

The Impact of Diabetes Duration on Cardiac and Vascular Remodeling

Saidakbarova F. T.^{1,*}, Srojedinova N. Z.²

¹Postdoctoral Student, Republican Specialized Scientific and Practical Medical Center of Cardiology Tashkent, Uzbekistan
²MD, Republican Specialized Scientific and Practical Medical Center of Cardiology Tashkent, Uzbekistan

Abstract To evaluate the effect of disease duration on cardiac and vascular remodeling in patients with atherosclerotic cardiovascular disease (ASCVD) and type 2 DM. This study included 285 patients aged 35–80 years with HNT and DM who were treated in an inpatient setting. The average age of the patients was 64.11±1.2 years, with 34% male and 66% female. Patients with preserved ejection fraction (LVEF ≥ 50%) were included in this study. Patients were divided into two groups according to the duration of type 2 DM: Group 1 included patients with DM duration of up to 5 years (n=236), and Group 2 included patients with DM duration of more than 5 years (n=49). Statistical analysis was performed using IBM-SPSS 27.0 software package. When comparing the central hemodynamic parameters, it was observed that these measures were larger in Group 2. ESD – 3.42±0.49 cm vs 3.8±0.65 cm, p=0.001; EDD – 5.08±0.5 cm vs 5.33±0.5 cm, p=0.002. EDV – 124.7±27.7 mL vs 138.8±29.8 mL, p=0.0002; ESV – 49.9±18.5 mL vs 65.18±28.6 mL, p=0.001; IVST – 1.16±0.13 cm vs 1.19±0.1 cm, p=0.05; LVPWT – 1.14±0.14 cm vs 1.18±0.12 mm, p=0.03; EF- 60.78±7.05% vs 54.59±10.6%, p=0.001. LVMM (234.9±63.7 g/m² vs 266.77±58.97 g/m², p=0.005) and LVMMi (152.79±41.9 g/m² vs 173.4±43.5 g/m², p=0.002) were significantly higher in Group 2 than in Group 1. Left ventricular hypertrophy was more common in Group 2 patients (67% vs. 89%, $\chi^2 = 4.7$, p=0.05). When evaluating peak velocity indicators in both groups, it was found to be non-significantly lower in Group 2: E wave, 0.68±0.15 vs. 0.63±0.14 m/s, p=0.09; A wave, 0.78±0.1 vs. 0.78±0.13 m/s, p=0.9; E/A, 0.89±0.3 vs. 1.04±1.3 m/s, p=0.15. e' – 0.09±0.06 m/s vs 0.07±0.02 m/s, p=0.01. The E/e' ratio was found to be significantly lower in Group 2 (0.75 ± 1.3 vs. 0.8 ± 1.6 m/s, p = 0.043). When evaluating the brachiocephalic vessels, the right intima-media thickness (IMT) was 1.0±0.18 vs. 3.0±0.89 mm (p = 0.002), the left IMT was 1.02±0.19 vs. 4.69±1.6 mm (p = 0.002), the right atherosclerotic plaque was 15.75±18.1 vs 24.37±19.7 mm, p=0.003; left Atherosclerotic plaque 30.7±18.7 vs 34.7±20.1 mm, p=0.05. DM is a major clinical problem for treating physicians. It is important to conduct early primary examinations and initiate standard treatment in patients with type 2 DM. This is because not diagnosing the disease for years causes rapid development of severe complications. Prolonging the duration of DM leads to remodeling of the heart and blood vessels.

