Impact of Myocardial Scars on Left Ventricular Deformation in Type 2 Diabetes Mellitus After Myocardial Infarction by Contrast-Enhanced Cardiac Magnetic Resonance

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Research Article

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Abstract

Background

Type 2 diabetes mellitus (T2DM) is a major risk factor for coronary artery disease and myocardial infarction (MI). The interaction of diabetic cardiomyopathy and MI scars on myocardial deformation in T2DM patients is unclear. Therefore, we aimed to evaluated myocardial deformation using cardiac magnetic resonance (CMR) in T2DM patients with previous MI and investigated the influence of MI on left ventricular (LV) deformation.

Methods

Two hundred and two T2DM patients, including 46 with MI (T2DM(MI+)) and 156 without MI (T2DM(MI−)), and 59 normal controls who underwent CMR scans were included. Myocardial scars were assessed by late gadolinium enhancement. LV function and deformation, including LV global function index, LV global peak strain (PS), peak systolic strain rate (PSSR), and peak diastolic strain rate (PDSR), were compared among these groups. Correlation analysis and multivariate linear regression analyses were used to investigate the relationship between myocardial scars and LV deformation.

Results

There was a decrease in LV function and LV global PS, PSSR, and PDSR in the T2DM(MI+) group compared with those of the other groups. Furthermore, reduced LV deformation ($p < 0.017$) was observed in the T2DM(MI+) group with anterior wall infarction. The increased total LV infarct extent and infarct mass of LV were related to decreased LV global PS (radial, circumferential, and longitudinal directions; $p < 0.01$), and LV global PSSR (radial and circumferential directions, $p < 0.02$). Multivariate analysis demonstrated that NYHA functional class and total LV infarct extent were independently associated with LV global radial PS ($\beta = −0.400$ and $\beta = −0.446$, respectively, all $p < 0.01$; model $R^2 = 0.37$) and circumferential PS ($\beta = −0.339$ and $\beta = −0.530$, respectively, all $p < 0.01$; model $R^2 = 0.41$), while LV anterior wall infarction was independently associated with LV global longitudinal PS ($\beta = −0.398$, $p = 0.006$).

Conclusions

The myocardial scarring size in T2DM patients after MI is negatively correlated with LV global PS and PSSR, especially in the circumferential direction. Additionally, different MI regions have different effects on the reduction of LV deformation, and relevant clinical evaluations should be strengthened.

Introduction

Diabetic cardiomyopathy (DCM) is defined as myocardial dysfunction that is independent of coronary artery disease and hypertension and can lead to heart failure.$^{1,2}$ Diastolic dysfunction is one of the important indicators of early left ventricular (LV) dysfunction prior to reduced LV ejection fraction in DCM, and impaired global longitudinal strain was associated with cardiovascular events in type 2 diabetes mellitus (T2DM) patients.$^{3−5}$ As DCM develops, myocardial microvascular dysfunction, remodeling of the extracellular matrix are also related in contractile dysfunction in DCM.$^6$ Coronary artery disease and myocardial infarction (MI) are major causes of global morbidity and mortality, and T2DM is considered a major risk factor for coronary artery disease, T2DM patients are at high risk of MI and have a poor prognosis.$^7,8$ Previous studies have pointed out that the MI size and transmurally in MI patients has an important effect on the prognosis and survival. In patients with previous MI, myocardial scarring causes weakened or even contradictory LV wall movement, fibrotic repair of the infarcted area, and compensatory cardiomyocyte hypertrophy in remote infarcted areas, all of which have an impact on the LV myocardial deformation.$^9$ At present, few studies have been carried out on the effect of myocardial scar on myocardial deformation after MI in T2DM patients with DCM.

Cardiac magnetic resonance (CMR) imaging, which has been commonly used in the last decades in clinical practice, provides information on various characteristics of cardiac structure, function, and myocardial tissue.$^{10−12}$ CMR feature tracking has been used to measure myocardial deformation.$^{13}$ The late gadolinium enhancement (LGE) sequence detects and assesses myocardial scar location with high spatial resolution and quantifies the area of the MI.$^{14}$ Therefore, this study aimed to evaluate myocardial deformation using CMR in T2DM patients with previous MI and to investigate the influence of MI scar on LV deformation.
Study population

