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Serum Myonectin and Adropin Levels in Predicting Diabetes

Diyabeti Öngörmede Serum Miyonektin ve Adropin Düzeyleri

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ABSTRACT

Background: Myonectin is a myokine associated with type 2 diabetes mellitus (T2DM) and insulin resistance (IR), and adropin is a peptide hormone that prevents IR and impaired glucose tolerance (IGT). Adropin is produced by the liver and regulates energy homeostasis. This research aimed to examine the serum levels of myonectin and adropin levels among prediabetes, newly-diagnosed type 2 diabetes mellitus (nT2DM), and healthy controls.
Material and Methods: For this cross-sectional study, a total of 167 individuals were divided into 3 subgroups using OGTT and HbA1c; 61 prediabetes (36.5%), 62 nT2DM (37.1%), and 44 healthy controls (26.3%). Serum levels of myonectin and adropin were assayed using enzyme-linked immunoassay kits. The anthropometric (age, gender, weight, height, waist/hip ratio -WHR-, waist and hip circumference, and body mass index -BMI-) and biochemistry findings of the participants were evaluated between the groups.
Results: Our study showed that myonectin levels are associated with nT2DM and WHR ($p = 0.028$ and $p = 0.015$, respectively). The serum levels of myonectin are significantly correlated with systolic blood pressure values in the prediabetes group ($p = 0.017$). Linear regression analysis revealed that nT2DM affects the serum levels of myonectin, but not adropin values. The adropin levels are correlated with LDL-cholesterol, total cholesterol, and triglyceride levels in the nT2DM group ($p = 0.002$, $p= 0.004$, and $p = 0.035$, respectively).
Conclusion: The findings of the previous studies are supported by those of this study and indicated that the serum levels of myonectin may be associated with newly-diagnosed T2DM patients. Serum myonectin levels could be a valuable marker for predicting diabetes mellitus.

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ÖZET

Amaç: Miyonektin insülin direnci (IR) ve tip 2 diyabetes mellitus (T2DM) ile ilişkili bir miyokin iken adropin, IR'yi ve bozulmuş glukoz toleransını (BGT) önleyen bir peptit hormondur. Adropin karaciğer tarafından üretilir ve enerji homeostazını düzenler. Çalışmamızda yeni tanı almış-tedavisiz- tip 2 diyabetes mellitus (nT2DM), prediyabet ve sağlıklı kontrollerde serum miyonektin ve adropin düzeylerinin değerlendirilmesi amaçlanmıştır.
Gereç-Yöntem: Çalışmamızda toplam 167 kişi OGTT ve HbA1c bakılarak 3 alt gruba ayrıldı; 61 prediyabet (%36.5), 62 nT2DM (%37.1), 44 kontrol (%26.3). Serum miyonektin ve adropin seviyeleri, ELISA kitleri kullanılarak test edildi. Katılımcıların antropometrik (yaş, cinsiyet, kilo, boy, bel çevresi, kalça çevresi, bel/kalça oranı, vücut kitle indeksi) ve biyokimyasal bulguları tüm gruplar arasında değerlendirildi.
Bulgular: Çalışmamız nT2DM ve bel/kalça oranının miyonektin düzeylerini etkileyebileceğini gösterdi ($p = 0.028$ ve $p = 0.015$; sırasıyla). Prediyabet grubunda, miyonektin değeri ile sistolik kan basıncı değeri arasında anlamlı bir korelasyon saptandı ($p = 0.017$). Grupların ortalama miyonektin ve adropin seviyeleri arasında anlamlı fark yoktu. Lineer regresyon analizi, nT2DM'nin miyonektini etkilediğini ancak adropin değerlerini etkilemediğini ortaya koydu. Adropin düzeyleri nT2DM grubunda total kolesterol, LDL-kolesterol ve trigliserit düzeyleri ile koreleydi ($p = 0.002$, $p = 0.004$ ve $p = 0.035$; sırasıyla).
Tartışma: Bu çalışmadan elde edilen bulgular önceki çalışmaları desteklemektedir ve yeni tanı almış T2DM'li hastalarda serum miyonektin düzeylerinin değişebileceğini göstermiştir. Serum miyonektin seviyeleri, diyabetes mellitusu öngörmede değerli bir belirteç olabilir.

