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# Cardiac Magnetic Resonance feature tracking for quantifying left and right Ventricles deformation in Type 2 Diabetic patients

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Diabetes Mellitus Type 2 (T2DM) related mortality and morbidity are mainly caused by cardiovascular complications. Cardiovascular Magnetic Resonance feature tracking (CMR-FT) was used as a novel tool to provide assessment quantitatively of Left and Right Ventricular. However, inadequate assessment of Right Ventricular (RV) deformation in T2DM has been reported. To determine whether the use of CMR-FT in LV and RV is effective in detecting global and regional myocardial deformations in diabetics and healthy individuals. This study involved 80 patients, 40 of whom had Type 2 DM and 40 of whom controls, who were subjected to cardiac MRI. Post-processing was done offline using CMR feature tracking followed by SPSS analysis of the data. T2DM patients and controls did not demonstrate any significant differences in the study. There was a significant reduce in the End Diastolic Volume (EDV), End Systolic Volume (ESV) and Ejection Fraction (EF) of both LV and RV in Diabetic patients as compared to healthy controls ($p < 0.001$). The LV Global Longitudinal Strain (LV GLS), LV Global Radial Strain (LV GRS), RV Global Longitudinal Strain (RV GLS), RV Global Circumferential Strain (RV GCS), RV Global Radial Strain (RV GRS) values among T2DM patients was decreased significantly ($p < 0.001$) in comparison to normal controls. The CMR-FT method could identify the LV an RV deformation and subclinical dysfunction in diabetic patients, even in those with normal EF. This study recommends that CMR-FT would be incorporated into the clinical practices due to their positive results in diagnosing myocardial deformation.

**Keywords: Cardiac magnetic resonance imaging, Feature tracking, left ventricle, Right ventricle, Type 2 Diabetes Mellitus**

## INTRODUCTION

Diabetes mellitus (DM) is one of the non-communicable chronic diseases and a major public health concern accompanied by high healthcare costs, morbidity, and early mortality (Alanazi et al. 2018).

This metabolic disorder has sharply elevated due to

a lack of physical activity, poor food habits, and obesity (Alanazi et al. 2018). According to the International Diabetes Federation (IDF), about 537 million who aged between 20 and 79 years are likely to be involved by diabetes by 2021 which means one out of every ten adults. This number would be expected to increase to 643 million by 2030, and 783 million by 2045. There are 73 million diabetics in the Middle East and North Africa, and the number is expected to rise to 135.7 million by 2045 (International Diabetes Federation, 2013).

DM is described by elevated blood sugar levels. This may leads to major macrovascular and microvascular complications such as neuropathy, retinopathy, renal failure, and cardiovascular disorder (Alanazi et al. 2018).

Diabetes-related mortality and morbidity are mainly caused by cardiovascular complications. When diabetes is untreated or ineffectively treated, it can lead into overt diabetic cardiomyopathy. Myocardial dysfunction is the most common complication of diabetes, causing clinically silent myocardial dysfunction (Gertz et al. 2018).

Diabetic cardiomyopathy can be categorized as either having coronary artery disease or hypertension (Petrie etal. 2018). In addition to advanced glycation end products, atherosclerosis, microinfarctions in the subclinical stage, mitochondrial dysfunction, and lipotoxicity, several metabolic impairments contribute to diabetic cardiomyopathy (Barrett et al. 2017). These impairments may affect both left Ventricle (LV) and right Ventricle (RV), due to their systematic nature (Aschauer et al. 2018).

It is believed that cardiovascular diseases represent a significant correlation between the RV dysfunction and myocardial disease prognosis (Aschauer et al. 2018). Furthermore, the typical parameter that defines LV or RV function and Ejection Fraction (EF), has substantial restrictions due to its volumetric nature, suboptimal reproducibility, and a loss of ability to reflect local LV function. As a result, LV and RV mechanics can be more totally illustrated by evaluating myocardial deformity (strain) non-invasively (Smiseth et al. 2016).