The study protocol was approved by Biomedical Research Ethics Committee of our hospital. Initially, we retrospectively enrolled 698 patients who were diagnosed with T2DM according to the World Health Organization standards, between January 2015 and May 2021, and all the patients have completed CMR examinations\(^{15}\). Exclusion criteria were as follow: (1) known cardiomyopathy, congenital heart disease, or valvular heart disease (confirmed by echocardiography, electrocardiogram, or coronary computed tomographic angiography); (2) uncontrolled hypertension (systolic blood pressure > 160 mmHg); and (3) severe renal failure (estimated glomerular filtration rate, eGFR < 30 ml/min). Following these criteria, a total of 227 T2DM patients were included in this study, of which 156 T2DM patients (48 males and 106 females; mean age 55.55 ± 11.8 years) had no previous MI or coronary revascularization, 25 T2DM patients had acute or subacute MI during CMR examination, and 46 T2DM patients (28 males and 18 females; mean age 61.54 ± 9.11 years) had previous acute MI (> 6 months). Final, we exclude the 27 T2DM patients had acute or subacute MI. In this study, the MI was defined according to the European Society of Cardiology/American College of Cardiology/American Heart Association committee criteria\(^{16}\). In addition, age-, sex-, and body mass index-matched healthy volunteers were recruited in the controls group. Exclusion criteria for the control group were as follows: (1) DM or impaired glucose tolerance; (2) known acute or chronic disease such as hypertension; (3) presence of dyspnea, chest pain, palpitation or other cardiovascular disease-related symptoms; (4) electrocardiogram abnormalities; and (5) cardiovascular abnormalities detected by CMR (perfusion defect, local, or diffuse myocardial late-gadolinium enhancement, abnormal ventricular motion, valvular stenosis, etc.). Hence, 59 healthy controls (27 males and 32 females; mean age 58.53 ± 8.23 years) were included in this study. A detailed flow chart of the present study is provided by Fig. 1.

Clinical characteristics, family history, surgery history, medication, and serum biochemical indexes of all patients and healthy controls were collected. Blood sampling for serum biochemical indexes was performed within one week of the CMR scan without changing the subject's medication regimen.

CMR scanning protocol

All subjects underwent CMR scan using a 3.0-T whole-body scanner (Skiya; Siemens Medical Solutions, Erlangen, Germany) in the supine position. A standard ECG-triggering device was used and end-inspiratory breath holding were performed. Following a survey scan, cine images such as long-axis four-chamber views and short-axis two-chamber views were acquired using a steady-state free-precession sequence (temporal time = 39.34 ms, echo time = 1.22 ms, flip angle = 40°, slice thickness = 8 mm, field of view = 360 × 300 mm\(^2\), matrix size = 256×166). Gadobenate dimeglumine (MultiHance; Bracco, Milan, Italy) was intravenously injected at a dose of 0.2 ml/kg body weight at an injection rate of 2.5–3.0 ml/s, followed by a 20 ml saline flush at a rate of 3.0 ml/s. Late gadolinium enhancement (LGE) images were acquired in the corresponding slice position as the cine imaging 10–15 min after contrast injection. The images were obtained using a phase-sensitive inversion recovery sequence with the follow parameters: temporal time = 300ms, echo time = 1.44 ms, flip angle = 40°, slice thickness = 8 mm, field of view = 275 × 400 mm\(^2\), matrix size = 256×184.

CMR data analysis

All CMR images data to an offline workstation using a semi-automated software (Cvi42; Circle Cardiovascular Imaging, Inc., Calgary, Canada). Endocardial and epicardial traces were delineated manually by two experienced radiologists in the serial short-axis slices during the end-diastolic and end-systolic phases(figure 2.). Papillary muscles were considered as part of the ventricular cavity, and epicardial fat was excluded. Subsequently, LV functional parameters and LV mass were automatically determined. LV remodeling was characterized by the ratio of LV mass to LVEDV (LVMVR). The LV global function index (LVGFI) was calculated using the following formula:

\[
\text{LVGFI} = \left( \frac{\text{LSSV}}{\left( \frac{\text{LVEDV} + \text{LVESV}}{2} \right) + \left( \frac{\text{LV mass}}{1.05} \right)} \right) \times 100
\]

For analysis of LV myocardial strain, long-axis 2-chamber, 4-chamber, and short-axis slices were loaded into the 3-dimensional tissue tracking module, and the LV global myocardial strain parameters were acquired automatically, including radial, circumferential, and longitudinal peak strain (PS), peak systolic strain rate (PSSR), and peak diastolic strain rate (PDSR). For LGE imaging analysis, LV segment–based analysis was performed in accordance with the 16-segment model of the American Heart Association. The hyper-enhanced myocardium area was defined as myocardial scar on the LGE short-axis images when the signal intensity was five standard deviations above the mean intensity of the normal myocardium (Figure 2)\(^{17}\). We assessed the extent of the LGE regions involving the LV wall, dividing it into the interventricular septum, anterior wall, inferior wall and lateral wall using the 16-segment model. Two radiologists evaluated the images separately, and if the results were inconsistent, they discussed and agreed on the result.

