



# Obvious or Subclinical Right Ventricular Dysfunction in Diabetes Mellitus (Type II): An Echocardiographic Tissue Deformation Study

Mozhgan Parsaee, MD\*, Parvaneh Bahmanziari, MD, Maryam Ardeshiri, MD, Maryam Esmaeilzadeh, MD

Rajaei Cardiovascular, Medical and Research Center, Tehran University of Medical Sciences, Tehran, Iran.

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## Abstract

**Background:** Diabetes mellitus is capable of impairing the myocardial function. Several studies have documented the influential impact of diabetes mellitus on the left ventricular function. The right ventricular function plays a significant role in the overall myocardial contractility; hence, this study was undertaken to evaluate the effect of diabetes mellitus type II on the right ventricular function.

**Methods:** Twenty-two diabetic patients without any coronary artery disease, hypertension, or left ventricular dysfunction were studied. The right ventricular end diastolic diameter, tricuspid plane systolic excursion, right ventricular inflow Doppler parameters, longitudinal myocardial velocities, and deformation indices from the basal and apical segments of the right ventricular free wall of the case group were measured. The control group consisted of 22 healthy individuals.

**Results:** The tricuspid annular plane systolic excursion (TAPSE) and tricuspid peak early to peak late diastolic flow velocities ratio (E/A) in the diabetic patients were significantly lower than those of the control group patients (18.9 vs. 23.2,  $p$  value  $< 0.001$  and 0.96 vs. 1.21,  $p$  value = 0.012), but there were no significant differences in the right ventricular end diastolic diameter and the right ventricular Tei index between the two groups ( $p$  value = 0.72). The right ventricular basal peak myocardial systolic velocity (SM) (12 cm/sec vs. 13.4 cm/sec;  $p$  value = 0.03), basal and apical right ventricular free wall systolic strain (-13.3% and -18.7% vs. -20.2% and -25.7%;  $p$  value = 0.001), and apical strain rate (-1.2 1/s vs. -1.6 1/s;  $p$  value = 0.008) were significantly lower in the study group. There was a weak correlation between the right ventricular function and HbA1c as well as the duration of diabetes mellitus and C-reactive protein.

**Conclusion:** Our results suggest that diabetes mellitus type II can influence the right ventricular function in the absence of coronary artery disease, diastolic dysfunction, and pulmonary hypertension.

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**Keywords:** Echocardiography • Diabetes mellitus • Ventricular function, right

\*Corresponding Author: Mzhgan Parsaee, Assistant Professor of Cardiology, Department of Echocardiography, Rajaei Cardiovascular, Medical and Research Center, Vali-Asr Ave. Adjacent to Mellat Park, Tehran, Iran. 1996911151. Tel: +98 21 23922930. Fax: +98 21 2055594. E-mail: [parsaemozhgan@yahoo.com](mailto:parsaemozhgan@yahoo.com).

## Introduction

Diabetes mellitus (DM) increases the risk of heart failure development even in the absence of coronary artery disease, hypertension, or other comorbidities<sup>1, 2</sup> and could result in a two to fourfold greater mortality in heart failure patients. Indeed, DM is capable of impairing the myocardial function: this is initially a clinically silent condition; nevertheless, if left unrecognized and insufficiently managed, it could beget overt diabetic cardiomyopathy.

The right ventricular (RV) function plays a significant role in the overall myocardial contractility.<sup>3</sup> Nevertheless, most of the previous studies regarding diabetes-induced changes in myocardial dysfunction were dedicated to the left ventricle (LV) at the cost of ignoring the role of the right heart chambers. The existing literature of course does contain a limited number of studies on the RV cardiomyopathies of patients with DM type I; however, to our knowledge, there is only one recent study probing into DM type II drawing up on three-dimensional strain and strain rate.

The objectives of the present study were to evaluate the RV systolic and diastolic functions using conventional echocardiography, tissue Doppler imaging (TDI), and deformation indices (strain and strain rate) in patients with DM type II and without coronary artery disease or LV dysfunction.

## Methods

The study group was comprised of 22 diabetic patients (9 men and 13 women) aged  $55.6 \pm 6.0$  years. These patients either referred to the DM Clinic of Rajaei Cardiovascular, Medical and Research Center or were amongst the hospital staff. The control group consisted of 22 healthy individuals (9 men and 13 women). All the diabetic patients enrolled in this study were asymptomatic, without any clinical evidence of either systolic or diastolic heart failure. The control subjects were considered to have a low probability of coronary disease or heart failure based on clinical data.

