptal, mid inferior, and apical inferior), and the left circumflex (LCX, including basal inferolateral, basal anterolateral, mid inferolateral, mid anterolateral, and apical lateral).

In the analysis of the T2* map, the region of interest was selected in the septal part from the basal, mid-cavity and apical view, because the T2* relaxation time from this region might be less prone to susceptibility artifact caused by adjacent veins [21]. In addition, the T2* relaxation time from the septal part could be highly correlated with values from the whole left ventricle region [22]. The mean values of T2* relaxation time from each septal region were recorded.

Statistical analysis

Statistical analysis was performed in SPSS (SPPS Inc., Chicago, IL, USA). The difference in height, weight, body mass index (BMI, weight (kg)/height^2 (m)), blood pressure, and ejection fraction were evaluated by using Student's T-Test (for sex) and analysis of variance (ANOVA, among different age groups), respectively. *Post hoc* testing was performed using the least significant difference method. The partial correlation was used to examine the association between 1) the relaxation time and age, and 2) the clinical parameters and the relaxation times from each heart partition by controlling for the BMI alone or age and BMI, respectively, because both were highly associated with blood pressure and pulse rate [23] and ejection fraction. The p-value smaller than 0.05/n (Bonferroni correction, n is the number of partitions in different territories of the coronary artery) was regarded as significant.

Results

Demographic description

Difference in age

No significant difference in BMI, systolic, and diastolic pressure, ejection fraction, and pulse rate was observed either among three age groups or in each sex and all participants [Table 1].

Difference in sex

The male group has increased BMI than the female in the middle-aged group [Table 1]. In young groups, the male also has increased systolic pressure. However, the female group has an increased pulse rate than the male in the middle-aged group [Table 1].

T1 relaxation time in different age and sex

The difference in myocardium T1 and T2* relaxation time was examined for its age and sex dependence. Table 2 summarized the T1 relaxation time as measured from each partition and territory of three coronary arteries. Overall, males had a lower averaged T1 than the females no matter in a different part of the left ventricle or territory of coronary arteries, which also could be reflected in the minimal average T1 relaxation time. The minimal averaged T1 relaxation time in basal, mid-cavity and apical of all age were 1157.0 ± 43.9, 1145.5 ± 27.4, and 1143.1 ± 72.0 msec in the male participants, and 1190.4 ± 64.1, 1180.1 ± 54.5, 1210.9 ± 60.0 msec in the female ones, respectively. For the territory of the coronary artery, the minimal averaged T1 relaxation time of LAD, RCA and LCX territory were 1167.3 ± 17.2, 1181.2 ± 19.1, and 1164.6 ± 28 msec in the male participants, and 1226.2 ± 31.5, 1231.1 ± 37.1, and 1212.4 ± 26.4 msec in the female ones, respectively.

Difference of T1 relaxation time in sex or age groups

In the young group, the male participants had lower T1 relaxation time when compared with the female ones ($p < 0.01$), noticeably in the partitions located in mid (anterior, anteroseptal, and anterolateral) and apical (anterior, septal, inferior and lateral) and in each of the three coronary artery territories ($p < 0.05$) [Table 2, Fig. 1A & B]. Similar lower value in T1 relaxation time can also be noticed in the male than in the female in the middle-aged group, which was located in partitions of basal (anterior and anterolateral), mid (anteroseptal and anterolateral), and apical (anterior and septal) [Fig. 1C & D] and in each of the three coronary artery territories ($p < 0.01$). Significant higher T1 relaxation time from basal anterior, mid anteroseptal, and RCA territory were observed in old than young or middle-aged groups in the male participants [Table 2 and Fig. 1E].

Correlation between T1 relaxation time and age

The potential influence of age to T1 relaxation time was evaluated by partial correlation. Mild correlation between age and T1 relaxation time was noticed in the basal anterior ($r = 0.291$, $p = 0.006$), basal anterolateral ($r = 0.277$, $p = 0.009$) and mid inferoseptal ($r = 0.276$, $p = 0.009$) part of myocardium of all participants [Fig. 2A–C], basal anterolateral ($r = 0.416$, $p = 0.007$), mid anterior ($r = 0.437$, $p = 0.004$), mid anterospetal ($r = 0.539$, $p < 0.001$), mid inferoseptal ($r = 0.533$, $p < 0.001$), and mid inferolateral ($r = 0.429$, $p = 0.005$) of male [Fig. 2C–H], and apical inferior in female ($r = -0.312$, $p = 0.009$) [Fig. 2I].

