



Body Composition and the Components of Metabolic Syndrome in Type 2 Diabetes: The Roles of Disease Duration and Glycemic Control

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Purpose: Data about body compositional changes throughout the course of type 2 diabetes (T2D) are limited and inconsistent. We investigated the roles of the disease duration and glycemic control in T2D-associated changes of body composition and the components of metabolic syndrome (MetS).

Patients and Methods: A total of 25 non-diabetic controls and 92 individuals aged 20–60 years with T2D were included in a case–control study conducted at King Faisal Specialist Hospital, Saudi Arabia. Based on disease duration (newly diagnosed: within the first year and long duration: ≥ 5 years) and glycemic control (glycated hemoglobin [HbA1C] level $\leq 7\%$), the patients were divided into the following groups: newly diagnosed and controlled (N&C, $n=25$), newly diagnosed and uncontrolled (N&U, $n=17$), old and controlled (O&C, $n=25$), and old and uncontrolled (O&U, $n=25$). Blood samples were collected to assess fasting blood glucose level, HbA1C level, and lipid profile. Anthropometric data were evaluated, and body composition was assessed using a bio-impedance analyzer. Nonparametric tests and multivariable logistic regression analyses were performed.

Results: Compared to the control group, the fat mass (FM) was significantly higher in all groups; furthermore, the fat mass/fat-free mass (FM/FFM) ratio was significantly higher in the N&C. The N&U and O&U groups showed significantly higher percentages of all components of MetS. Among all selected independent factors, only age increased the likelihood of MetS diagnosis by 7% (OR: 1.07; 95% CI: 1.004–1.149; $P<0.05$). Besides, age, gender, adherence to diet regimen, and T2D duration showed lower odds of increased FM/FFM ratio.

Conclusion: This study provided evidence about the impact of T2D on body composition and the other components of MetS. Thus, further characterization of T2D contributes to defining the etiology of the disease to detect and treat poor cardiometabolic health.

Keywords: type 2 diabetes, metabolic syndrome, disease duration, HbA1C, FM/FFM ratio, HOMA-IR

Introduction

Type 2 diabetes (T2D) is a highly prevalent metabolic disorder characterized by a state of insulin resistance and relative insulin deficiency.^{1–3} Currently, the condition affects more than 425 million people worldwide, and the number of individuals who will develop T2D can exceed 629 million by the year 2045.² Meanwhile, multiple lifestyle and genetic factors contribute to the pathogenesis of T2D,^{1,3–5} and the specific etiologies of the disease are not yet fully understood. Moreover, several cases of T2D may remain undiagnosed long after its onset, thereby leading to severe life-threatening

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health problems.^{1,3–5} Thus, it is important from a clinical perspective that studies continually evaluate factors associated with poor health outcomes in T2D. Indeed, such research is essential in the prevention, early detection, and treatment of poor cardiometabolic health.

Atherosclerotic cardiovascular disease is the leading cause of morbidity and mortality in individuals with T2D.^{6–8} A high risk of cardiovascular disease is correlated to obesity and the other components of metabolic syndrome (MetS), including hyperlipidemia and insulin resistance, in those with T2D.^{9,10} Thus, appropriate research aiming to define factors contributing to poor T2D-related health outcomes must focus particularly on these metabolic impairments. Indeed, most individuals with T2D are overweight or obese,¹¹ and T2D patients who are not considered overweight or obese may still have a high percentage of body fat primarily in the abdominal region.^{11–13}

Current studies have indicated that impaired glycemic control and disease duration are the two major contributing factors that affect body composition in individuals with T2D.^{14,15} However, data about fat distribution and variations in individuals with T2D are limited and equivocal. Besides, the impact of T2D on hyperlipidemia and insulin resistance is not fully elucidated. Considering this result, the current study investigated the roles of disease duration and glycemic control in T2D-associated changes in body composition and the other components of MetS.

Patients and Methods

Population

A total of 92 patients with known T2D and 25 healthy individuals aged 20–60 years were enrolled in a case–control study conducted at King Faisal Specialist Hospital and Research Centre in Riyadh, Saudi Arabia. The potential participants were then interviewed to collect detailed data, and a written informed consent was obtained from all those who wanted to participate. The exclusion criteria included individuals diagnosed with type 1 diabetes; those with a history of other endocrine diseases, neurological disorders, and/or renal comorbidities; and pregnant and lactating women. The study protocol was in accordance with the Declaration of Helsinki and was approved by the ethics committee of the College of Applied Medical Sciences, King Saud University (at all sites; approval letter no: CAMS 30/3536).