Coronary artery disease was excluded if there was a negative Dobutamine stress echocardiographic examination or a negative treadmill exercise electrocardiographic test. In a few cases, coronary artery disease was excluded on the evidence of equivocal non-invasive stress tests and normal coronary angiograms. The other exclusion criteria included valvular or congenital heart disease, left ventricular ejection fraction (LVEF) less than 50%, rhythms other than normal sinus rhythm, documented pulmonary diseases or pulmonary hypertension, and tricuspid regurgitation more than a mild degree.

All the diabetic patients were on a diet and treatment with oral hypoglycemic drugs. Plasma glucose and HbA1c were observed periodically and controlled by the endocrinologist

in the aforementioned clinic. None of the patients had such diabetic complications as progressive and complex diabetic retinopathy, neuropathy, and nephropathy.

The study participants in the two groups underwent echocardiographic examinations (Vivid 7, GE Vingmed). The variables measured are presented as follows:

1. The RV dimension and tricuspid annular plane systolic excursion (TAPSE) were measured from the apical four-chamber view.

2. The RV Doppler parameters of the diastolic function (peak early [A] and peak late diastolic flow velocity [E], together with their ratio [E/A] and deceleration time [DT]) were recorded. The trans-tricuspid flow was measured in the apical four-chamber view using pulsed Doppler, with the sample volume positioned at the tips of the tricuspid leaflets. The measurements were averaged from three end-expiratory cycles.

3. TDI was conducted to assess the RV longitudinal myocardial function in the apical four-chamber view. Color TDI was used in addition to two-dimensional images, with adjustment of the depth and sector angle to obtain an acceptable frame rate. The TDI variables of peak systolic velocity (Sm), peak early diastolic velocity (Em), peak late diastolic velocity (Am), myocardial performance index (MPI), and acceleration time of the isovolumetric contraction time (IVCT) were analyzed online.

4. The deformation indices were measured by adjusting the imaging angle to achieve a parallel alignment of the beam with the myocardial segment of interest. The images were stored on a remote archive of the echocardiography machine so that they could be analyzed offline. The myocardial deformation curves were investigated from the basal segment of the RV free wall, which belongs to the inflow part of the RV, and also from the apical segment, which belongs to the trabecular portion of the RV.

5. The strain rate and strain were measured based on the standard deformation measurement, and the peak of the R on the electrocardiography (ECG) was utilized to define end diastole. End systole was determined using the pulsed Doppler velocity profile of the left ventricular outflow tract (LVOT) as the aortic valve closure, and the RV end systole was determined using the pulsed wave profile of the right ventricular outflow tract (RVOT) at end expiration. The analysis of the myocardial strain and strain rate data included the assessment of the systolic strain ( $\epsilon$ ), peak systolic strain rate (SRs), and peak early diastolic strain rate (SRe).

The data are expressed as Mean  $\pm$  SD and percentages. The Student unpaired t-test was used to evaluate the differences between the groups, and the chi-square test was employed to compare the categorical variables. The Pearson correlation coefficients were utilized to pair the continuous variables. A two-tailed p value  $< 0.05$  was considered significant. For the statistical analyses, the statistical software SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL) was used.



## Results

The demographic characteristics and clinical parameters of the participants are depicted in Tables 1. There were no significant differences between the two groups in terms of sex, age, body mass index, creatinine, total cholesterol level, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and being a smoker. The diabetic group, however, showed a higher level of triglyceride ( $p$  value = 0.049), but this was statistically, and not clinically, significant.

The echocardiographic and Doppler data of the studied groups are illustrated in Table 2. There were no significant differences between the two groups as regards the right ventricular end diastolic diameter (RVEDD) (mm), and tricuspid E velocity, whereas the tricuspid annular plane systolic excursion (TAPSE), and tricuspid E/A ratio of the diabetic patients ( $18.9 \pm 2.1$  vs.  $23.2 \pm 2.9$  and  $0.96 \pm 0.2$  vs.  $1.21 \pm 0.3$ , respectively) were significantly lower. The tricuspid A velocity and E wave deceleration time of the diabetic patients ( $0.5 \pm 0.1$  m/s vs.  $0.4 \pm 0.1$  m/s and  $289.2 \pm 67$  msec vs.  $250.9 \pm 57.1$  msec) were significantly higher.