T2* relaxation time in different age and sex

Table 3 summarizes the T2* relaxation time as measured from the septal part of basal, mid-cavity, and apical. Overall, young participants had a higher averaged T2* relaxation time than

Table 2 The T1 relaxation time from partitions of myocardium.

Segment	Young			Middle-aged			Old		
	All	Male	Female	All	Male	Female	All	Male	Female
Basal_A	1175.2 (58.2)	1157.9 (46.8)	1190.4 (64.1)	1187.3 (51.7)	1157.0 (43.9)	1210.5 (45.6)**	1217.8 (63.2)	1218.2 (75.3)[a,b]	1217.5 (51.7)
Basal_AS	1206.8 (76.1)	1203.9 (101.2)	1209.3 (48.1)	1209.2 (68.3)	1196.9 (73.1)	1218.5 (65.1)	1231.4 (42.8)	1227.3 (52.9)	1235.2 (31.8)
Mid_A	1174.9 (47.4)	1145.5 (27.4)	1200.6 (46.8)**	1164.1 (48.8)	1143.3 (30.9)	1180.1 (54.5)	1181.9 (45.9)	1177.4 (41.8)	1186.1 (50.4)
Mid_AS	1207.3 (40.3)	1180.8 (20.6)	1230.6 (39.2)**	1203.4 (39.1)	1174.8 (25.6)	1225.3 (33.2)**	1229.1 (51.1)	1217.2 (45.5)[c,d]	1240.3 (54.8)
Apical_A	1228.8 (68.3)	1182.6 (46.0)	1269.2 (58.8)**	1209.6 (79.0)	1149.7 (46.6)	1255.4 (67.4)***	1187.6 (79.0)	1162.9 (90.6)	1210.9 (60.0)
Apical_S	1246 (93)	1185.8 (50.1)	1298.7 (90.6)**	1230.4 (65.9)	1182.1 (30.8)	1267.3 (61.8)***	1242.8 (65.2)	1216.3 (72.4)	1267.8 (46.9)
LAD	1206.5 (47.7)	1176.1 (21.0)	1233.1 (45.5)***	1200.7 (41.2)	1167.3 (17.2)	1226.2 (31.5)***	1215.1 (41.7)	1203.2 (46.9)	1226.3 (33.7)
Basal_IS	1193.2 (72)	1184.2 (92.2)	1201.1 (50.1)	1193.4 (57.7)	1180.9 (41.0)	1202.9 (67.5)	1242.9 (85.7)	1255.7 (118.6)	1230.9 (34.5)
Basal_I	1193.8 (70.4)	1182.8 (31.4)	1203.4 (92.3)	1205.4 (81.7)	1178.2 (45.9)	1226.2 (97.2)	1230.0 (42.8)	1213.0 (45.1)	1245.9 (34.7)
Mid_IS	1203.8 (52.2)	1182.3 (34.0)	1222.6 (58.8)	1203.8 (41.7)	1188.5 (26.6)	1215.5 (47.9)	1225.9 (52.0)	1220.0 (55.5)	1231.4 (49.5)
Mid_I	1205.9 (60.6)	1178.6 (40.7)	1229.8 (66.0)	1196.8 (59.1)	1167.2 (42.7)	1219.4 (60.9)	1212.9 (63.0)	1195.7 (63.2)	1229.2 (60.1)
Apical_I	1262.9 (110.9)	1190.7 (45.5)	1326.1 (113.3)**	1255.1 (132.4)	1191.1 (37.0)	1304.0 (157.8)	1222.5 (84.2)	1227.3 (90.4)	1217.9 (80.4)
RCA	1211.9 (54.6)	1182.4 (5.0)	1236.6 (61.4)***	1210.9 (41.0)	1181.2 (19.1)	1232.4 (36.1)***	1226.8 (39.8)	1222.3 (43.2)[e,f]	1231.1 (37.1)
Basal_IL	1209.1 (105.9)	1191.9 (41.8)	1224.3 (140.2)	1202.0 (54.1)	1191.0 (50.8)	1210.5 (56.5)	1215.6 (46.6)	1207.8 (46.8)	1222.9 (46.5)
Basal_AL	1186.1 (48.8)	1168.0 (38.9)	1202.0 (52.1)	1195.1 (47.7)	1163.4 (44.7)	1219.3 (34.5)**	1211.1 (47.6)	1206.3 (55.2)	1215.6 (40.4)
Mid_IL	1177.9 (58.8)	1160.4 (31.2)	1193.2 (72.8)	1194.9 (62.8)	1166.6 (33.3)	1216.5 (71.9)	1198.3 (55.5)	1192.9 (63.4)	1203.4 (48.3)
Mid_AL	1188.7 (46.1)	1162.5 (26.3)	1211.6 (48.1)**	1191.6 (57.7)	1158.7 (47.5)	1216.7 (52.8)***	1193.6 (45.1)	1191.9 (59.0)	1195.1 (28.1)
Apical_L	1233 (78.5)	1190.9 (41.7)	1269.9 (85.5)**	1223.9 (107.6)	1143.1 (72.0)	1285.6 (88.0)***	1199.1 (100.5)	1171.6 (134.3)	1225.0 (42.8)
LCX	1199 (52.6)	1176.0 (14.2)	1220.2 (61.6)*	1201.5 (47.9)	1164.6 (28)	1230.2 (28.1)***	1203.5 (42.5)	1194.1 (54.1)	1212.4 (26.4)