Keywords Arterial hypertension, Type 2 diabetes mellitus, NT-proBNP, Cardiac remodeling, Left ventricular diastolic function, Left ventricular systolic function

1. Introduction

According to the World Health Organization, Coronary Heart Disease (CHD) and hypertension (HNT) are the leading causes of death, ranking first among the top ten causes. The risk of developing CHD and HNT in individuals with Diabetes Mellitus (DM) is 3-5 times higher than that in non-diabetic patients [1]. The longer the duration of DM, the greater is the risk. DM is considered an international epidemic. Type 2 DM is the most prevalent form of the disease, accounting for approximately 90% of all cases. The prevalence of DM is rapidly increasing in both developing

and developed countries. The prevalence of diabetes among the working-age population increased from 4.7% in 1980 to 8.5% in 2014. Currently, its global average prevalence is estimated to be approximately 11.8% (4.7-13.3%) [2]. Globally, deaths from diabetes are more widespread among women than men, which may be due to the higher cardiovascular risk in women. In our country, the incidence of DM in the population aged 20 to 79 years is 7.5-7.6%, and in the population over 60 years of age, it is 0.74% [1]. CHD and HNT are the main causes of heart failure in patients with DM; however, diabetic cardiomyopathy also plays a key role in its development. The longer the duration of DM, the faster the remodeling of the heart develops, along with the development of macro- and microvascular complications [3].

Objective: To evaluate the effect of disease duration on cardiac and vascular remodeling in patients with atherosclerotic cardiovascular disease (ASCVD) and type 2 DM.

* Corresponding author:

saidakbarova.feruza92@mail.ru (Saidakbarova F. T.)

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2. Materials and Methods

The study was conducted in the Department of "Cardiometabolic Disorders and Endocrinology" of the Republican Specialized Scientific-Practical Medical Center of Cardiology (RSSPMCC). The study included 285 patients aged 35–80 years with HNT and DM who were treated in an inpatient setting. The average age of the patients was 64.11 ± 1.2 years, with 34% male and 66% female. All patients received commonly prescribed antihypertensive and hypoglycemic medications.

The analysis of comorbidities was conducted based on the history of cardiovascular and chronic diseases recorded in the patients' medical records. The presence of comorbidities was determined based on the results of examinations conducted in an inpatient setting. Patients with preserved ejection fraction ($LVEF \geq 50\%$) were included in this study. Patients were divided into two groups according to the duration of type 2 DM: Group 1 included patients with DM duration of up to 5 years ($n=236$), and Group 2 included patients with DM duration of more than 5 years ($n=49$).

The structural and functional states of the myocardium and remodeling process were assessed using Doppler echocardiography. Examinations were performed using an ultrasound "ACUSON X 700 PV 2.0" apparatus (SIEMENS,

Germany). The examination was performed using the transthoracic method in M and B modes according to the recommendations of the American Society of Echocardiography. According to the recommendations, LVEF is measured based on the disc method (Simpson's method) in biplane (apical 4-chamber and apical 2-chamber) view. Left ventricular end-diastolic (LVEDV) and end-systolic volumes (LVESV) were obtained from the 4- and 2-chamber views. The following structural parameters of the heart were assessed in the EchoCG examination: end-diastolic dimension (EDD), end-systolic dimension (ESD), interventricular septal thickness (IVST), left ventricular posterior wall thickness (LVPWT), left atrial index (LAI), aorta, left ventricular myocardial mass (LVMM), LVMM index (LVMMi), and relative wall thickness (RWT). Left ventricular systolic function was determined using the Simpson method: end-diastolic volume (EDV), end-systolic volume (ESV), left ventricular ejection fraction (LVEF), and stroke volume (SV), which is the difference between EDV and ESV. Myocardial diastolic function was assessed using the following indicators: peak early diastolic filling velocity (E wave), peak late diastolic filling velocity (A wave), and E/A ratio. Ultrasonography of the brachiocephalic vessels was performed using an ultrasound apparatus. NT-pro BNP was measured using an electrochemiluminescence immunoassay (ECLIA; Roche).