Table 1. Demographic characteristics of the studied groups\*

	Diabetic group	Control subjects	P value
Age (y)	54.5±7.0	49.8±8.4	0.05
Male	9 (40.9)	9 (40.9)	0.69
Hypertension	9 (40.9)	4 (18.2)	0.07
Smoking	2 (9.1)	3 (13.6)	0.82
Body mass index (Kg/m <sup>2</sup> )	28.7±3.1	26.4±3.8	0.05
Systolic blood pressure (mm Hg)	125.6±15.4	120.5±13.4	0.28
Diastolic blood pressure (mm Hg)	79.5±11.6	76.1±10.5	0.32
Creatinine (mg/dl)	1.0±0.2	1.1±0.1	0.47
Total cholesterol (mg/dl)	178.4±40.0	166.0±37.0	0.39
Duration of diabetes (y)	7.0±3.0	-	-
Triglyceride (mg/dl)	186.0±82.0	130.0±67.0	0.04
Low-density lipoprotein cholesterol (mg/dl)	90.0±26.0	89.0±27.0	0.96

\*Data are presented as mean±SD or n (%)

Table 2. Echocardiographic and Doppler data of the studied groups\*

	Diabetic group	Control subjects	P value
Right ventricular end diastolic diameter (mm)	28.0±2.9	28.0±3.7	0.56
Tricuspid annular plane systolic excursion (mm)	18.9±2.1	23.2±2.9	< 0.01
Tricuspid E velocity (m/s)	0.47±0.05	0.46±0.08	0.52
Tricuspid A velocity (m/s)	0.5±0.1	0.4±0.1	0.04
Tricuspid deceleration time (msec)	289.2±67.0	250.9±57.1	0.04
E/A ratio	0.9±0.2	1.2±0.3	0.01

\*Data are presented as mean±SD

E/A, Tricuspid peak early to peak late diastolic flow velocities ratio

Table 3. Tissue Doppler imaging data of the studied groups\*

	Diabetic group	Control subjects	P value
Right ventricular basal segment Sm (cm/s)	12.0±1.9	13.4±2.1	0.03
Right ventricular basal segment Em (cm/s)	8.5±2.1	11.6±2.4	< 0.01
Right ventricular basal segment Am (cm/s)	12.6±2.7	14.7±3.3	0.03
Myocardial performance index	0.42±0.11	0.40±0.09	0.72
Acceleration time of the isovolumetric contraction time (ms)	37.8±8.4	35.4±8.4	0.45
E/Em ratio	0.05±0.01	0.04±0.01	< 0.01

\*Data are presented as mean±SD

Sm, Peak myocardial systolic velocity; Em, Peak early diastolic velocity; Am, Peak late diastolic velocity; E, Peak late diastolic flow velocity

Table 4. Deformation indices data of the studied groups\*

	Diabetic group	Control subjects	P value
Right ventricular basal $\epsilon$ (%)	-13.3 $\pm$ 4.3	-20.2 $\pm$ 7.3	< 0.01
Right ventricular basal SRs (1/s)	-1.0 $\pm$ 0.5	-1.37 $\pm$ 0.9	0.18
Right ventricular basal SRe (1/s)	0.9 $\pm$ 0.3	1.2 $\pm$ 0.5	0.05
Right ventricular apical $\epsilon$ (%)	-18.7 $\pm$ 4.3	-25.7 $\pm$ 8.2	< 0.01
Right ventricular apical SRs (1/s)	-1.2 $\pm$ 0.3	-1.6 $\pm$ 0.6	< 0.01
Right ventricular apical SRe (1/s)	1.2 $\pm$ 0.4	1.9 $\pm$ 0.7	< 0.01

\*Data are presented as mean $\pm$ SD

$\epsilon$ , Systolic stain; SRs, Peak systolic strain rate; SRe, Early diastolic strain rate

The TDI data of the study population are shown in Table 3, according to which the RV basal segment Sm, Em, Am, and E/Em (12  $\pm$  1.9 cm/sec vs. 13.4  $\pm$  2.1 cm/sec, 8.5  $\pm$  2.1 cm/sec vs. 11.6  $\pm$  2.4 cm/sec, 12.6  $\pm$  2.7 cm/sec vs. 14.7  $\pm$  3.3 cm/sec, and 0.05  $\pm$  0.01 vs. 0.04  $\pm$  0.01, respectively) were significantly lower in the case group than in the control group. There were no significant differences between the two groups with respect to the MPI of the RV and the acceleration time of the IVCT.