Data are presented as means (standard deviations in parentheses). The unit of T1 relaxation time is in msec. * Male versus female in same age group, $p < 0.05$, ** Male versus female in same age group, $p < 0.01$, *** Male versus female in same age group, $p < 0.001$. Abbreviations: A: anterior; AS: anteroseptal; S: septal; IS: inferoseptal; I: inferior; IL: inferolateral; AL: anterolateral; L: lateral; LAD: left anterior descending artery; RCA: right coronary artery; LCX: left circumflex.

[a,c,e], Age Old versus age Young in male, p value < 0.05.

[b,d,f], Age Old versus age Middle-aged in male, p value < 0.05.

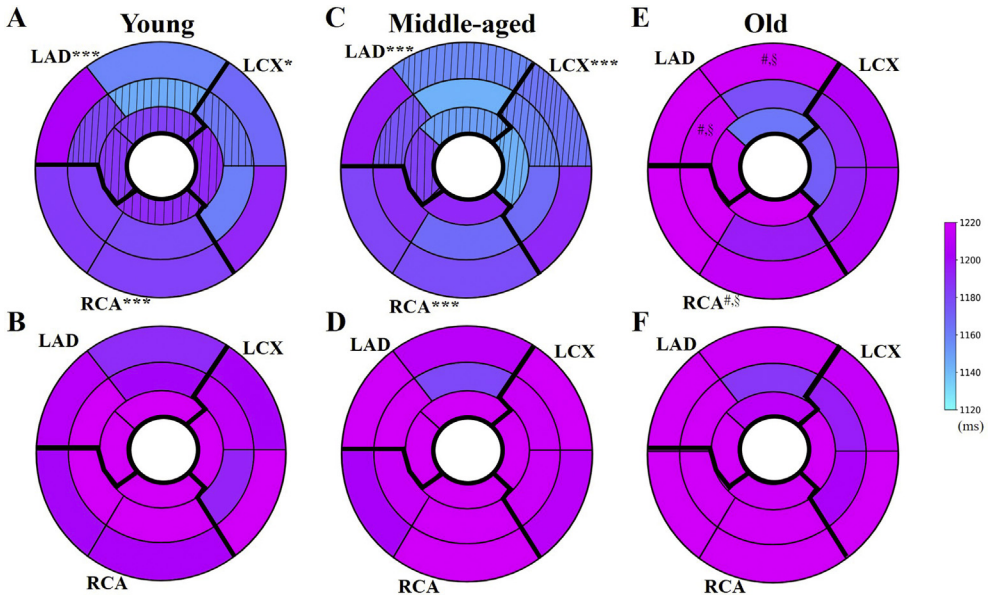

Fig. 1 Bull's eye plot of T1 relaxation time from different age groups. Fig. 1 plots the T1 relaxation time for each myocardial partition, including the basal (outer ring), mid-cavity (middle ring) and apical (central ring) planes in male (top row) and female (bottom row), respectively. The age groups are young (Panel A, B), middle-aged (Panel C, D), and old (Panel E, F) groups. The partitions with a significant difference between males and females are highlighted in shadow labeling. The unit of T1 relaxation time is given in msec. In the male group, # indicated a significant difference between old and young group; § indicated a significant difference between old versus middle-aged groups. Abbreviations used: LAD: left anterior descending; RCA: right coronary artery; LCX: left circumflex.

