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Echocardiographic Evaluation of Pulmonary Vascular Resistance in Patients with Type2 Diabetes Mellitus Concerning Diabetic Duration and HbA1c Level and its Effect on the Right ventricular Function

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Abstract

Objective The study aims to non-invasive assessment of PVR by echocardiography in type 2 DM and its relation to duration of DM and HbA1c level and association of PVR to RV systolic and diastolic function.

Methods This cross-sectional comparative and analytic study was conducted on 62 consisting of patients with type 2 diabetes mellitus without a history of hypertension, established coronary artery disease, and chronic obstructive pulmonary disease. All diabetic patients were studied for age, sex. BMI, HbA1c level, and duration of diabetes, and echocardiography was performed to assess PVR systolic (TAPSE. MPI) and diastolic (E/A, E/ē) function of RV.

Results The study reveals there is no significant difference in PVR RV systolic and diastolic function concerning HbA1c level and DM duration. While there is significantly higher PVR and significantly lower TAPSE and E/A in DM ($P < 0.05$) in comparison with normal control subjects. In correlation of PVR with systolic and diastolic function of RV, there were showed a strong negative relationship between PVR and systolic function and weak positive relationship with diastolic dysfunction P-value <0.05.

Conclusion Significant-high pulmonary vascular resistance in type 2 DM and inverse correlation to systolic function and linear correlation to diastolic dysfunction of the right ventricle, while there is no relation of PVR to HbA1c level and duration DM.

Keywords Pulmonary vascular resistance, pulmonary hypertension, right ventricle function, diabetic state, diastolic and systolic function, HbA1c

Introduction

Diabetes mellitus (DM) is an endocrine disorder that quickly develops among the population that affects millions of people worldwide causing serious consequences and effects.[1] It is defined as a progressive disorder because of resistance to insulin utilization from body organs and frequently decreased insulin secretion from pancreatic cells in adults.[2] The standard investigation of DM is HbA1c that is used for blood glucose control level as follows - pre-diabetes as HbA1c 5.7 --- 6.4% -diabetes person as HbA1c > 6.4%). -Good-control DM. HbA1c < 7%, -poor or bad control DM HbA1c > 7%).[3] There is evidence that DM may contribute to endothelial dysfunction of the pulmonary system via the release of inflammatory cytokines (vasoconstrictive) substances such as (endothelin and platelet-activating factors) and decrease availability of nitric oxide (vasodilator). Recently showed that DMs have a high risk of hospitalization (left ventricular) (LV) with (RV) hypertrophy and higher concentrations of biomarkers that relate to oxidative stress, inflammation, and fibrosis.[3] The majority of methods for estimating pulmonary vascular resistance (PVR) effects are based on invasive RV heart catheterization (RHC) such approach using for conclusive diagnosis while the ratio of tricuspid peak velocity (TRV) to velocity time integral (VTI) of right ventricular outflow tract (RVOT) calculated by echo give a valuable guide to PVR estimation.[4] The aim of study was to determine the association between pulmonary vascular resistance (PVR) and type 2 diabetes mellitus duration and the HbA1c level (glycaemic control) and its relation to right ventricular systolic & diastolic function.

Method

A self-constricted questionnaire form prepared to known information from the Patients selected included information and history regarding sex, age, diabetic period, smoking, weight, and height were calculated. Medical history for any cardiovascular disease, renal disease, respiratory, and hypertension disease. After complete the questionnaire, participants evaluated with relevant investigations like fasting blood sugar with postprandial blood sugar, HbA1c level, the patients were subdivided into 2 groups (according to HbA1c): good control group when HbA1c < 7% and bad poor control (≥7%), and (according to diabetic duration): patients ordered into 3 groups (1) below 5 years, (2) from 5–10 years and (3) above than 10 years. Exclusion criteria: all patients with cardiac diseases like valvular heart disease, ischemic, hypertensive heart disease, congestive heart failure, cardiomyopathy, renal failure, chronic pulmonary disease, severe anaemia, and hemoglobinopathies. The study was conducted by the ethical principles that have their origin in the Declaration of Helsinki. The study protocol and the subject information and consent form were reviewed and approved by a local Ethics Committee. All participants were invited to do echocardiographic examinations, which were done on all individuals with the same protocol by using a general electric medical system vivid 9-ultrasound machine equipped with 5 MHz sector transducer probe. All participants placed in the left lateral position and echo examination have been done according to the guidelines/recommendations of the American Society of Echocardiography (ASE)/European Association of Echocardiography (EAE).[5]