Variability analysis
To determine intra-observer variability, LV deformation and LGE parameters in 70 random cases that included 50 T2DM patients and 20 normal controls were measured twice within a week interval by a radiologist. Then, a second radiologist, who was blinded to the first investigator's results reperformed the measurements to assess the inter-observer variability.

**Statistical analysis**

Statistical analyses were performed with commercially available SPSS (version 21.0 for windows; SPSS, Inc., Chicago, IL, USA). Continuous variables are presented as the mean ± standard deviation, or as median values and interquartile ranges. One-way analysis of variance test was performed to evaluate the differences among the following groups: T2DM with MI, T2DM without MI and normal control. Based on Bonferroni's correction for multigroup comparisons, p-values of < 0.017 were considered as statistically significant. Spearman's and Pearson's correlation analysis were conducted to identify the relationship between infarction and cardiac deformation. Moreover, multivariable stepwise linear regression analysis was employed to identify the relationship between infarction parameters and cardiac dysfunction. Variables with a prob- ability value of 0.1 in the univariable analyses were then included in a stepwise multivariable analysis based on a linear regression model. A p-value of < 0.05 was considered statistically significant.

**Results**

**Patient characteristics**

Of the 202 T2DM patients, 156 were in T2DM(MI-) group (48[30.7%]) males, mean age 55.55±11.80 years) and 46 in T2DM(MI+) group (28[60.8%]) males, mean age 61.54±9.11 years). Table 1 presents their baseline characteristics, cardiovascular risk factors, metabolic parameters, and medications. The results showed that there were no statistically significant differences in the baseline characteristics among these groups, except that there were more males in the T2DM(MI+) group than in T2DM(MI-) group. As for cardiovascular risk factors, more patients were previous or current smoker (50.5% vs. 28.3%) in T2DM(MI+) group than that in T2DM(MI-) group. For cardiovascular risk factors, metabolic parameters, and medications. The results showed that there were no statistically significant differences in the baseline characteristics among these groups, except that there were more males in the T2DM(MI+) group than in T2DM(MI-) group. As for cardiovascular risk factors, more patients were previous or current smoker (50.5% vs. 28.3%) in T2DM(MI+) group than that in T2DM(MI-) group, but there was no difference in hyperlipidemia or family history of T2DM between the groups. HbA1c and GLU showed no statistically significant differences between the T2DM(MI+) and T2DM(MI-) groups.

In the T2DM(MI+) group, 20 patients received percutaneous coronary intervention, and one patient received coronary artery bypass grafting surgery. A total of 34 patients were identified with culprit vessels, among which 14 (30.43%) were the left anterior descending coronary artery (LAD), 6 (13.0%) were the left circumflex coronary artery (LCx) and 14 (30.43%) were the right coronary artery (RCA).

**Comparison of the LV function and deformation among three groups**

The CMR imaging results for LV function and deformation are summarized in Table 2. LVESVi was higher in the T2DM(MI-) group than in the control group. LVESVi, and LV mass were higher (all p < 0.005) in the T2DM(MI+) group compared with the T2DM(MI-) and normal control groups. Meanwhile, LVMiVi (T2DM(MI+) vs. T2DM(MI-): 39.33(31.96–46.71) vs. 48.17(41.04–54.36); T2DM(MI+) vs. control: 39.33(31.96–46.71) vs. 47.52(42.13–53.67), p < 0.001) and LVGFI (T2DM(MI+) vs. T2DM(MI-): 27.37(18.12–40.02) vs. 39.99(44.38–54.33); T2DM(MI+) vs. control: 27.37(18.12–40.02) vs. 51.56(48.03–56.06), p < 0.001) were lower in the T2DM(MI+) group compared with the T2DM(MI-) and control groups.

Regarding LV deformation, the global radial PS, global circumferential PS, and global longitudinal PS (all p < 0.001) were lower in the T2DM(MI+) group than in the T2DM(MI-) and control groups. The global circumferential PS (p = 0.001) were lower in the T2DM(MI-) group than in the control group. There was no statistically significant difference in global radial PS between the T2DM(MI-) and control group. The global radial, circumferential and longitudinal PSSR and PDSR (all p < 0.001) were significantly lower in the T2DM(MI+) group than those in the T2DM(MI-) and control groups. except for longitudinal PDSR in the T2DM(MI+) group compared with the T2DM(MI-) group. For the T2DM(MI+) group, the circumferential and longitudinal PDSR were lower than those in the control group (p < 0.017).