A myocardial strain is a deformation caused by the application of force to the myocardium and characterized by the rate at which the myocardial length changes from relaxed to contracted (Alsharari et al. 2021). As opposed to strain, ejection fraction (EF) offers the possibility of examining components of contractions in longitudinal (LS), circumferential (CS), and radial directions (RS). Non-invasive methods to analyze myocardial deformation, incudes cardiac magnetic resonance feature tracking (CMR-FT) and speckle tracking echocardiography (STE) (Katogiannis et al. 2020).

With cardiac magnetic resonance feature tracking (CMR-FT), a novel method has been developed for quantifying left and right ventricular myocardial deformation using high-resolution images (Liao et al. 2022; Lange et al. 2021; Mor-Avi et al. 2011). However, there is a lack of information about CMR-FT for both LV and RV deformation evaluation in DM patients. Thus, this study aimed to assess LV and RV longitudinal, radial and circumferential strains with features tracked through Cine SSFP CMR in diabetic patients.

## MATERIALS AND METHODS

The Institutional Ethics Review Board of the King Salman Hospital approved this study and in compliance with proper guidelines for medical research, we adhere to the Declaration of Helsinki (2000 edition). 94 volunteers were participated in this study, 14 participants were excluded, 40 subjects were diagnosed with diabetes mellitus and 40 were healthy subjects, at King Salman Specialist Hospital (KSSH)- Hail city and underwent routine CMR-FT examination between November 2021 and June 2022.

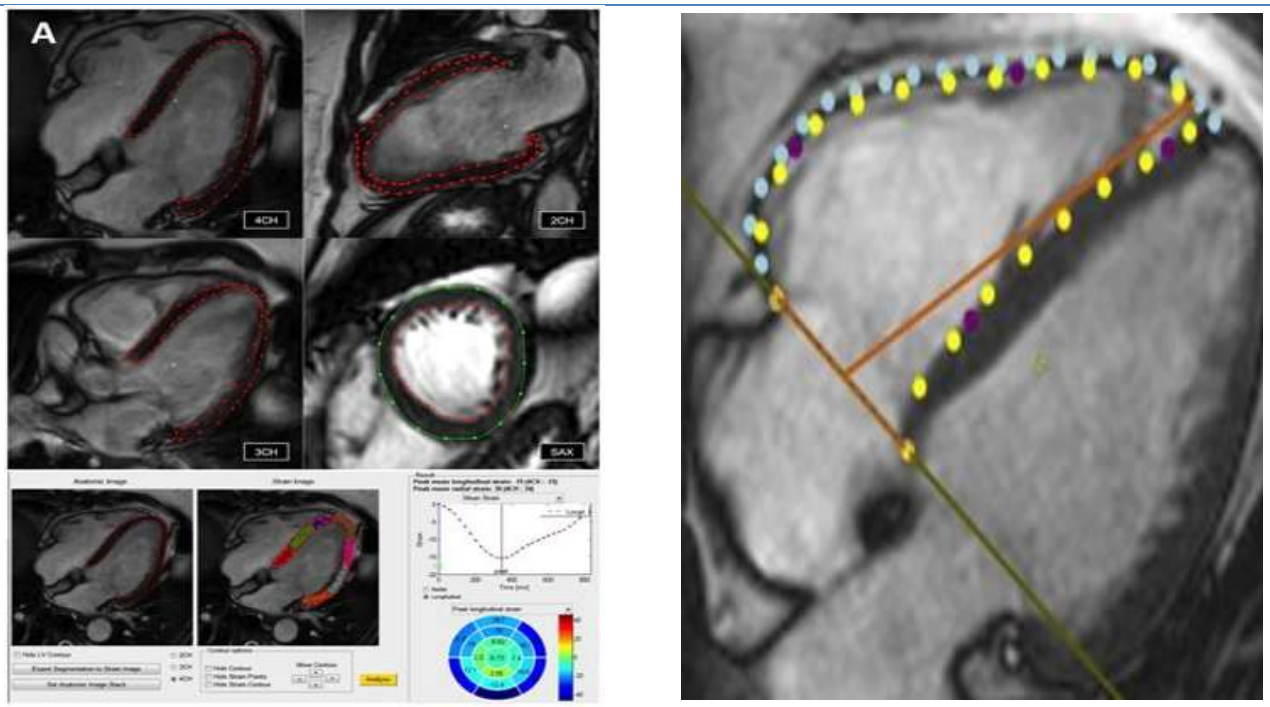
A diagnosis of Type 2 Diabetes (T2DM) at age 18 was required, without any symptoms, signs, or history of heart disease (known coronary artery disease, cardiomyopathy, or valvular heart disease); sinus rhythm; normal ejection fraction over 55%; and absence of contraindications to MR imaging.