Assessments of Pulmonary Vascular Resistance

For estimation, VTI-RVOT (cm/s) 1–2-mm placed of PW Doppler sample volume in RVOT when imaged from the parasternal short-axis view. The volume sample was placed in very closing but not opening click of pulmonic valve than an apical 4CV view where continuous wave (CW) Doppler sample volume placed in between tricuspid leaflets for measurement of TRV (m/s) an average of 3 cardiac cycles measurements were done then the formula applies PVR = tricuspid velocity (TRV)/velocity-time integral {PVR = TRV/VTI-RVOT X 10 + 0.16 (WU)}.[6]

Assessments of RV Systolic Function

(2DE) and M mode measurements for the RV systolic function of tricuspid annular plane systolic excursion (TAPSE) by the apical 4-chamber view (A4CV). An M-mode beam parallel to the motion of the lateral wall is oriented to cross the lateral part of the tricuspid annulus. An average of 3 measurements were taken to avoid error. The right myocardial performance index (RMPI) was measured by applying tissue Doppler imaging (TDI) to the lateral tricuspid annulus in apical 4-chamber view and calculated using the ratio of the isovolumic contraction and relaxation times to divide on the ejection time that encompasses both systolic and diastolic functions.[7]

Assessments of RV Diastolic Function

For measurements of E/A ratio of tricuspid apical 4CV, align the Doppler pulse wave volume sample (PW) beam with the inflow direction. Place a 1–3 mm between the tricuspid leaflet tips with reduction of adjustment Doppler gain so that modal frequency is seen and use a sweep speed of 90–100 mm. Dual imaging applied and TDI of lateral annulus for calculation of (ē wave) so E/ē automatically appear on screen.[8]

Data was analysed using a statistical package for social sciences (SPSS version 23) computer software program. Descriptive statistics presented as a frequency table and figure of continuous variables were expressed as mean ± SD and categorical variables as numbers and percentages. Analytical statistics as a student – *t*-test, ANOVA test, and correlation test were used to find an association between categorical variables and continuous variables. The *P*-value below or equal to 0.05 was considered statistically significant for a 95% confidence interval (C.I.).

Results

In our research 120 participants enrolled, 62 participants had T2DM and 67 participants had a negative history of DM (control subjects). The age mean in the diabetic group was 51.6 (±0.4) years, while the age means in the control group was 46 (±9.3) years. In the diabetes group, the male represents 64.5 % (40) of participants and the female was 35, 5% (22) of participants while in the control group the male represents 46.3 % (31) of participants and the female 53.7% (36) of participants. The BMI mean in the diabetic group was 28.6 that is approximately the same mean for the control group (28.7). In diabetic patients, the duration mean of T2DM was 10.2 (±6.8) in which 30.6% (19) of them have DM for less than 5 years, 27.4% (17) of them have DM between 5–10 years, and 41.09. (26) Of them have DM more than 10 years. Regarding HbA1c level in diabetic participants, 43.5% (27) of them have HbA1c level below or equal to < 7. 56.5% (35) of them have HbA1c levels above ≥ 7. The mean of PVR was higher in diabetic participants than the normal control subjects with statistical *P*-value was significant for mean difference between them (*P* value = 0.03*) which less than 0.05, while TAPSE and E/A had lower in DM participants than normal control individual the statistical mean difference between them, *P*-value = 0.003* and 0.03* respectively, which are less than 0.05 as in the following Table 1.

The PVR was matched with MPI and TAPSE, showing there are significantly negative (inverse) relationships between these variables (increase in PVR, there was a decrease in MPI and TAPSE). While the PVR showed (positive) correlation with diastolic dysfunction increased (E/ē and E/A) with increased PVR, Table 2.

Table 1. **Comparison in PVR, systolic and diastolic RV function between diabetic and control**

Variable		Mean (±SD)		*P*-value
		DM patients	Control	
Systolic function	MPI	0.46 (±0.15)	0.48 (±0.09)	0.48
	TAPSE	22.4 (±3.8)	24 (±4.3)	0.003*
Diastolic function	E/ē	4.9 (±1.6)	4.5 (±1.9)	0.28
	E/A	1.1 (±0.9)	1.4 (±0.4)	0.03*
Pulmonary vascular resistance		1.2 (±0.35)	1 (±0.29)	0.03*

*Correlation test, significant *P* value < 0.05.