**LV infarct characteristics analysis**

**Association between LV deformation and LGE size in T2DM patients with MI**
In this study, the range of infarct size of LV and total LV infarct extent were 17.96(11.07-25.26) and 17.12(9.58-27.53), respectively. As shown in Table 3, for T2DM(MI+) patients, there was a negative correlation between increased infarction size and decreased LVGFI (all \(p < 0.001\) and LV global PS in all three directions (all \(p < 0.01\)). LV global radial and circumferential PSSR were inversely correlated with total LV infarct extent (\(r = -0.353, p = 0.016; r = 0.533, p < 0.001,\) respectively), enhanced mass of LV (\(r = -0.302, p = 0.042; r = 0.525, p < 0.001,\) respectively), and enhanced area of LV (\(r = -0.297, p = 0.045; r = 0.528, p < 0.001,\) respectively) in T2DM patients with chronic MI. However, LV global longitudinal PSSR and global PDSR in the three directions showed no significant relationship with infarction size (all \(p > 0.05\)).

Multivariate linear regression analysis demonstrated that NYHA functional class and total LV infarct extent were independently associated with global radial PS (\(\beta = -0.400, p = 0.002;\) and \(\beta = -0.446, p = 0.001,\) respectively; model \(R^2 = 0.37\)) and global circumferential PS (\(\beta = -0.339, p = 0.006;\) and \(\beta = -0.530, p = 0.001,\) respectively; model \(R^2 = 0.41\)).

**Association between LV deformation and LGE area in T2DM patients with MI**

Regarding infarction-involve regions in the T2DM(MI+) group, 28 patients had LGE areas involving the interventricular septum, 20 involving the LV inferior wall, 13 involving the LV lateral wall, and 12 involving the LV anterior wall. There were no LGE areas detected in the T2DM(MI−) group.

For the LGE area in different regions of the LV wall, patients with anterior wall infarction had lower LV global radial PS (anterior vs. non-anterior: 11.91 ± 1.924 vs. 18.45 ± 1.671, \(p = 0.037\)), circumferential PS (anterior vs. non-anterior: -8.447 ± 0.7525 vs. -13.24 ± 0.8778, \(p = 0.034\)). figure.3 and longitudinal PS (anterior vs. non-anterior: -5.289 ± 0.4827 vs. -8.351 ± 0.6052, \(p = 0.006\)). Patients with interventricular septum infarction have lower LV global longitudinal PS (interventricular septum vs. non-interventricular septum: -6.515 ± 0.708 vs. -8.503 ± 0.6702, \(p = 0.043\)) (Figure.4). In addition, LV anterior wall infarction was independently associated with global longitudinal PS (\(\beta = -0.398; p = 0.006,\) model \(R^2 = 0.16;\) Table 4).

**Inter- and Intraobserver variability**

Table 5 summarizes the inter- and Intraobserver variability for LV deformation and LGE analysis. The ICCs for intra- and interobserver variability were 0.828–0.959 and 0.777–0.955, respectively, for LV deformation, and 0.827–0.895 and 0.882–0.893 respectively, for LGE parameters, which suggesting that both techniques are in agreement.

**Discussion**

T2DM is a chronic metabolic disease involving multiple organs, and the main reason for the increasing mortality of patients with T2DM is DCM. In addition, T2DM is a high-risk factor for cardiovascular events such as coronary heart disease and MI\(^{18,19}\). In this study, the following principal findings were obtained: 1) T2DM (MI−) patients have reduced LV longitudinal deformation, while T2DM (MI+) patients have reduced deformation in all three directions, especially circumferential deformation; 2) in T2DM (MI+) patients, LV global PS, and PSSR are decreased, which is related to the extent of myocardial scarring; and 3) anterior wall infarction, and then ventricular septal infarction, are more likely to lead to decreased LV deformation in T2DM (MI+) patients.

The pathogenesis of DCM is complex and multifactorial, and several causative mechanisms, include metabolic effects on myocytes, myocardial steatosis, myocardial fibrosis, microangiopathy, and autonomic nervous dysfunction\(^{20–22}\). Microvascular ischemia of DCM is most likely to occur in the sub-endocardium, where the longitudinal myocardial fibers are predominantly located; therefore, a reduction in longitudinal LV deformation occurs in the early stages of DCM. As in previous studies, our results show reduced longitudinal PS but preserved circumferential and radial PS in T2DM (MI−) patients compared to control subjects\(^{23}\). However, for T2DM patients after MI, deformation in all three directions of LV global PS were decreased, and were especially reduced in the circumferential rather than the longitudinal direction. We speculate that after MI and scar formation in T2DM (MI−) patients, the myocardial cells in the scar area are replaced by the fibrous matrix, and local ventricular wall movement is reduced or impaired to varying degrees. Different from the longitudinal myocardial fibers, circumferential myocardial fibers are mainly located subepicardial, resulting in significantly reduced circumferential LV deformation\(^{24}\). Additionally, reduced longitudinal and circumferential PDSR suggests that diastolic dysfunction begins in the initial stage of DCM, which we have shown in our previous research\(^{25,26}\). LV enlargement, especially LVESV, and reduced LVEF, are common cardiac morphological changes after MI, which was more significant than the early diastolic functional damage of DCM. Therefore, in our study, T2DM(MI+) patients had not only decreased PDSR, but also decreased PSSR in all three directions.
LGE-CMR is considered the best available technique for noninvasive assessment of myocardial scar tissue following MI, and it quantitatively evaluates the myocardial scar, discriminates the infarction transmurally, and defines the infarct territory of the LV ventricular wall\textsuperscript{27}. Scarring extent and size are strictly related not only to adverse cardiac remodeling but also to cardiovascular events\textsuperscript{28}. Scar recognition is also a potential predictor for arrhythmia substrates, Histological examination has shown that isolated bundles of surviving myocytes are interwoven within strands of fibrous tissue. These viable cells can form reentry circuits within fibrous tissue, thus contributing to ventricular tachycardia\textsuperscript{29}.