Participants with severe renal impairment (estimated glomerular filtration rate = 30 mL/min/1.73 mm2), uncontrolled blood pressure at rest (systolic blood pressure > 180mmHg and/or diastolic blood pressure > 100mmHg), or contraindicated for MRI were excluded.

### Procedure

The research design is to analyze retrospectively CMR-FT offline data, using the software of circle CVI-42 that measures the strain in a 17-segment software-generated mode, in a different direction. Global longitudinal strain (GLS) is measured on the long axis (2,3 4 chambers views) while circumferential (GCS) and radial strains (GRS) are measured on the short axis without the need to use additional sequences.

At end-diastole, the epi- and endocardial borders were defined on all pictures. Following the initiation of an automated calculation, the used software program automatically demarcated the boundary all through the cardiac cycle. The efficiency of the tracking and contouring is visually assessed and manually corrected as appropriate. Left ventricular ejection fraction (LVEF), Right Ventricular ejection fraction (RVEF) LV and RV end diastolic volume, LV and RV end systolic volume, LV and RV stroke volume were computed based on serial short axis cine-CMR Images.




a) b)

**Figure 1: FT-CMR Myocardial strain is measured with Feature-tracking cardiac magnetic resonance imaging of LV, a) and RV, b) which are used for the analysis of myocardial segmentations and global longitudinal strains. A four-chamber view is called a 4CH; a two-chamber view is called a 2CH and a three-chamber view is called a 3CH.**

**Feature tracking CMR**

A 1.5 Tesla MRI scanner was used to perform CMR imaging. We recorded 2- and 4-chamber CVs with ECG-gated b-SSFP cine sequences as well as a short-axis stack. As a result, we used the following parameters for scanning the cardiac cycle: 40 frames per cardiac cycle, 0.8mm x 0.8mm pixel spacing, 8mm slice thickness, 1.5mTR, and 3ms TE. In order to evaluate the LVEF, the SA stack was used.

For the measurement of strain in CMR-FT, commercial software available from "CVI" was used (CVI42, Version 5.6.5, Circle Cardiovascular Imaging Inc., Calgary, Canada) (Figure 2). An FT was performed at the diastole's end. An endocardial and epicardium boundary scan was conducted on the left ventricle. The RV boundaries could also be tracked using CV in the same way. During the cardiac cycle, the tissue properties have been traced by applying tracking algorithms. The tracking accuracy was verified visually, and any modifications were made only to the initial outlines if necessary. Then, the process was recurring three times and the average was used. A global longitudinal strain measurement (GLS) was performed on the LV and RV, along with a global circumferential strain measurement (GLS/GRS) on the LV. The GLS was determined using two, three, and four long-axis CVs and averaging peak strains. In contrast, the RV strain was exclusively derived from the 2-CV and 4-CV strains. Global short axis (SA) strains (GCS and GRS) were calculated from an average of three slices: basal slices (last slices showing the entire circular myocardium with no outflow tract), midventricular slices, and apical slices (blood pool maintained throughout the cardiac cycle).

**Data analysis**

Using SPSS, the data will be analyzed (v23). If relevant, data are reported as percentages or standard deviations with a confidence level of 95%. (CI). p-values less than 0.05 were deemed statistically significant.