Table 2. **Correlation between PVR and systolic and diastolic parameters**

Variable		Mean (±SD)	Correlation coefficient	*P*-value in correlation with PVR
Systolic function	MPI	0.46 (±0.15)	−0.46	0.00001*
	TAPSE	22.4 (±3.8)	−0.25	0.046*
Diastolic function	E/ē	4.9 (±1.6	0.29	0.022*
	E/A	1.1 (±0.9)	0.28	0.025*
Pulmonary vascular resistance		1.17 (±0.35)		

*Correlation test, significant *P* value < 0.05.

Table 3. **Relation of some parameters with the duration of DM**

Variable		Duration of DM (±SD)			*P*-value
		<5 years	5–10 years	>10 years	
Systolic function	MPI	0.46 (±0.17)	0.5 (±017)	0.44 (±0.15)	
	TAPSE	22.8 (±4)	21 (±3.6	22.5 (±3.8)	0.404
Diastolic function	E/ē	5 (±1.3)	4.3 (±1.5)	5.1 (±1.9)	0.644
	E/A	1 (±0.8)	1.1 (±0.6)	1.2 (±1.1)	0.27
Pulmonary vascular resistance		1.2 (±0.31)	1.1 (±0.31)	1.1 (±0.41)	0.63

ANOVA test, significant *P*-value <0.05.

Table 4. **Relation of some parameters with the HbA1c level**

Variable		Level of HbA1c mean (±SD)		*P*-value
		≤7 (controlled DM)	>7 (poor controlled DM)	
Systolic function	MPI	0.49 (±0.16)	0.44 (±0.14)	0.19
	TAPSE	23.1 (±4.4)	21 (±3.2)	0.21
Diastolic function	E/ē	4.8 (±1.5)	4.9 (±1.7)	0.78
	E/A	1.1 (±0.8)	1.1 (±1)	0.98
Pulmonary vascular resistance		1.1 (±0.3)	1.1 (±0.34)	0.72

Student *t*-test, significant *P* value <0.05.

The right ventricular systolic, diastolic function, and pulmonary vascular resistance had no meaningful statistical difference with the duration of DM (*P*-value > 0.05), Table 3.

The RV systolic, Diastolic function, and pulmonary vascular resistance had no meaningful statistical difference with HbA1c level (*P*-value > 0.05), Table 4.

Discussion

DM is the commonest endocrine disease that influences all general body vascular systems[1] but Its effects on PVR have not yet studied well. Our original research design to non-invasive echo assessment of association between PVR andT2DM concerning diabetic duration and HbA1c level with correlation to RV function in comparison with normal control non-diabetic individuals, therefore the study is cross-sectional comparative and analytic one. The study demonstrated that there is a statistically significant high (PVR) in DM compared with normal non-DM (control subjects). This may be due to the impact of DM on the endothelium of the pulmonary vasculature system (pulmonary artery, precapillary arteriole, pulmonary capillary bed, and pulmonary veins) causing endothelial dysfunction of this system leading to synthesize some peptides, endothelin and platelet activating factors which is an extremely potent vasoconstrictor causing elevated PVR.[9] In this study, the correlation of PVR with systolic parameters (MPI and TAPSE) show a reverse negative relationship $P < 0.05$ when elevated PVR may cause elevated back pressure (afterload pressure) which caused RV thickening, hypertrophy, stiffens and fibrosis of RV, leading to decreased contractility and decreased MPI and TAPSE.[10,11] Another explanation, the elevated PVR in diabetic subjects causing loss of RV-PA coupling[11] leading to elevated RV pressure afterload causing decreased RV contractility and compliance due to RV hypertrophy which decreased MPI and TAPSE which causing increased E/ē and E/A ratio in T2DM.[8] In our study, it was demonstrated that there is no statistically significant difference between PVR, systolic and diastolic RV, DM duration, and HbA1c level. However, this may be a smaller number size ($N = 62$) or a very short period of research. However, the present study is in agreement with some other similar studies. The Browning[9] in his study reported RV function in type one and type two DM, using TDI, was showing no any difference in the (E/A, E/ē, TAPSE and MPI) among normal and diabetic subjects and he said in his study that there is no relation between the echo estimated parameters and indices of diabetic control (plasma glucose and HbA1c) and the duration of diabetes. Su et al.[11] concluded in his long prospective study on patients with T2DM, there is a modest but not statistically significant relation between HbA1c level and *cardiovascular* events.

Conclusion

Significant-high pulmonary vascular resistance in type 2 DM and inverse correlation to systolic function and linear correlation to diastolic dysfunction of the right ventricle, while there is no relation of PVR to HbA1c level and duration DM.

Conflicts of Interest

None of the authors has any conflicts of interest relevant to what is written.

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