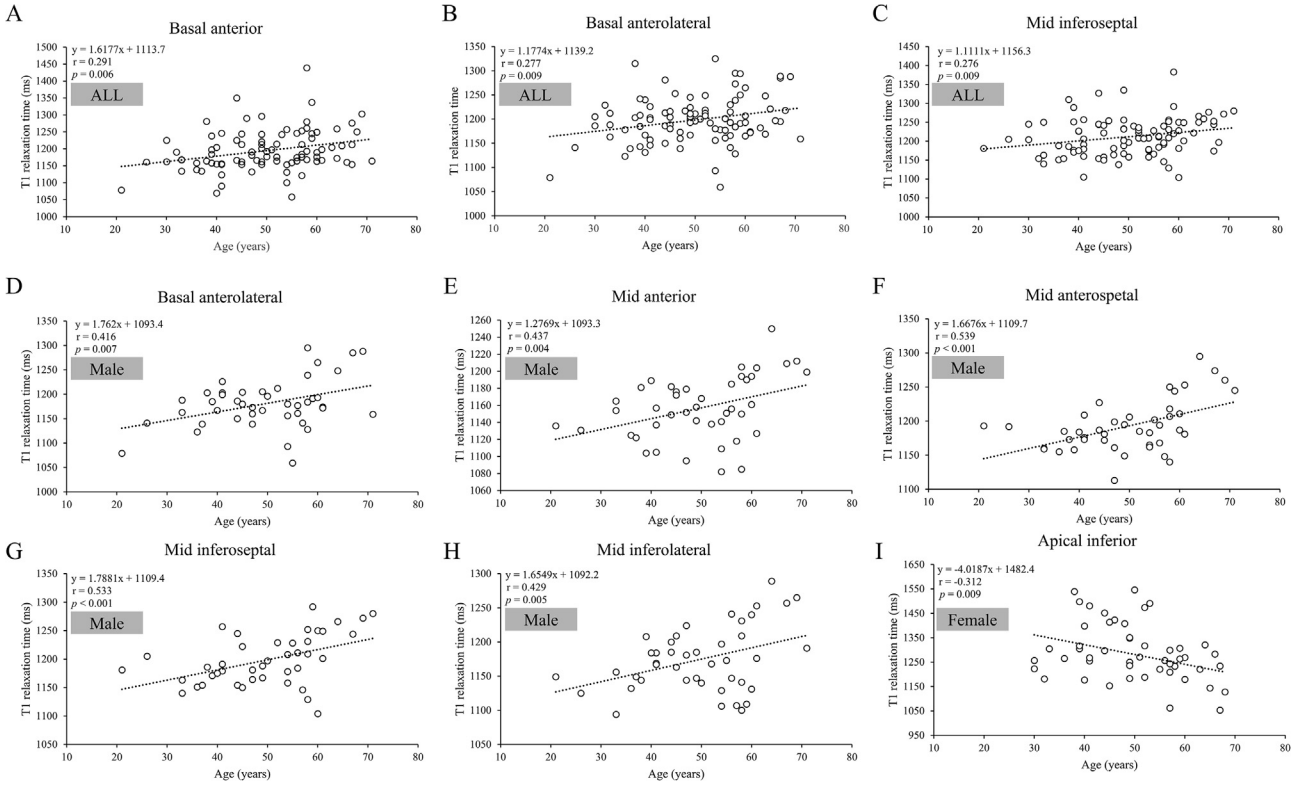

Fig. 2 T1 relaxation time for myocardial partition correlates with age. T1 relaxation time was correlated with age in the myocardial partitions of all (Panel A–C), male (Panel D–H), and female participants (Panel I) after control the individual's body mass index. The equation and statistical results, including correlation coefficient *r* and *p* values, are depicted for each analysis.

Table 3 The T2* relaxation time from partitions of myocardium.