**RESULTS**

The inclusion criteria were met by a total of 54 patients. Fourteen participants were removed from the trial as a result of low-quality pictures (n=5), tachycardia (n=6), or an irregular pulse (n=3). In the study overall number of 80 patients was first separated into two groups: healthy individuals (n=40, mean age 52±13 years, 20 men) and T2DM patients (n=40, mean age 54±11 years, 21 men).

There was a significant difference between the levels of arterial blood pressure, fasting blood glucose, and HbA1c in patients with T2DM compared to healthy controls (p0.05), however, the level of low-density lipoprotein was not significantly different (P>0.05), this is summarized in Table 1

**Table 1: Characteristics of STE and CMR-FT in type 2 diabetes mellitus subjects and control subjects.**

| | Normal subjects (40) | T2DM (40) | p-value |
|---|---|---|---|
| **Age (yrs)** | 52±13 | 54±11 | 0.36 |
| **Male%** | 20 (50) | 21(55) | 0.84 |
| **BMI (kg/m$^2$)** | 22±1.4 | 23±1.7 | 0.21 |
| **Heart rate (bpm)** | 72±9 | 75±11 | 0.34 |
| **LVEF%** | 66±4 | 60±3 | <0.001 |
| **DBP (mmHg)** | 74±10 | 77±9 | 0.19 |
| **SBP (mmHg)** | 121±12 | 125±11 | 0.38 |
| **Fasting Plasma glycose (mmol/L)** | 4.97±0.6 | 14±3.9 | <0.001 |
| **HbA1c (%)** | 5.18±0.5 | 10.20±2.09 | <0.001 |
| **TCH (mmol/L)** | 3.8±0.7 | 3.9±0.6 | 0.62 |
| **TG (mmol/L)** | 1.1±0.2 | 1.1±0.5 | 0.34 |
| **HDL (mmol/L)** | 1.24±0.2 | 1.20±0.4 | 0.42 |
| **LDL (mmol/L)** | 2.1±0.5 | 2.2±0.6 | 0.17 |
| **CMR** | | | |
| **LVEDV (ml)** | 129±23 | 118±26 | <0.001 |
| **LVESV (ml)** | 58±17 | 42±11 | <0.001 |
| **LVSV (ml)** | 72±16 | 71±17 | 0.08 |
| **LVEF (%)** | 64±6 | 59±8 | <0.001 |
| **RVEDV (ml)** | 105±26 | 99±35 | <0.001 |
| **RVESV (ml)** | 50±17 | 40±12 | <0.001 |
| **RVSV (ml)** | 60±17 | 52 ±16 | <0.001 |
| **RVEF (%)** | 58±7 | 51±5 | <0.001 |

CMR-FT, Cardiac Magnetic Resonance Feature Tracking; GLS, Global Longitudinal Strain; GRS, Global Radial Strain; GCS, Global Circum ferential Strain, BMI, Body Mass Index, SBP Systolic Blood Pressure, DBP Diastolic Blood Pressure, TCH Total Cholesterol, TG Triglyceride, HDL High-Density Lipoprotein, LDL Low-Density Lipoprotein, LAD Left Atrial Diameter, LVEF Left Ventricular Ejection Fraction

Patients with T2DM showed levels that were noticeably lower than those in healthy individuals when compared to the values of LV GLS, LV GRS, RV GLS, RV GCS, RV GRS ($p < 0.001$). In terms of LV GCS, there were no significant differences between normal LV GCS and T2DM LV GCS. This is summarized in Table 2.

LV GCS (SAX) Left ventricle Global Circumferential Strain (Short axis), LV GRS (SAX) left ventricle Global Radial Strain (Short axis), LV GLS (LAX) left ventricle Global Longitudinal Strain (Long axis). RV GCS (SAX) Right ventricle Global Circumferential Strain (Short axis), RV GRS (SAX) Right ventricle Global Radial Strain (Short axis), RV GLS (LAX) Right ventricle Global Longitudinal Strain (Long axis).