Table 1. Comparative characteristics of patients in groups

	DM duration > 5 years (n = 236)	DM duration < 5 years (n = 49)	P (value)
Average age	62.6±7.4	65.5±7.8	0.4
Male	102 (42%)	29 (59%)	χ^2 -5.78 P-0.017
Female	134 (58%)	20 (41%)	χ^2 -5.78 P-0.017
Weight, kg	80.9±11.2	89.1±14	0.04
Height, cm	162.5±8.1	164.6±8.1	0.18
Body Mass Index (BMI), kg/m ²	30.7±5.6	33.1±4.9	0.022
CHD	236 (100%)	49 (100%)	0
Post-infarction cardiosclerosis	0	0	0
Controlled Hypertension	138(58%)	21 (42%)	χ^2 -5.1 P-0.024
Stage 1 HNT	42 (18%)	10 (22%)	χ^2 -0.5 P-0.48
Stage 2 HNT	20 (9%)	2 (4%)	χ^2 -2.05 P-0.15
Stage 3 HNT	36 (15%)	16 (32%)	χ^2 -8.038 P-0.005
Duration of DM	1.36±0.9	11.9±4.6	0.0000
Stage I CHF	98 (42%)	10 (20%)	χ^2 -11,3 P-0.001
Stage II CHF	138 (58%)	39 (80%)	χ^2 -11,3 P-0.001
History of acute cerebrovascular accident	4 (2%)	4 (8%)	χ^2 -3.8 P-0.05

Statistical analysis of the results was performed in two stages: preparation for statistical analysis and specific statistical analysis. Statistical analysis was performed using IBM-SPSS 27.0 software package. The arithmetic mean (M), standard deviation (SD), median (Me), and lower (Q1) and upper (Q3) quartiles were calculated. Student's t-test was used to compare the arithmetic means of the two groups (control and experimental). To analyze the validity of the qualitative features, the χ^2 criterion was used.

Differences were considered statistically significant at $P \leq 0.05$. The relationship between the studied indicators was assessed by calculating Pearson's (r) or Spearman's (R) correlation coefficient with the results of the correlation analysis and subsequently determining its significance using the t-criterion.

There was no significant difference in age between the groups. The number of male patients was higher in Group 2 ($p = 0.017$). The number of female patients was higher in Group 1 ($p = 0.017$). The body weight and body mass index of the patients were also higher in Group 2 ($p = 0.022$). Ischemic Heart Disease (CHD) was diagnosed in all patients in both groups. A history of post-infarction atherosclerosis was not observed in either group of patients. Hypertension was diagnosed in both groups of patients. Controlled hypertension was found in a significantly higher number of patients in Group 2 ($p = 0.024$). No statistically significant differences were obtained for degrees 1 and 2 hypertension between the two groups. However, 3rd-degree hypertension was diagnosed in a significantly higher number of patients in Group 2. Chronic Heart Failure (CHF) was observed in both patient groups. Stage I CHF was more common in Group 1 patients ($p = 0.001$). Stage II CHF was significantly more common in Group 2 ($p = 0.001$). When the duration of diabetes mellitus was analyzed by year between the groups, it was found that the duration was significantly longer in Group 2 ($p = 0.000$). A history of acute cerebrovascular accident was also significantly more common in Group 2 ($p = 0.05$).

3. Results

Table 2. Analysis of Blood Pressure Indicators and Laboratory Tests Between Groups

	Diabetes duration > 5 years (n = 236)	Diabetes duration < 5 years (n = 49)	P (value)
SBP, mmHg	132.66±17.7	134.5±18.04	0.5
DBP, mmHg	84.04±9.7	84.7±9.9	0.7
Heart Rate	73.85±14.4	73.67±8.8	0.9
NT-proBNP, pg/mL	62[22.5±123.5]	105[53.7±296.0]	0,0001
Fasting glucose level, mmol/L	5.8±1.9	10.15±2.9	0,0001

The two groups were compared for ambulatory Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) values. No differences were found when comparing the SBP

and DBP values. When comparing NT-proBNP values, a significantly higher value was obtained in Group 2 (62[22.5 ± 123.5] pg/mL vs. 105[53.7±296.0] pg/mL; ($p=0.001$). When comparing fasting glucose levels in both groups, it was found that the levels were significantly higher in Group 2 (5.8 ± 1.9 mmol/L vs. 10.15 ± 2.9 mmol/L, $p = 0.0001$).