Young			Middle-aged			Old		
All	Male	Female	All	Male	Female	All	Male	Female
26.6 (4.3)[a,b]	24.5 (8.0)	27.3 (4.7)	21.9 (8.0)	23.0 (6.3)	21.0 (9.2)	22.9 (6.5)	23.1 (5.0)	22.7 (4.8)
25.3 (5.0)[c]	24.6 (4.9)	25.6 (5.2)	21.6 (7.2)	19.5 (8.9)	23.5 (4.9)	23.2 (4.7)	23.0 (5.1)	23.4 (4.0)
23.4 (4.7)	22.8 (5.0)	23.6 (4.7)	22.6 (7.4)	21.0 (7.8)	24.0 (6.9)	23.4 (5.0)	23.2 (5.1)	23.6 (5.0)

Table summarized the T2* relaxation time from partitions of myocardium for each age and sex groups, respectively. Data are presented as means (standard deviations). The unit of T2* relaxation time is in msec.
[a] Age Young *versus* age Middle-aged in all, p value = 0.037.
[b] Age Young *versus* age Old in all, p value = 0.027.
[c] Age Young *versus* age Middle-aged in all, p value = 0.014.

the middle-aged one in the septal part of the basal and middle cavity. The T2* relaxation time in septal part of basal, mid-cavity and apical of all age ranged in 23.0 ± 6.3–24.5 ± 8.0 msec, 19.5 ± 8.9–24.6 ± 4.9 msec, 21.0 ± 7.8–23.2 ± 5.1 msec in the male participants, and 21.0 ± 9.2–27.3 ± 4.7 msec, 23.4 ± 4.0–25.6 ± 5.2 msec, 23.2 ± 4.7–24.0 ± 6.9 msec in the female ones, respectively. Fluctuation could be found that males had a low minimum value of averaged T2* relaxation time in the septal part of mid-cavity and apical.

Difference of T2 relaxation time in sex or age groups*

T2* relaxation time in the young group was higher when compared with that of middle-aged (in the septal part of basal and mid-cavity) in all participants [Table 3]. However, no significant difference in T2* relaxation time from individual heart partition was observed among three age groups in the male, female participants and between sex in each age group [Table 3].

Correlation between T2 relaxation time and age*

The potential influence of age to T2* relaxation time was evaluated by partial correlation. Negative correlation with age was noticed in T2* relaxation time of the septal part in basal ($r = -0.366$, $p = 0.007$) in the female [Fig. 3A]. No partition of T2* relaxation time would be found in the male.

Correlation between T1, T2* relaxation time and clinical parameters

The correlation between T1, T2* relaxation time and cardiac-related clinical parameters were shown in Fig. 4. In the male participants, the correlation was found in the middle-aged and old groups. Correlation with the pulse rate and T2* relaxation time was noticed in regions located in the basal ($r = -0.888$, $p < 0.001$) and mid-cavity ($r = -0.739$, $p < 0.001$) in the middle-aged group [Fig. 4A]. The correlation with the ejection fraction was found in the segment of apical septal ($r = 0.797$, $p = 0.001$) [Fig. 4B] in the old group. In the female participants, the correlation with the systolic blood pressure was found in the young group. The regions included mid inferoseptal ($r = -0.556$, $p = 0.003$), mid anterolateral ($r = -0.552$, $p = 0.004$), which are located in either the RCA or LCX territory [Fig. 4C]. Besides, correlation with the pulse rate was noticed in regions located in the mid anteroseptal ($r = -0.615$, $p = 0.008$) and mid inferoseptal ($r = -0.635$, $p = 0.007$) [Fig. 4D] from the young group.

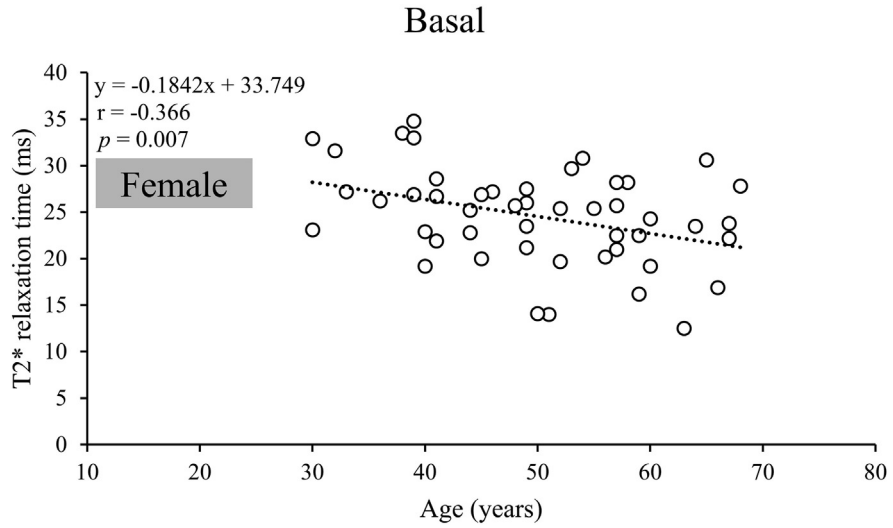

Fig. 3 T2* relaxation time for myocardial partition correlates with age. T2* relaxation time was negatively correlated with age in the septal part of basal of female participants after control the individual's body mass index. The equation and statistical results, including correlation coefficient r and p values, are depicted for each analysis.