**Table 2: Characteristics CMR-FT in type 2 diabetes mellitus subjects and control subjects**

| | Normal subjects (40) | T2DM (40) | p-value |
|---|---|---|---|
| **Feature tracking CMR** | | | |
| **LV GCS% (SAX)** | -24±6 | -22±5 | 0.32 |
| **LV GRS% (SAX)** | 22±11 | 16±7 | <0.001 |
| **LV GLS% (LAX)** | -20±5 | -15±2 | <0.001 |
| **RV GCS% (SAX)** | -8±1 | -4±2 | <0.001 |
| **RV GRS% (SAX)** | 23±5 | 19±9 | <0.001 |
| **RV GLS% (LAX)** | -12±2 | -8±4 | <0.001 |

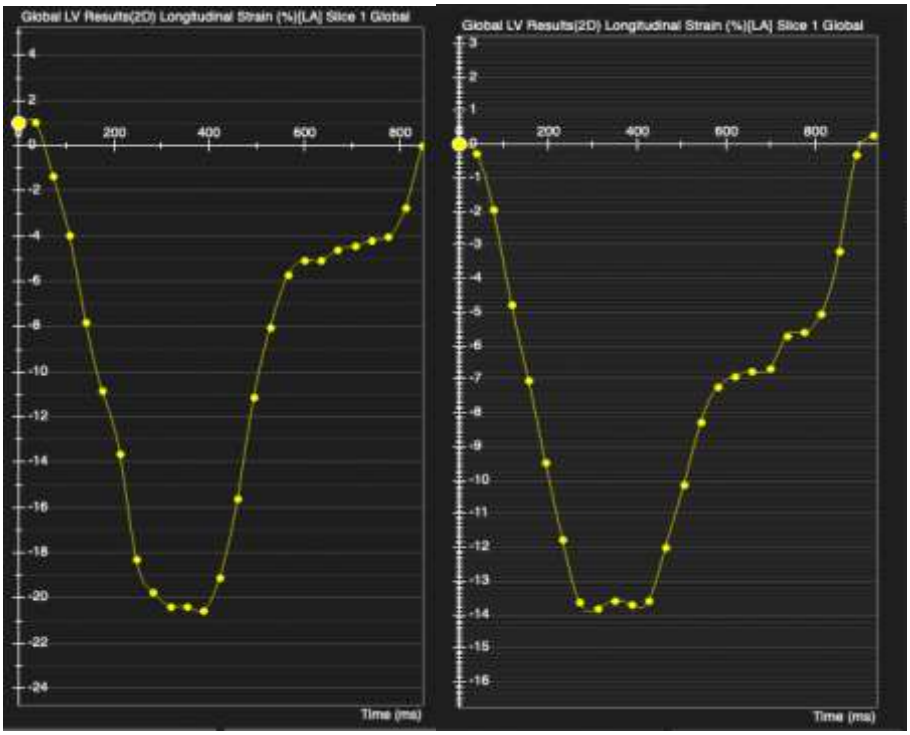



**Figure 2 : LV GLS in Control (left) and diabetic subject (right). The GLS in control = -21% and in diabetic patients = -14%.**

## DISCUSSION

In current study, global and regional myocardial deformations in diabetics are quantified and healthy individuals by using CMR-FT of both left and right myocardial ventricles. In addition, to quantifying LV myocardial deformation in T2DM patients, the result demonstrated that the CMR-FT could assess the subclinical RV dysfunction even with normal EF.

Presently, Cardiovascular Magnetic Resonance imaging (CMR) technique is the most accurate and reproducible available imaging tools for assessing the volumes of the ventricles and the Ejection Fraction. It generally agree of that there is no non-invasive "gold standard" imaging technique that can be applied in humans at the present to assessing LV mechanics (Castillo et al. 2005). While numerous studies have demonstrated the accuracy and reliability of MRI tagging for measuring myocardial mechanics including myocardial strain, limited availability and expertise have significantly limited its use in comparative research with echocardiography (Lima et al. 1993; Germans et al. 2010; Yeon et al. 2001; Rademakers et al. 2006).