Previous studies have shown that there is a correlation between the extent of MI and LV deformation in acute MI patients\textsuperscript{9,30}. However, after acute MI, with the absorption of myocardial edema and inflammation, or infarction core fiber gliosis, the delayed enhancement area of LGE imaging changes. We found that on the basis of DCM, which inherently exists myocardial deformation and damage, myocardial scarring after MI has a significant negative correlation with LV radial, circumferential, and longitudinal PS and PSSR. This indicates that after acute MI, the recovery of LV myocardial systolic function and deformation, is affected by the extent and quality of MI, especially in the circumferential direction. Furthermore, we also found that T2DM (MI+) patients had reduced LV global PDSR in the three directions compared to T2DM (MI-) patients, but there was no correlation between LV global PDSR and the extent of myocardial scarring. The decreasing in PDSR does not seem to be directly related to the local myocardial scarring, but may be secondary to reduced LV systolic function. Decreased LV function may further lead to myocardial metabolic disorder, and hyperglycemia may have an additive effect on diastolic dysfunction, which further leads to reduced LV PDSR. These speculations need to be verified by further studies.

At present, a few studies have explored the relationship between MI territory (involving the interventricular septum, anterior wall, lateral wall or inferior wall) and LV global deformation and peak strain rate. The results in this study show that if MI involved in the LV anterior wall, the LV global PS in all three directions is significantly affected, and anterior wall involvement is an independent factor for the decrease in LV global longitudinal PS. Most of the Culprit vessel in the infarction of the LV anterior wall was LAD, while the right bundle branch and left anterior fasicular are slender, and the LAD is the only blood supply. When LAD stenosis and the blood supply is blocked, there might be an effect on LV deformation. More studies have focused on the stratification effects of MI size on prognosis and survival risk, and these studies have shown that MI size is an important predicator for the quality of life of patients\textsuperscript{31,32}. However, the MI involved different areas of the LV wall may result in different prognoses, implying that more attention should be paid to LV infarction involvement in future clinical evaluation.

**Limitations**

There are several limitations to our study. First, this study was a single-center study, so there may be some biases influencing the results. Second, the medication and the NT-proBNP of the control group was not measured. However, the detailed history and the physical examination report were carefully checked to ensure that inclusion criteria were met. Thirdly, since this was a retrospective study, the long term development in T2DM patients after myocardial infarction should be further investigated in follow-up in the future.

**Conclusions**

The study found that systolic dysfunction is more likely to occur in T2DM patients after MI, with a significant reduction in LV global circumferential deformation. The size of myocardial scarring is negatively correlated with the LV global PS and PSSR. In addition, MI in different regions has different effects on the reduction of LV deformation. Therefore, more attention should be paid to MI scarring and involved scope in T2DM patients in clinical evaluations.

**Abbreviations**

DM: diabetes mellitus; T2DM: Type 2 diabetes mellitus; DCM: diabetic cardiomyopathy; CMR: cardiac magnetic resonance; LGE: late gadolinium enhancement; LV: left ventricular; LVGFI: left ventricular global function index; MI: myocardial infarction; PDSR: peak diastolic strain rate; PS: peak strain; PSSR: peak systolic strain rate; LAD: left anterior descending coronary artery; EDVi: End-diastolic volume index; ESVi: End systolic volume index; SVi: Stroke volume index; LVEF: Left ventricle ejection fraction; ICC: Intraclass correlation coefficient.

**Declarations**

**Ethics approval and consent to participate**
The study complied with the Declaration of Helsinki and was approved by the West-China hospital of Sichuan University biomedical research ethics committee (Chengdu, Sichuan, China; No. 2016-24).

Consent for publication
Not applicable.

Availability of data and materials
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest
The authors declare that there are no conflicts of interest.