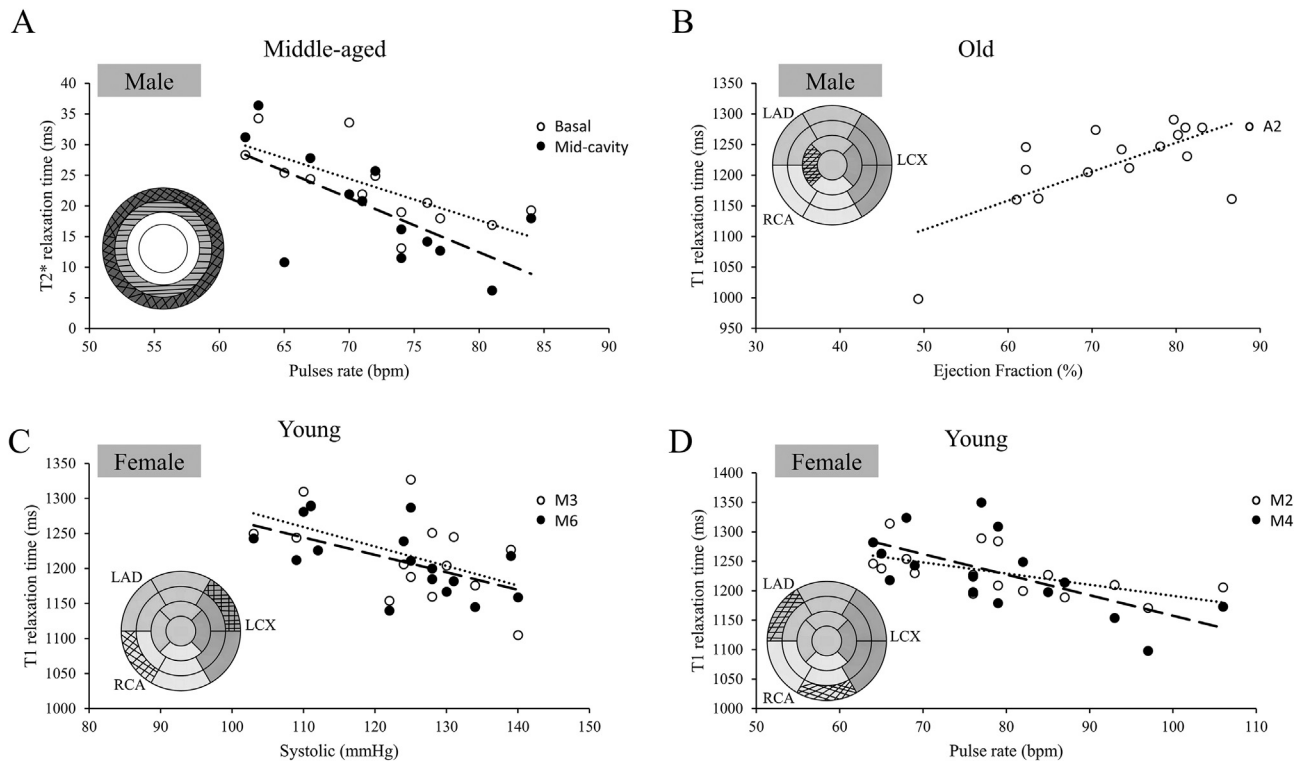

Fig. 4 T1 and T2* relaxation time for the myocardial partitions correlates with the clinical parameters. T1 and T2* relaxation time was correlated with the clinical parameter in the myocardial partitions of male (Panel A, pulse rate; Panel B, ejection fraction) and female (Panel C, systolic pressure; Panel D, pulse rate) after control the individual's body mass index and age. Crossline labeling areas represented the partitions with a significant correlation between the specific clinical parameter and T1 relaxation time. B1, basal anterior; B3, basal inferoseptal; B4, basal inferior; B5, basal inferolateral; B6, basal anterolateral; M2, mid anteroseptal; M3, mid inferoseptal; M6, mid anterolateral; A2, apical septal.