1. Background

Prediabetes is a relatively new clinical term that was first defined in 2002 in the United States by the American Diabetes Association (ADA) and the Department of Health and Human Services (1). Prediabetes is associated with an increase in blood glucose levels that are higher than usual but not high enough for the diabetes mellitus (DM) diagnosis (2). Prediabetes; is the condition of having one or more impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) and/or hemoglobin A1c (HbA1c)

≥ 5.7 - < 6.5% (3). The terms IFG and IGT describe the stages between normal glucose balance and DM (4).

Myonectin (C1q/Tumor Necrosis Factor-related protein-CTRP-15) is a kind of myokine identified in 2012 by Seldin et al. (5). Myonectin belongs to the CTRP family produced by skeletal muscle regulating the metabolism of whole-body fatty acid and is released into the circulation through the increased calcium level during exercise due to muscle contraction (6). Exercise positively affects the energy balance and systemic insulin sensitivity, yet the mechanisms underlying them are obscure. Physical exercise reduces circulating fatty acid by significantly increasing myonectin expression and circulating levels, increasing fatty acid reuptake into cells. Seldin et al. (5) and Pourranjbar et al. (7) observed increased muscle and circulating myonectin expression following eight weeks of aerobic exercise. In the studies by Petersen and Abedi, myonectin and insulin resistance (IR) were decreased due to exercise (8,9). In Li K's study, circulating myonectin levels stayed the same after an exercise of 45 minutes (10). Thus, it is possible to suggest that myonectin is not affected by acute changes, therefore, suggesting that it may be a promising marker to diagnose prediabetes and DM.

Adropin is a recently identified peptide hormone playing essential roles in metabolic homeostases, such as preventing IR, IGT, and dyslipidemia as well as controlling fatty acid metabolism. In their study, Kutlu et al. reported a negative relationship between nonalcoholic fatty liver disease (NAFLD), IR, total cholesterol and triglyceride levels, and adropin levels (11). Initially, adropin was isolated in the liver and brain of mice and expressed through the "Energy Homeostasis Associated Gene" (Enho) (12). Adropin mediates the mechanism of increased adiposity, IR, glucose, and lipid metabolism (13,14). As a result of the studies, a significant increase in the level of serum adropin and changes in IR and glucose intolerance were observed in the rats on a high-fat diet (15). Moreover, the effect of adropin on the expression of inducible nitric oxide synthase was discovered (16), which could explain its potential role in preventing endothelial disorders in patients with DM (17). It has been claimed that treatment with adropin may lower blood glucose in rats with diabetes induced by streptozotocin and improve IR (18). In the literature, limited data focuses on the relationship between serum adropin concentrations and T2DM.

In this research, the primary purpose was to investigate the serum myonectin and adropin levels of individuals with prediabetes, newly diagnosed T2DM (nT2DM) patients who have not received antidiabetic treatment and non-diabetic/normoglycemic healthy controls.

2. Materials and Methods

2.1. Patients and study design

A total of 167 individuals with prediabetes, nT2DM and healthy subjects that admitted to the Department of Internal Medicine, participated in this cross-sectional study. The individuals were scheduled for a nutrition program that contains at least 200 gr of carbohydrates per day at least three days before the OGTT. The initial fasting blood samples were collected between 08:00-09:00 following ten hours of fasting (OGTT 0th hour) (in the meantime, blood samples were taken for other metabolic parameters). Then, a 75-gram solution of anhydrous glucose dissolved in 300 mL of water in 5 minutes was given to the individuals, and postprandial glucose was measured 2 hours later. Individuals who underwent OGTT, per the ADA diagnostic criteria, were divided into three groups (3):

Group 1 (prediabetes): FPG (OGTT 0th hour) values ≥100-<126 mg/dL as impaired fasting glucose (IFG) and/or postprandial glucose (OGTT 2nd hour) values ≥ 140-<200mg/dL as impaired glucose tolerance (IGT) and/or HbA1c % values ≥ 5.7-< 6.5 included 61 individuals.

Group 2 (newly diagnosed T2DM-nT2DM): nT2DM group included 62 individuals with FPG values (OGTT 0th hour) ≥126 mg/dL and/or postprandial glucose values (OGTT 2nd hour) ≥200 mg/dL and/or HbA1c ≥ 6.5%.

Group 3 (control): FBG (OGTT 0th hour) values <100 mg/dL and postprandial glucose (OGTT 2nd hour) values <140 mg/dL and HbA1c % value <5.7 included 44 individuals without any other disease and normal glucose tolerance.