The results of this study indicate that the values of LV GLS, LV GRS RV GLS, RV GCS, RV GRS ($p<0.001$) in type2 diabetes patients were considerably less than those in control subjects and that no significant changes were observed in LV GCS between healthy and T2DM patients. With feature tracking CMR, it has been demonstrated that patients with type 2 diabetes could use this technique to assess RV myocardial deformation before clinically evident RVEF reductions. These measurements provide objective evaluations of subclinical RV dysfunction before clinically obvious RVEF reductions (Hu et al. 2019).

As the RV complex shape and motion, it is often difficult to assess the RV function. Thus, the CMR is a gold standard imaging technique to evaluate RV function and mechanics.

Currently, SSFP sequences has a very good spatial resolution of the that are being used in MRI, which allows differentiating between myocardium and trabeculae. Myocardial deformation techniques, including myocardial strain, are the emerging modalities to estimate LV and RV function quantitively (Smiseth et al. 2016). The usefulness of myocardial strain with echocardiography using doppler and speckle tracking has been investigated (Kosmala et al. 2004). It is limited to quantify RV function and chamber size which concluded that the RV myocardial strain is reduced compared to healthy subjects (Kosmala et al. 2004). However, the myocardial deformation in T2DM using CMR is still not fully investigated. Thus, our result provides more accurate assessment on regional and global RV strain in T2DM.

Myocardial Tagging is established to quantify LV regional strain. However, it is limited to RV regional strain and the time-consuming post processing procedure. Conversely, the CMR-FT is a promising tool to overcome these limitations (Yang et al. 2021).

The CMR Feature Tracking technique has recently been recognized as a novel method of assessing the quantitative function of the biventricular myocardium (Fischer et al. 2022). This technology is based on tissue voxel motion-tracking technology derived from CMR SSFP cine imaging. A primary advantage of this technique is that it requires relatively small post-processing time. In addition, this method has been averaged to require a 5 - 10-minute post-processing time for each subject implies, therefore, providing the integrated possibility into routine use (Schuster et al. 2015; Zoroufian et al. 2014; Alaa et al. 2023; Abdelmalik et al. 2023, Qurain et al. 2022; Salih et al. 2022; Alshammari et al. 2022; Salih et al. 2021; Alshammari et al. 2022; Qurain et al. 2020).

Zia Ur Rahman et al (Rahman et al. 2017) conducted clinical research and stated that CMR feature tracking was assessed in the literature despite their potential validity, normal and abnormal values, advantages, and limitations. It is more feasible, accessible, and time-effective to use feature tracking to analyze myocardial function globally and segmentally than other CMR-based strain approaches (Rahman et al. 2017).

## CONCLUSIONS

CMR-FT methods of LV and RV can identify myocardial deformation in diabetic patients and would be used to assess early detection of subclinical myocardial dysfunction in T2DM patients. This study advised involving the software of Feature tracking (CMR-FT) in the clinical practices due to its positive outcome in the diagnosis of myocardial deformation.

### Supplementary materials

Not applicable

### Author contributions

Conceptualization, Q.T.A. and B.A.E.; methodology, R.M.A., R.O.A., and A.M.H.; formal analysis, H.A.A.; N.O.A., and K.A.S.; Data Collection, M.M.F.A. and A.M.N.; writing-original draft, A.A.A and W.K.A.; writing-review and editing, A.T.A. and S.S.A.; supervision, QTA. All authors have read and agreed to the published version of the manuscript.

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### Institutional Review Board Statement

The study was approved by the Bioethical Committee of the of the King Salman Hospital, Saudi Arabia

### Informed Consent Statement

Not applicable.

### Data Availability Statement

All of the data is included in the article/Supplementary Material.

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### Conflict of interest

The authors declared that present study was performed in absence of any conflict of interest.
OR The authors declare no conflict of interest.



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