Discussion

This study provided a reference value for the T1 and T2* relaxation time in different regions of the myocardium from healthy Taiwanese participants using a 3T MR scanner. The images which corresponded with T1 and T2* relaxation were divided and these partitions were also included separately with the territory of three coronary arteries. Our results noticed that the male participants had lower T1 relaxation time in partitions located in mid-cavity and apical before 55 years old than females. Lower T2* relaxation time could also be noticed in participants after 45 years old than youngers. The current study demonstrated the reference values of T1 and T2* relaxation time in healthy Taiwanese participants. As the variability of the quantitative maps among myocardial partitions might exist for healthy participants between different races, the range of T1 and T2* relaxation time in the Asian population should be evaluated more clear.

Cardiac imaging using MRI can be complicated which might require extensive processing effort [24,25]. The merit of image processing on a clinical scanner might consist of a motion correction technique incorporating parallel imaging to reduce the scan time, which further allowed the automatic online reconstruction of a quantitative T1 map. Increased field strength using a 3T scanner might allow for more accurate T2* mapping. Unfortunately, neither Bull's eye analysis nor quantitative T2* map was implemented as a standard procedure, which can only be performed in additional offline software.

T1 mapping

The averaged T1 relaxation time in the current study are 1206.5, 1197.8, and 1228.0 in the basal, mid-cavity, and apical of the myocardium, which was slightly higher than the values reported in Caucasian cohort (average T1 = 1157.1 (basal), 1158.7 (mid-cavity), and 1180.6 (apical)) [13]. In general, the T1 relaxation time of Caucasian ranged from 1100 to 1200 msec [11,13,14]. Studies demonstrated the difference of CMRI quantitative data between a small Asian cohort of healthy and patients, such as extracellular volume, T1, and T2 relaxation time [26–28]. Averaged T1 relaxation time in those healthy participants ranged between 1218 and 1283 msec, consistent with the value in the current study.

Several factors contributed to the T1 relaxation time within the voxel of interest, for example, water contents and substrate deposition. Increased water content in the regions of edema, such as myocardial infarction or myocarditis, might have increased T1 relaxation time [29,30]. In contrast, reduced T1 relaxation time might result from substrate deposition, such as glycosphingolipid in Fabry's syndrome [31] or iron

overload in the myocardium [32]. The current study showed that male participants had reduced T1 relaxation time in partitions of mid-cavity and apical in the young and middle-aged groups when compared with that in the female. Previous studies showed that the T1 relaxation time was lower in the male when compared with that in the female [24,33,34]. Our study further demonstrated the contribution can be from specific segments, for example, mid-cavity and apical. Because T1 relaxation time can be prone to motion artifact in the lateral part lower than septum [24], we cannot rule out the contribution from the measurement fluctuation. Alternatively, the changes might be related to the heart rate difference between sex [35], which might prolong T1 mapping [36]. Although the current scheme of acquisition in one breathhold (MOLLI 5 (3)3, i.e. 8 heartbeats with 3 beats between inversion pulses) in our study was less sensitive to heart rate when compared to the conventional one (5 (3)3 (3)3, i.e. 11 heartbeats with 6 beats in between) one [25], the effect from the heart rate difference might still contribute the reduced relaxation time in our study.

The changes in the relaxation time might be related to an age-dependent interstitial myocardial fibrosis [37] or potential iron deposition [32]. Further investigation using post-contrast images (e.g. extracellular volume) with complete biochemistry study including serum ferritin level might be required in order to shed new light on the status of the myocardium. This subtle difference between the health and sub-health cohort might prompt new interest in the future by using a longitudinal design.

T2 mapping*

The current study demonstrated the reduction of T2* relaxation time in the septal part of basal, especially in the female participants. The averaged T2* relaxation time from healthy Taiwanese participants in the current study was consistent with the values from previous studies, which ranged between 20 and 30 msec in Caucasian [15,38]. Our study did not report any significant difference in T2* relaxation among the female groups. Although iron load can be different in females before and after menopause [39], we did not observe reduced T2* values as a result of changes in iron load. The relationship between the T2* values in the myocardium and the serum iron load can be complicated.