When comparing the central hemodynamic parameters, it was observed that these measures were larger in Group 2.

Table 3. Comparative Characteristics of Central Hemodynamic Parameters Between Groups

	DM duration > 5 years (n = 236)	DM duration < 5 years (n = 49)	P (value)
EDD, cm	5.08±0,5	5.33±0,5	p=0,002
ESD, cm	3.42±0,49	3.8±0,65	p=0,001
IVST, cm	1.16±0.13	1.19±0.1	p=0,05
LVPWT, cm	1.14±0,14	1.18±0,12	p=0,03
EDV, mL	124.7±27.7	138.8±29,8	p=0,0002
ESV, mL	49.9±18,5	65.18±28,6	p=0,001
LVMM, g	234.9±63.7	266.77±58.97	p=0.005
LVMMi, g/m ²	152.79±41.9	173.4±43.5	P=0.002
Stroke Volume	76.95±13.8	80.32±9.1	p=0,1
EF	60,78±7,05	54,59±10.6	p=0,001
E peak, m/s	0.89±0,3	0.63±0,14	p=0,09
A peak, m/s	0.78±0,1	0.78±0,13	p=0,9
E/A ratio	0.89±0,3	1.04±1.3	p=0,15
e' peak, m/s	0.09±0.06	0.07±0.02	p=0,01
E/e' ratio	0.8±1.6	0.75±1.3	p=0,043

When comparing the central hemodynamic parameters, it was observed that these measures were larger in Group 2. ESD – 3.42±0.49 cm vs 3.8±0.65 cm, $p=0.001$; EDD – 5.08±0.5 cm vs 5.33±0.5 cm, $p=0.002$. EDV – 124.7±27.7 mL vs 138.8±29.8 mL, $p=0.0002$; ESV – 49.9±18.5 mL vs 65.18±28.6 mL, $p=0.001$; the interventricular septum was found to be statistically significantly thicker in Group 2 – IVST – 1.16±0.13 cm vs 1.19±0.1 cm, $p=0.05$; LVPWT – 1.14±0.14 cm vs 1.18±0.12 mm, $p=0.03$; the left ventricular ejection fraction showed a statistically significant difference between the two groups: 60.78±7.05% vs 54.59±10.6%, $p=0.001$. LVMM (234.9±63.7 g/m² vs 266.77±58.97 g/m², $p=0.005$) and LVMMi (152.79±41.9 g/m² vs 173.4±43.5 g/m², $p=0.002$) were significantly higher in Group 2 than in Group 1. Left ventricular hypertrophy was more common in Group 2 patients (67% vs. 89%, $\chi^2 = 4.7$, $p = 0.05$).

When evaluating peak velocity indicators in both groups, it was found to be non-significantly lower in Group 2: E wave, 0.68±0.15 vs. 0.63±0.14 m/s, $p=0.09$; A wave, 0.78±0.1 vs. 0.78±0.13 m/s, $p=0.9$; E/A, 0.89±0.3 vs. 1.04±1.3 m/s, $p=0.15$. e' – 0.09±0.06 m/s vs 0.07±0.02 m/s, $p=0.01$. The E/e' ratio was found to be significantly lower in Group 2 (0.75 ± 1.3 vs. 0.8 ± 1.6 m/s, $p = 0.043$).

When evaluating the brachiocephalic vessels, the right intima-media thickness (IMT) was 1.0±0.18 vs. 3.0±0.89

mm ($p = 0.002$), the left IMT was 1.02 ± 0.19 vs. 4.69 ± 1.6 mm ($p = 0.002$), the right atherosclerotic plaque was 15.75 ± 18.1 vs. 24.37 ± 19.7 mm, $p = 0.003$; left Atherosclerotic plaque 30.7 ± 18.7 vs. 34.7 ± 20.1 mm, $p = 0.05$.