Patients with one or more of the following conditions that may affect metabolic parameters were excluded from the study: hyperthyroidism or hypothyroidism, renal failure, hepatic failure, heart failure, alcoholism, malignancy, pregnancy, pancreatic diseases, steroid or hydrochlorothiazide use, previous diagnosis of DM, or those taking medication for DM.

2.2. Laboratory measurement

Blood glucose was measured using the Siemens Advia 1800 device with the photometric method. The chemiluminescence immunoassay method (Siemens Advia Centaur) was employed to analyze insulin levels. Blood samples were obtained simultaneously for myonectin and adropin analysis. The samples were immediately cooled; centrifugation was used to separate the serum, and it was kept at -80°C until the procedure. The serum concentrations of serum levels of myonectin and adropin were assayed in duplicate with enzyme-linked immunoassay (ELISA) kits (Myonectin Catalog Number: SEU540Hu; Adropin Catalog

No.: SEN251Hu; Cloud-Clone Corp. 23603 W. Fernhurst Dr., Unit 2201, Katy, TX 77494, USA) in accordance with the protocol of the producer. The inter-assay and intra-assay coefficients of the variations for myonectin and adropin were <10% and <12%, respectively. The microplate offered in this kit has been pre-coated with an antibody specific to adropin. Standards or samples were then included in the suitable microplate wells with a biotin-conjugated antibody specific to adropin. Then, Avidin conjugated to Horseradish Peroxidase (HRP) was included in the microplate wells and incubated. After adding the solution of TMB substrate, only the wells containing adropin, biotin-conjugated antibody and enzyme-conjugated Avidins showed a change of color. The enzyme-substrate reaction was completed by addition of sulphuric acid solution and change of color was measured spectrophotometrically (Smart Microplate Reader; USCN KIT INC.) at a 450nm ± 10 nm wavelength. The adropin concentration in the samples was then found by comparing the O.D. of the samples with the standard curve. All these applications are valid for myonectin.

2.3. Ethics issues

Before conducting the study, we obtained ethical clearance from the Clinical Research Ethics Committee with protocol no. date: IRB Number: 2019.03.3.04.033 (March 29, 2019). All participants confirmed and signed their written informed consent. The authors declare that there is no potential conflict of interest relevant to this article.

2.5. Statistical analyses

The Statistical Package for the Social Sciences (SPSS) version 25.0 software (SPSS Inc., Chicago, IL, USA) was used to analyze the data. The results were presented as percentages, frequencies, standard deviations (SD), and means. When the numerical variables were normally distributed, the Kolmogorov-Smirnov test was employed. The one-way ANOVA was used to compare data meeting parametric assumptions, while The Chi-Square test was performed to compare categorical variables. The Pearson correlation analysis was used to assess the correlations between the numerical variables. Finally, a linear regression analysis was performed to check the variables independently that affect myonectin and adropin levels. A p-value of <0.05 was regarded as 'statistically significant'.

3. Results

The data were analysed for 167 individuals 61 (36.5%) prediabetes, 62 (37.1%) nT2DM, and 44 (26.3%) controls. The mean age of the individuals was 41.5±12.2. The control group consisted of much younger individuals than other groups (p = 0.001). Additionally, we detected some significant differences between the groups with regard to the anthropometric features (Table 1).

Table 1. The anthropometric features of the prediabetes, newly diagnosed diabetes mellitus patients and controls

	Groups							
	Prediabetes		Newly diagnosed DM		Control			
	Mean	SD	Mean	SD	Mean	SD	F*	p
Age (years)	43.85	10.95	47.40	9.01	30.13	10.44	39.632	<0.001
Height (cm)	162.70	9.67	163.45	8.59	165.64	9.14	0.914	0.404
Weight (kg)	85.99	15.48	84.96	16.01	79.11	14.35	1.862	0.160
BMI (kg/m^2)	32.83	7.31	31.84	4.72	29.13	5.51	3.264	0.042
Waist circumference (cm)	96.8	12.8	96.8	9.4	86.5	11.6	10.888	<0.001
Hip circumference (cm)	107.1	13.0	105.1	8.5	100.8	10.8	3.597	0.030
Waist/hip ratio (WHR)	0.91	0.08	0.92	0.07	0.86	0.08	7.171	0.001

*One-way ANOVA, SD: Standard Deviation, BMI: Body Mass Index.