Although iron overload could be one of the major factors that affect T2* relaxation time in the myocardium [40], iron concentration in the myocardium might be stable even though the serum ferritin increased in the post-menopause period [41], which only started to increase at more than five-times of overload in serum (>1000 mg) [42] when it could be detected by MRI [38]. Because no participants suffered from diseases which might cause pathogenic iron deposition, such as thalassemia or cirrhosis, we believed that the T2* values in our female group might be stable before and after menopause, which is further supported by the observation of T2* relaxation time in the normal range (>12 msec in 3T MRI). However, a complete biochemistry study from a larger population, including serum ferritin level, is required in order to understand the relationship between iron load in the myocardium and the corresponding relaxation measurement.

Correlation between age and quantitative mapping

Correlation of the T1 relaxation time and age could be found in partitions located in the anterior, septal, and inferior region of the basal and mid-cavity part in the male participants, and apical inferior in the female. T2* relaxation time also negatively correlated with age in the septal part of the basal region. No significant difference in T1 relaxation time could be observed between males and females in the old group, indicated the increasing trend in T1 relaxation time in male participants during aging. Roy et al. showed T1 relaxation time in males significantly increased with aging, but not in females [15]. Liu et al. also demonstrated an age-dependent increase for T1 relaxation time were stronger in male than in female, even after adjusted by cardiovascular risk factor and cardiac function [43]. The difference of correlated pattern between T1 relaxation time and age might be associated with variation of physiological and anatomical issues of heart from sex. In physiology, the female heart responds well to cardiovascular risks under the protection by the hormone, such as pressure, volume overload, and age [44]. In anatomy, the size and number of myocytes did not change in the senescent female heart but significantly reduced in the senescent male heart [45]. Whether these factors might make the male heart more susceptible to attribute the increase of T1 relaxation time during aging was needed to be further evaluated in the animal study.

T2* relaxation time mainly affected by iron overload in tissue. Female has no significant iron overload until menopause because of their continuous loss of iron during the period of the menstrual cycle, pregnancy, and parturition [46]. The iron overload increased after menopause, which consisted of the result of the negative correlation between T2* relaxation time and age in the female participants. In contrast, studies for Caucasian healthy participants demonstrated the T2* relaxation time was not correlated with age and sex [15,47]. Both studies did not control potential confounding parameters such as BMI [43] or age, during analysis, which might be the reason for these controversial results. The reference value of T2* relaxation time in the Taiwanese participants was reported, which could be used to determine the susceptibility difference for the healthy participant in myocardium with or w/o iron overload in the future study.

Correlation between clinical parameters and T1 and T2 values*

The significant correlation between the T1, T2* relaxation time and the clinical parameters can be observed in different partitions of the myocardium in healthy participants. The location is consistent with the territory of the coronary artery. T1 relaxation time in female participants existed a negative correlation with systolic pressure and pulse rate before 45 years old. In contrast, T1 and T2* relaxation time in male participants were positively and negatively correlated with ejection fraction and pulse rate after 45 years old, respectively.

Sex and age itself indeed caused a change in cardiac function. Intrinsic cardiac aging increased the prevalence of

ventricular hypertrophy, atrial fibrillation, and change of diastolic function [48]. Ejection fraction and maximum heart rate during exercise were also lower in the older populations than the younger ones [49]. Similar to age, studies demonstrated sex plays a role in the maintenance of cardiac function, which had been known as the effect of sex hormone [50,51]. The prevalence of coronary heart disease for the male is also twice higher than in female at each age stage before 65 years old [17,52]. Following the different prevalence of the cardiac disease by sex and age, participants were separated and grouped by sex and different age range to control the potential confounding factors in the current study. The correlation between T1 relaxation time and clinical parameters varied and whether the involvement of anatomical and physiological differences from sex might be needed to be further evaluated.

Study limitation

The limitation on the participants group is mainly from the quantitation fluctuation due to acquisition parameters such as scanner types and imaging parameters [53]. However, the values of T1 and T2* mapping is valid for a 3 T scanner. Besides, the potential factors, such as the blood supplement, hormone protection, and effect of other cardiovascular risk factors, should be further controlled and investigated the reference values from CMRI of healthy participants in the multiple-center study.

Conclusion

The current study demonstrated the reference values of T1 and T2* relaxation time of healthy Taiwanese participants in a single center. These reference values could be used to compare whether cardiac quantitative mapping from healthy participants in different studies is consistent. The relationship between clinical parameters (pulses rate, blood pressure, and ejection fraction) and T1 relaxation time from specific cardiac partitions was also established.

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Conflicts of interest

All authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bj.2020.08.013.

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