Table 4. Comparative Characteristics of Large Vessels Between Groups

	DM duration > 5 years (n = 236)	DM duration < 5 years (n = 49)	p (value)
Right IMT	$1.0 \pm 0,18$	$3.0 \pm 0,89$	0.002
Left IMT	$1.02 \pm 0,19$	$4.69 \pm 1,6$	0.002
Right Atherosclerotic Plaque	15.75 ± 18.1	24.37 ± 19.7	0.003
Left Atherosclerotic Plaque	30.7 ± 18.7	34.7 ± 20.1	0,05

At the same time, a direct correlation was found between the duration of DM and relative wall thickness ($r = 0.2$, $p < 0.001$), EDD ($r = 0.11$, $p = 0.05$), ESD ($r = 0.69$, $p = 0.004$), interventricular septal thickness ($r = 0.29$, $p = 0.001$), left ventricular posterior wall thickness ($r = 0.18$, $p = 0.001$), EDV ($r = 0.19$, $p = 0.024$), ESV ($r = 0.32$, $p = 0.001$), LVMM ($r = 0.13$, $p = 0.03$), LVMMi ($r = 0.12$, $p = 0.05$); and an inverse correlation with EF ($r = -0.205$, $p = 0.001$).

Table 5. Correlation Analysis of DM Duration

DM duration	Rx	P (value)
Relative wall thickness	0.29	0.001
EDD	0.11	0.05
ESD	0.69	0.004
IVST	0.29	0.001
LVPWT	0.18	0.001
EDV	0.19	0.024
ESV	0.32	0.001
LVMMi	0.12	0.019
LVMM	0.13	0.03
EF	-0.205	0.001
NT- proBNP	0.33	$p = 0.001$

4. Discussion

Early diagnosis of HF in patients with type 2 DM at early stages of development, that is, during the period when reversible changes in organs may develop, can reduce the development of cardiovascular complications, disability, and risk of death. This is because the duration of DM directly affects the development of complications of DM. Uncontrolled DM can cause complications that are twice as severe. In DM, initial changes in the heart may begin with left ventricular (LV) diastolic dysfunction. Left ventricular diastolic dysfunction is a sign of early heart damage and can be diagnosed long before clinical signs of the disease develop. Left ventricular diastolic dysfunction is the only functional disorder of the heart that can be detected by echocardiography (EchoCG) [4,7]. According to the recommendations of the European

Society of Cardiology, the determination of blood brain natriuretic peptide hormone (BNP) and its NT-pro BNP fraction is important in the diagnosis of CHF [5]. In our study, even though patients with preserved left ventricular EF were included, the amount of NT-pro BNP in the blood was significantly high and correlated with the duration of DM.

The development of CHF in patients with type 2 DM is rapid [6]. In all patients with DM included in the study, the presence of two stages of CHF was observed. An increase in the duration of diabetes mellitus was associated with the development of severe heart failure. Therefore, timely diagnosis of LV dysfunction is important in this patient category. The main diagnostic methods are echocardiography (EchoCG) and plasma BNP or NT-pro BNP analysis [8]. This study examined the association between type 2 DM duration and NT-pro BNP levels and structural changes in the heart. Despite the fact that the patients included in the study had preserved EF, we can see that NT-pro BNP was higher in patients with diabetes for more than 5 years. As the duration of DM increases, heart remodeling becomes more pronounced. In addition, the degree of atherosclerotic damage to the brachiocephalic vessels was more pronounced in patients with DM for more than 5 years. It was found that the stronger the heart remodeling, the higher the NT-pro BNP value in the patient. In addition, a direct correlation was observed between the duration of DM and NT-pro BNP values and LV dimensions.

5. Conclusions

DM is a major clinical problem for treating physicians. It is important to conduct early primary examinations and initiate standard treatment in patients with type 2 DM. This is because not diagnosing the disease for years causes rapid development of severe complications. Prolonging the duration of DM leads to remodeling of the heart and blood vessels.

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