No statistically significant differences were observed between myonectin, adropin and HDL levels of the three groups (p=0.194, p=0.213 and p=0.567; respectively). The mean total cholesterol and LDL- cholesterol levels of the control group were significantly lower than those of prediabetes and nT2DM (p=0.005/p=0.001 and p=0.006/p=0.001), while no statistically significant differences were observed between prediabetes and nT2DM (p=0.747 and p=0.341). The mean triglyceride levels of nT2DM were found to be statistically significantly higher than prediabetes and the control group (p=0.001/p=0.001). SBP and DBP averages of the control group were found to be statistically significantly lower than nT2DM (p=0.003 and p=0.007). Other biochemical parameters were shown in Table 2.

Table 2. The comparison of biochemical parameters and blood pressure between the groups

	Groups						
	Prediabetes (n = 61)		Newly diagnosed DM (n = 62)		Control (n = 44)		
	Mean	SD	Mean	SD	Mean	SD	p
Myonectin (ng/mL)	0.28	0.09	0.32	0.12	0.29	0.07	0.194[a]
Adropin (pg/mL)	1576.89	305.96	1691.13	319.39	1593.72	264.12	0.213[a]
Total cholesterol	217.07	45.01	222.94	41.97	190.61	35.66	0.001[b]
LDL cholesterol	145.36	32.05	153.78	32.84	125.25	30.76	0.001[b]
Trigliserid	133.26	72.86	214.89	132.51	113.37	48.52	0.001[a]
HDL cholesterol	47.82	8.65	45.9	9.73	46.58	9.85	0.567[b]
SBP (mmHg)	118.08	10.17	120	7.3	114.55	6.63	0.005[b]
DBP (mmHg)	72.24	6.28	74.1	4.96	70.68	5.46	0.009[b]

[a]Kruskal Wallis Test. [b]One-Way Analysis. SD: Standard Deviation. SBP: Systolic Blood Pressure. DBP: Diastolic Blood Pressure.

In the control group, means of AST, GGT and CRP were found to be statistically significantly lower than prediabetes and nT2DM (p=0.02/p=0.04, p=0.002/p=0.0001 and p=0.004/p=0.001; respectively), AST and CRP averages were not statistically significantly different between prediabetes and nT2DM, while GGT means in prediabetes were found to be statistically significantly lower than nT2DM (p=0.002). The AST/ALT means of the patients with nT2DM patients were significantly lower than those of the patients with prediabetes patients and the control group (p=0.003/p=0.001). The mean LDH levels of the control group were found to be statistically significantly lower than nT2DM (p=0.039). Other biochemical parameters were shown in Table 3.

Table 3. The **c**omparison of biochemical parameters between the prediabetes, newly diagnosed diabetes mellitus patients and controls

	Groups							
	Prediabetes		Newly diagnosed DM		Control			
	Mean	SD	Mean	SD	Mean	SD	F*	P
AST (U/L)	25.95	10.38	27.09	16.31	21.59	5.98	2.787	0.065
ALT (U/L)	29.85	21.18	36.20	24.96	23.67	13.09	4.539	0.012
AST/ALT ratio	1.01	0.31	0.85	0.24	1.10	0.43	7.400	0.001
ALP (U/L)	81.91	23.43	87.25	24.87	74.00	22.04	3.628	0.029
GGT (U/L)	31.36	24.28	38.56	21.67	22.26	14.90	7.046	0.001
LDH (U/L)	201.65	43.67	207.90	31.95	189.74	25.43	3.103	0.048
Albumin (g/dL)	4.43	0.29	4.29	0.28	4.36	0.29	2.928	0.057
CRP (mg/L)	4.64	3.84	7.03	9.58	2.98	3.69	4.928	0.008
TSH (mIU/L)	1.66	1.15	2.37	3.16	2.07	1.23	1.601	0.205
Free T4 (pg/ml)	0.78	0.12	0.78	0.15	0.93	1.12	0.954	0.387

*One-way ANOVA, SD: Standard Deviation. AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; ALP: Alkaline Phosphatase; GGT: Gamma-Glutamyltransferase; LDH: Lactate Dehydrogenase; CRP: C-Reactive Protein; TSH: Thyroid-Stimulating Hormone.