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Authors’ Contributions
YG and ZGY designed the study. YG performed the experiments, and wrote the manuscript. YL participated in the study design, analyzed the data, drafted the manuscript and editing and review of the manuscript. YZG supervised the overall study and contributed to study design, editing and review of the manuscript. YG and HYX performed the experiments and review the manuscript. YG, XLW and RS performed the experiments and was responsible for collecting, sorting and statistical data. ZGY is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Tables

Table 1

Baseline characteristics of the study cohort
|                          | Normal (n=59) | T2DM (MI -) (n=156) | T2DM (MI +) (n=46) |
|--------------------------|---------------|----------------------|--------------------|
| **Baseline characteristics** |               |                      |                    |
| Age, years               | 58.53±8.23    | 55.55±11.8           | 61.54±9.11         |
| Male, n (%)              | 27(48.2%)     | 48(30.7%)            | 28(60.8%) §        |
| BMI, kg/m²               | 23.17±3.14    | 23.67±3.06           | 25.32±3.35         |
| Systolic blood pressure, mmHg | 120.19±8.85 | 127.96±13.11         | 123.67±19.27       |
| Diastolic blood pressure, mmHg | 75.73±10.36 | 79.88±9.88           | 77.89±12.76        |
| Heart rate, bpm          | 73.28±10.85   | 72.67±15.42          | 73.80±14.60        |
| **Cardiovascular risk factors** |           |                      |                    |
| Previous/current smoker, n (%) | 9(15.2%)  | 44(28.3%)            | 23(50.5%) §        |
| Hyperlipidemia           |              |                      |                    |
| Family history of DM     | 0             | 32(20.5%)            | 11(23.9%)          |
| Pervious PCI, n (%)      | 0             | 0                    | 20(43.5) %         |
| Previous CABG, n (%)     | 0             | 0                    | 1(2.2) %           |
| **NYHA functional class, n** |           |                      |                    |
| I                        | -             | -                    | 3(6.5) %           |
| II                       | -             | -                    | 27(58.7) %         |
| III                      | -             | -                    | 15(32.6) %         |
| IV                       | -             | -                    | 1(2.2) %           |
| **Culprit vessel n (%)** |               |                      |                    |
| LM                       | -             | -                    | 0                  |
| LAD                      | -             | -                    | 14(30.43) %        |
| LCx                      | -             | -                    | 6(13.0) %          |
| RCA                      | -             | -                    | 14(30.43) %        |
| **Metabolic characteristics** |           |                      |                    |
| HbA1c, %                 | 5.46±0.34     | 7.82±0.87            | 8.10±1.32          |
| GLU, mmol/L              | 5.08±0.45     | 8.28±1.23            | 8.78±2.34          |
| eGFR, mL/min/1.73m2      | 107.23±8.45   | 95.84 ± 9.32         | 79.60±10.45        |
| NT-proBNP                |              |                      | 874(204.75-2032.75) |
| **Medication, n (%)**    |               |                      |                    |
| Aspirin                  | -             | 17(6.5) %            | 28(60.8) %         |
| β-blockers               | -             | 0                    | 11(19.6) %         |
| ACEI/ARB, n (%)          | -             | 5(3.2) %             | 16(34.7) %         |
| Diuretics                | -             | 1(0.06) %            | 13(28.2) %         |
| Calcium-channel blocker  | -             | 8(5.1) %             | 5(10.8) %          |
| Insulin                  | -             | 36(23.1) %           | 7(15.2) %          |
| Statin                   | -             | 6(3.8) %             | 14(30.4) %         |
T2DM: type 2 diabetes mellitus; MI: myocardial infarct; BMI: body mass index; PCI: Percutaneous Transluminal Coronary Intervention; CAGB: coronary artery bypass grafting; NYHA: New York Heart Association; HbA1c: glycated hemoglobin; Glu: glucose, eGFR estimated glomerular filtration rate; ACEI: angiotensin converting enzyme inhibitor.

* p < 0.017 versus normal group (Bonferroni's)
§ p < 0.017 versus T2DM patients without MI (Bonferroni's)