The data on the deformation indices of the two study groups are demonstrated in Table 4, according to which the RV basal segment systolic strain ( $\epsilon$ ) and RV apical segment ( $\epsilon$ , SRs, and SRe) of the case group were significantly lower than those in the control group (p value < 0.01). There were, however, no significant differences in regard to the RV basal segment SRs and SRe between the two groups.

There were no significant correlations between HbA1c, duration of diabetes, C-reactive protein (CRP), and measures of the RV systolic or diastolic dysfunction (based on conventional Doppler, TDI data, or deformation indices).

## Discussion

The present study shows that both systolic and diastolic RV functions are impaired in patients with DM type II and without coronary artery disease or ejection fractions of less than 50%. This finding was demonstrated by significantly lower RV systolic parameters (TAPSE, RV basal Sm, basal and apical RV free wall systolic strains, and apical SRs) and lower RV diastolic parameters (E/A ratios, Em, Am, E/Em ratios, and apical early diastolic strain rate [SRe]) in our case group than those in a normal, sex- and age-matched control group. There were no statistically significant differences in the RV basal segment SRs and SRe between the diabetic and control subjects, which may be due to difficulties in drawing basal RV strain rate curves.

Our results chime in with those of the Kosmala et al.,<sup>4</sup> study, which reported the impairment of both basal and apical segments of the RV free wall performance. In that study, however, the apical segments exhibited more pronounced systolic impairment than did the basal segments and it

was concluded that the RV might be divided into the three components of the inflow or sinus, the trabecular, and the outflow portions. Geva et al.,<sup>5</sup> stated that the inflow region, compared with the other parts of the RV, had significant predominance in fiber shortening and contribution to the global RV systolic function. As the basal segment of the RV free wall is a part of the inflow component, and the apical segment refers to the trabecular portion of the RV, they suggested that the differences seen in their cohort might be related to the regional inhomogeneity of the RV in patients with DM.

The Kosmala et al., study<sup>4</sup> reported RV diastolic dysfunction in a non-uniform type I and type II diabetic cohort using TDI and demonstrated significantly lower values of Em and Em-to-Am ratio in the basal and mid-segments and longer isovolumic relaxation time (IRTm) in the mid-segment. Nonetheless, that study failed to show any difference in the E/A ratio, Em, and systolic parameters (Sm and TAPSE) between the diabetic patients and normal subjects. Furthermore, the said study found no significant correlations between the estimated echocardiographic parameters and indices of diabetic control (plasma glucose and HbA1c) as well as the duration of diabetes.

In another study, Kosmala et al.,<sup>4</sup> evaluated non-uniform type I and type II diabetic groups and showed impairment of the RV systolic function according to deformation studies (RV systolic stain and SRs in the basal and apical segments of the RV free wall) and impairment of the RV diastolic function (decreased SRe in both RV segments). In a study by Karamitsos et al.,<sup>6</sup> type I diabetic patients were found to have an impaired RV diastolic function (trans-tricuspid E velocity, A velocity, E/A ratio, Em, and Am). Nevertheless, the RV systolic function was preserved in the authors' diabetic population.

Consistent with the findings of the present study, Gaber et al.,<sup>7</sup> assessed patients with DM type II and demonstrated impairment of the RV systolic and diastolic functions according to deformation studies via three-dimensional echocardiography (systolic strain, SRs, and SRe in both RV basal and apical segments).

The present study, in agreement with some other similar studies,<sup>4, 8, 9</sup> found no importance for the impact of the



duration of diabetes on the RV function. This finding could suggest that controlling diabetes mellitus is more important than its duration.

## Conclusion

Whether the RV diastolic abnormalities have prognostic implications in the clinical course of patients with DM type II remains to be investigated. We believe that serial echocardiography measurements are warranted in this diabetic population if the progression from subclinical RV involvement to symptomatic RV dysfunction is to be followed. In addition, subclinical RV systolic and diastolic abnormalities should be considered when planning pharmacotherapy to prevent the development of symptomatic RV dysfunction.

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