In the prediabetes group, there was a weak positive correlation between myonectin values and systolic blood pressure (SBP) values (p = 0.017). Moreover, in the nT2DM group, there were weak positive correlations between adropin levels and total cholesterol, low-density lipoprotein (LDL) cholesterol and triglyceride values (p = 0.002, p = 0.004 and p = 0.035; respectively) (Table 4). Other biochemical parameters were shown in Table 4.

Table 4. The correlation of blood pressure and biochemical parameters between groups

		Prediabetes		Newly diagnosed DM		Control	
		Myonectin	Adropin	Myonectin	Adropin	Myonectin	Adropin
SBP (mmHg)	r	0.315	0.068	-0.057	-0.013	0.001	-0.228
	p	0.017	0.615	0.667	0.922	0.998	0.141
DBP (mmHg)	r	0.244	0.051	-0.111	0.048	0.157	-0.069
	p	0.067	0.709	0.401	0.718	0.316	0.661
HbA1c	r	-0.005	-0.03	-0.056	-0.197	-0.077	-0.140
	p	0.974	0.832	0.670	0.131	0.624	0.372
Glukoz	r	0.087	0.059	0.030	-0.121	-0.204	-0.081
	p	0.522	0.666	0.820	0.359	0.190	0.605
Total cholesterol	r	-0.072	0.248	0.122	0.441	0.222	-0.115
	p	0.611	0.073	0.403	0.002	0.152	0.462
LDL cholesterol	r	-0.06	0.198	0.225	0.377	0.221	-0.067
	p	0.667	0.152	0.095	0.004	0.155	0.668
Trigliserid	r	0.14	0.202	0.162	0.285	-0.207	-0.228
	p	0.309	0.139	0.238	0.035	0.183	0.142
HDL cholesterol	r	0.030	0.126	-0.083	-0.153	0.167	0.039
	p	0.833	0.370	0.571	0.293	0.289	0.804

Pearson Correlation test. SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HbA1c: Hemoglobin A1c.

Linear regression analysis was performed to assess elements affecting the levels of adropin and myonectin by controlling the potentially confounding factors. Age, BMI, WHR, and AST/ALT ratio were independent factors entered into the models. Additionally, the presence/absence of prediabetes and nT2DM were entered as dummy variables ($p = 0.015$ and $p = 0.028$). While WHR and the presence of nT2DM were significantly affecting myonectin levels, none of the included variables significantly affected the adropin levels (Table 5).

Table 5. The linear regression analysis for myonectin and adropin

	Unstandardized Coefficients		t	P	95% CI	
	B	SE			Lower	Upper
Dependent variable: Myonectin (ng/mL)						
Age (years)	0.000	0.001	-0.256	0.798	-0.002	0.002
BMI (kg/m^2)	0.001	0.002	0.354	0.724	-0.003	0.004
Waist/Hip ratio	-0.334	0.135	-2.479	0.015	-0.602	-0.066
AST/ALT ratio	-0.037	0.030	-1.228	0.223	-0.096	0.023
Prediabetes	0.020	0.028	0.703	0.484	-0.037	0.077
Newly diagnosis DM	0.072	0.032	2.229	0.028	0.008	0.136
Dependent variable: Adropin (pg/mL)						
Age (years)	-0.652	3.399	-0.192	0.848	-7.403	6.099
BMI (kg/m^2)	-7.969	5.291	-1.506	0.135	-18.478	2.540
Waist/Hip ratio	605.744	448.330	1.351	0.180	-284.809	1496.297
AST/ALT ratio	-48.562	99.131	-0.490	0.625	-245.474	148.350
Prediabetes	-22.085	94.593	-0.233	0.816	-209.981	165.812
Newly diagnosis DM	88.980	107.233	0.830	0.409	-124.025	301.984

SE: Standard Error.

4. Discussion

In this study, we determined that myonectin levels could be associated with nT2DM and WHR. Moreover, we found a positive correlation between myonectin and SBP in the prediabetes group. Also, a positive correlation was detected between adropin values and total cholesterol, LDL cholesterol, and triglyceride levels of the nT2DM group.