Table 2

CMR findings between normal individuals, T2DM (MI-) group and T2DM (MI+) group
|                         | Normal (n=59) | T2DM (MI (−)) (n=156) | T2DM (MI (+)) (n=46) |
|-------------------------|---------------|------------------------|----------------------|
| LVEDVi, ml/m²           | 70.75(63.97-80.18) | 76.49(67.45-84.18) | 114.56(80.18-137.75) |
| LVESVi, ml/m²           | 23.64(19.16-28.39) | 26.46(20.92-32.32) | 72.52(39.62-102.18) |
| LVSVi, ml/m²            | 47.52(42.13-53.67) | 48.17(41.04-54.36) | 39.33(31.96-46.71) |
| LCO, l/min              | 5.54(5.00-6.63) | 5.85(4.56-7.00) | 5.11(3.95-6.25) |
| LVEF, %                 | 66.14(62.85-70.86) | 64.74(59.32-69.69) | 38.26(24.75-55.68) |
| LV mass, g/m²           | 77.61(68.40-88.32) | 91.86(74.13-111.40)| 127.80(103.68,156.91) |
| LVGFI, %                | 51.56(48.03-56.06) | 48.99(44.38-54.33) | 27.37(18.12-40.02) |
| PS, %                   |               |                       |                       |
| Radial                  | 35.32(32.38-40.72) | 32.11(25.73-38.83) | 14.71(9.29-22.83) |
| Circumferential         | -20.92(-22.67-(-18.84)) | -19.56(-21.47-(-17.64)) | -11.11(-16.10 -(-8.68)) |
| Longitudinal            | -15.03(-16.68-(-12.31)) | -12.24(-14.67-(10.08)) | -7.41(29.95(-4.75)) |
| PSSR, 1/s               |               |                       |                       |
| Radial                  | 2.05(1.77-2.48) | 1.745(1.41-2.26) | 0.83(0.61-1.44) |
| Circumferential         | -1.02(-1.15-(-0.92)) | -0.98(-1.13-(-0.86)) | -0.61(-0.81-(-0.45)) |
| Longitudinal            | -0.75(-0.87-(-0.67)) | -0.69(-0.86-(-0.55)) | -0.38(-0.56(-0.20)) |
| PDSR, 1/s               |               |                       |                       |
| Radial                  | -2.80(-3.22-(-2.12)) | -2.05(-2.65-(-1.58)) | -0.83(-1.24-(-0.51)) |
| Circumferential         | 1.32(1.19-1.53) | 1.12(0.97-1.36) | 0.65(0.50-0.93) |
| Longitudinal            | 0.93(0.70-1.11) | 0.79(0.60-0.97) | 0.49(0.33-0.62) |
| Infarct size, g         | -               | -                       | 20.69(11.69-32.12) |
| Infarct size, g % of LV | -               | -                       | 17.96(11.07-25.26) |
| Total LV infarct extent (%) | -               | -                       | 17.12(9.58-27.53) |
| Infarct territory, n (%) |               | -                       | -                       |
| Interventricular septum | -               | -                       | 22(47.8%) |
| Inferior                | -               | -                       | 20(43.4%) |
| Lateral                 | -               | -                       | 13(28.2%) |
| Anterior                | -               | -                       | 12(26.09%) |

Notes: Data are presented as median (25th, 75th percentile).
LVEDVi, left ventricular end diastolic volume index; LVESVi, left ventricular end systolic volume index; LVSVi, left ventricular stroke volume index; LVEF, left ventricular ejection fraction; LVGFI: left ventricular global function index; MI: myocardial infarction; PDSR: peak diastolic strain rate; PS: peak strain; PSSR: peak systolic strain rate

* p < 0.017 versus normal group (Bonferroni’s)
§ p < 0.017 versus T2DM patients without MI (Bonferroni’s)
Table 3

Correlation analysis of LV global strain parameters with the myocardial infarction parameters

|                  | Total LV infarct extent (%) | enhanced mass (g % of LV) | enhanced area (ml % of LV) |
|------------------|-----------------------------|---------------------------|-----------------------------|
|                  | r                           | P                         | r                           | P               |
| LVGFI, %         | -0.533**                    | <0.001                    | -0.507**                    | <0.001          |
|                  |                             |                           | -0.506**                    | <0.001          |
| PS, %            |                             |                           |                             |                 |
| Radial           | -0.455**                    | 0.001                     | -0.437**                    | 0.002           |
|                  |                             |                           | -0.435**                    | 0.001           |
| Circumferential  | 0.538**                     | <0.001                    | 0.530**                     | <0.0001         |
|                  |                             |                           | 0.533**                     | 0.000           |
| Longitudinal     | 0.395**                     | 0.007                     | 0.434**                     | 0.003           |
|                  |                             |                           | 0.431**                     | 0.007           |
| PSSR, %          |                             |                           |                             |                 |
| Radial           | -0.353*                     | 0.016                     | -0.302*                     | 0.042           |
|                  |                             |                           | -0.297*                     | 0.045           |
| Circumferential  | 0.533**                     | <0.001                    | 0.525**                     | <0.001          |
|                  |                             |                           | 0.528**                     | <0.001          |
| Longitudinal     | 0.097                       | 0.520                     | 0.106                       | 0.484           |
|                  |                             |                           | 0.110                       | 0.465           |
| PDSR, %          |                             |                           |                             |                 |
| Radial           | 0.160                       | 0.287                     | 0.163                       | 0.280           |
|                  |                             |                           | 0.172                       | 0.254           |
| Circumferential  | -0.235                      | 0.116                     | -0.220                      | 0.141           |
|                  |                             |                           | -0.218                      | 0.146           |
| Longitudinal     | -0.123                      | 0.417                     | -0.083                      | 0.586           |
|                  |                             |                           | -0.071                      | 0.639           |

*p < 0.05

**p < 0.01

Table 4

Univariable and multivariable linear regression analysis of LV global PS

Table 5

Inter- and intra-observer variability of tissue tracking and LGE
|                      | Radial PS (%) | Circumferential PS (%) | Longitudinal PS (%) |
|----------------------|---------------|------------------------|---------------------|
|                      | Univariable   | Multivariable          | Univariable         | Multivariable       | Univariable | Multivariable |
|                      | $r$           | $P$ value              | $r$                | $P$ value          | $r$         | $P$ value       |
| Age                  | -0.107        | 0.480                  | 0.057              | 0.707              | -0.045      | 0.768           |
| gender               | -0.262        | 0.079                  | 0.269              | 0.071              | 0.262       | 0.079           |
| NYHA functional class| -0.400        | 0.006                  | -0.400             | 0.002              | 0.322       | 0.029           |
| BMI                  | 0.160         | 0.287                  | -0.112             | 0.458              | -0.060      | 0.693           |
| Hyperlipidemia       | 0.151         | 0.318                  | -0.200             | 0.182              | -0.027      | 0.860           |
| Smoking              | -0.252        | 0.091                  | 0.310              | 0.026              | 0.336       | 0.022           |
| Total LV infarct extent (%) | -0.455 | 0.001                  | -0.446             | 0.001              | 0.538       | <0.001           |
|                      |              |                        |                    |                    | 0.395       | 0.007           |
| Anterior infarct     | -0.317        | 0.032                  | 0.433              | 0.003              | 0.410       | 0.005           |

|                      | Intra-observer (n = 70) | 95% CI            | Inter-observer (n = 70) | 95% CI            |
|----------------------|-------------------------|-------------------|-------------------------|-------------------|
| PS, %                |                         |                   |                         |                   |
| Radial PS (%)        | 0.959                   | 0.901–0.982       | 0.955                   | 0.905–0.979       |
| Circumferential PS (%)| 0.932                  | 0.851–0.969       | 0.938                   | 0.866–0.972       |
| Longitudinal PS (%)  | 0.923                   | 0.831–0.965       | 0.883                   | 0.745–0.947       |
| PSSR, 1/s            |                         |                   |                         |                   |
| Radial               | 0.938                   | 0.899–0.977       | 0.920                   | 0.833–0.962       |
| Circumferential      | 0.866                   | 0.862–0.968       | 0.915                   | 0.823–0.960       |
| Longitudinal         | 0.828                   | 0.717–0.935       | 0.849                   | 0.516–0.948       |
| PDSR, 1/s            |                         |                   |                         |                   |
| Radial               | 0.952                   | 0.871–0.970       | 0.925                   | 0.843–0.964       |
| Circumferential      | 0.934                   | 0.720–0.936       | 0.847                   | 0.596–0.934       |
| Longitudinal         | 0.864                   | 0.641–0.918       | 0.777                   | 0.485–0.913       |
| LGE                  |                         |                   |                         |                   |
| Infarct size, g      | 0.895                   | 0.790–0.898       | 0.893                   | 0.782–0.947       |
| Infarct size, g % of LV | 0.891              | 0.780–0.896       | 0.885                   | 0.667–0.923       |
| Total LV infarct extent (%) | 0.827 | 0.544–0.905       | 0.882                   | 0.651–0.893       |

**Figures**
Figure 1

Flow chart of the study
Figure 2

Measurement of LV global strain and enhanced area in LGE Cardiac magnetic resonance tissue tracking in short-axis and long-axis two-chamber and four-chamber cine images at end-diastole (A1-3) and end-systole (B1-3). LGE images for quantification of infarct size (A4, B4) the signal intensity of yellow region was five standard deviations above the mean intensity of the normal myocardium (blue circle).

Figure 3

CMR-LGE images and 3D pseudo-color images of LV circumferential strain in T2DM(MI+) patients. A1-3: T2DM(MI+) patient with LV anterior wall and interventricular septum infarction, female, 58 years old, left ventricular short axis (A1), end-diastolic 3D pseudo-color image(A2), end-systolic 3D pseudo-color image(A3). B1-3: T2DM(MI+) patient with LV inferior wall infarction, male, 69 years old, left ventricular short axis (B1), end-diastolic 3D pseudo-color image(B2), end-systolic 3D pseudo-color image(B3).
Figure 4

Left ventricular global PS in T2DM(MI+) patients with different area of myocardial infarct involved