Myonectin, involved in glucose and lipid metabolisms, draws attention as a new marker for predicting DM. Li Z's study showed that serum myonectin levels negatively correlated with obesity, BMI, and visceral and subcutaneous fat tissue measurement. Myonectin levels were decreased in T2DM patients and obese individuals, and serum myonectin levels correlated with metabolic markers of T2DM, suggesting that myonectin may be a useful marker for predicting obesity and T2DM development (19). Aerobic exercise (AE) alone does not alter circulating myokine levels in patients with T2D, whereas myonectin levels may increase with AE and decrease with obesity (5,19). In contrast, Park et al. reported that the myonectin levels in circulation significantly increased in diabetic/obese animals (20). The serum levels of myonectin correlated positively with WHR (10) in a study by Li K et al. On the other hand, in our study, we found that the myonectin levels were inversely associated with WHR. The literature review shows conflicting results but we expect that a larger sample may help provide more reliable results. In literature, in Li Z's study, serum myonectin levels were lower in T2DM patients than in the controls (19). Li et al found that the groups with T2DM and IGT had higher serum myonectin concentrations than the controls (10). Multivariate logistic regression analysis of the data in the same study showed that the serum myonectin levels were significantly correlated with T2DM and IGT (10). In our study, linear regression analysis displayed that nT2DM affects myonectin levels. In Li K's study, short-term hyperinsulinemia and hyperglycemia induced by OGTT in healthy individuals failed to change circulating myonectin levels (10). This result suggested that short-term hyperinsulinemia and hyperglycemia may not necessarily regulate myonectin in circulation. This may explain why myonectin was not associated with the prediabetes group but with the nT2DM group in our study. The findings from this study support those of previous studies and showed that serum levels of myonectin may decrease in newly-diagnosed T2DM patients.

Ghany and Reis's studies showed that prediabetes (21) and diabetes are both associated with left ventricular dysfunction (22). Patients with T2DM are at significant risk of developing cardiovascular disease (23,24), and the association of hypertension increases the possibility of cardiovascular complications (25). Studies have assumed that IR is the usual pathophysiological factor underlying hypertension and T2DM (26). Yet, its pathogenesis is complicated and has not been fully elucidated. Muscle tissue is a vital target element of IR and is regarded as an active endocrine organ. Myonectin is also primarily secreted and expressed from muscle tissue (6). This suggests that there may be a relationship between myonectin and hypertension. In this study, we determined a statistically significant positive correlation between myonectin and SBP values in the prediabetes group. Because most of the nT2DM group received antihypertensive drugs, no relationship was found between SBP and myonectin in the nT2DM group. Studies with nT2DM patients that do not receive antihypertensive drugs would be more demonstrative to confirm this relationship.

In literature many studies, adropin is associated with glucose, lipid, and energy metabolism, and antiatherosclerosis. Liu et al's study showed that serum adropin level is correlated with cardiovascular disease (27). In their study, adropin significantly reduced the level of triglyceride, total cholesterol, and LDL cholesterol depending on the dose in streptozotocin-induced diabetic rats (28). In Skrzypski et al's study, serum triacylglycerol and cholesterol levels were decreased in mice with T2DM treated with adropin (29). In their study among Taiwanese adolescents, Chang et al. found that serum adropin levels were not related to body composition and were not associated with lipid variables. Adropin's role in the progress of obesity is yet to be clarified (30). In our study, we observed a statistically significant positive correlation between adropin levels and total cholesterol, LDL cholesterol, and triglyceride values of the nT2DM group.

5. Conclusions

Consequently, this study revealed that the state of nT2DM affects myonectin levels. For this reason, myonectin may be a promising marker in the diagnosis of T2DM. Further studies with a larger number of patients are warranted to reach a more precise conclusion.

Limitations of the study

The presented research has several potential limitations: The lack of a DM group under antidiabetic treatment in our study design and the use of antihypertensive drugs by a large part of the nT2DM group. Further studies with nT2DM patients who do not use antihypertensive drugs would be demonstrative. And the other limitation, this study reports the experience of a single center. Therefore, the results are limited for generalization to other populations. Finally, the single-point measurement of variables may decrease the accuracy of the outcomes.

Conflict of Interest: The authors declare that there were no potential conflicts of interest with regard to the research, authorship and/or publication of this article.

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Authorship Contribution:

ES: Idea, design, data collection and processing, analysis and interpretation, literature review, critical review and writing the article.

ED: Data collection and processing, analysis and interpretation, and literature review.

ID: Data collection and processing, analysis and interpretation, and literature review.

MD: Analysis and interpretation, literature review, critical review and writing the article.

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