Patients with T2D who were enrolled in the study were grouped based on two factors: 1) duration of time since the

diagnosis of T2D, categorized as either new or old cases if the diagnosis of T2D was made within a year or if the diagnosis was confirmed at least 5 years prior, respectively,^{16,17} and 2) hemoglobin A1C (HbA1C, %) level, categorized as either controlled or uncontrolled, which is defined as HbA1C level \leq or $>7\%$, respectively.¹⁸ A control group was recruited by contacting healthy visitors at the hospital or relatives of the patients. Subsequently, five groups were included in this study: the healthy control (C) group (n=25), new and controlled cases (N&C) group (n=25), new and uncontrolled (N&U) group (n=17), old and controlled (O&C) group (n=25), and old and uncontrolled (O&U) group (n=25).

The sample size was calculated using an online calculator¹⁹ with consideration of the following: 95% confidence interval (CI), power of 80%, a control-to-case ratio of 1:1, the proportion of population without T2D who developed MetS in the 30–40-year-old population in Saudi Arabia (42.7%),²⁰ and proportion of individuals with T2D who developed MetS in Saudi Arabia (85.8%).²¹ Thus, the sample size was set at 20 individuals with T2D and 20 controls.

Anthropometric Measurements

Weight (kg) and height (cm) were measured twice while the patients were barefoot and wearing light clothes, and the body mass index (BMI) was calculated as weight (kg)/height²(cm). A trained nurse assessed other variables, such as waist circumference (WC in cm) and systolic blood pressure (SBP)/diastolic blood pressure (DBP).

Body Composition

Body composition was assessed using Tanita BC-418 (Tanita Corporation, Japan) – a segmental body composition analyzer used to measure the percentage of body fat (PBF), fat mass (FM), fat-free mass (FFM), total body water (TBW), and basal metabolic rate (BMR). Moreover, the FM-to-FFM ratio was calculated by dividing FM with FFM (FM/FFM ratio=FM_(kg)/FFM_(kg)).²²

Biochemical Assessment

Fasting blood glucose (FBG) level was analyzed with Cobas c 701 module (Roche Diagnostics, the UK).²³ Cobas c 311 (Roche Diagnostics, the UK) was used to analyze HbA1C level, which was measured in mmol/mol and then converted into percentages using a cutoff point of 7.0%.²⁴ Insulin level was measured using electrochemiluminescence immunoassay (Modular Analytics E170 and Cobas e411, 601,

and 602).²³ Serum total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein cholesterol, and triglyceride levels were assessed using Cobas c 701 modules (Roche Diagnostics, the UK).²³ The homeostasis model assessment-insulin resistance (HOMA-IR) score was used as an indicator of insulin resistance and was calculated using the following formula: fasting insulin (mIU/mL)×fasting glucose (mg/dL)/405.²⁵

Components of Metabolic Syndrome

Based on the consensus of the International Diabetes Federation,²⁶ the components of MetS used in this study were as follows: 1) central obesity defined as a WC of ≥ 94 cm for men or ≥ 80 cm for women, 2) hypertension defined as SBP ≥ 130 and/or DBP ≥ 85 mmHg or if the patient was already receiving pharmacological treatment for hypertension, 3) hyperglycemia defined as an FBG level ≥ 100 mg/dL, 4) low HDL cholesterol level defined as < 40 mg/dL in men or < 50 mg/dL in women or if the patient was already receiving treatment, and 5) elevated triglyceride levels defined as ≥ 150 mg/dL or if the patient was already receiving treatment. MetS was defined as WC higher than the previously mentioned cutoff values plus the presence of any positive two components.²⁶

Statistical Analysis

Descriptive statistics for non-categorical data were presented as means±standard deviations, and categorical parameters were recorded as absolute and relative frequencies. All data sets were tested for normality using the Kolmogorov–Smirnov, and Shapiro–Wilk tests, and they were found to be non-normally distributed, except for WC, BMI, FM, and creatinine level. Since most data had a non-normal distributed, all variables in the study groups were assessed using the Kruskal–Wallis test with performing multiple comparisons by the Mann–Whitney test. Categorical variables were compared using the chi-square test. The correlation between the study parameters was assessed with Spearman correlation coefficient. A multivariate binary logistic regression analysis was conducted to assess the independent factors for the risk of developing MetS (dependent variable), and a multiple linear regression analysis was performed to evaluate the association between the FM/FFM ratio and the same model of independent variables. The model included age, sex, physical activity, adherence to the dietary regimen, HbA1c levels, duration of T2D (in years), categories of glycemic control, and disease duration. A P value of ≤ 0.05 was considered statistically significant. Statistical analyses were conducted using the

Statistical Package for the Social Sciences version 25 (SPSS Statistics, IBM Corp., the USA).

Results

The total sample comprised men (56.5%) with a mean age of 45.58 ± 11.14 years. All patients who were assessed were instructed to follow healthy lifestyle habits, such as a balanced diet and daily physical activity for 30 min. Furthermore, they were instructed to take oral anti-diabetes agents regularly (metformin [100%], sulphonylureas [71%], and combination [56%]). Table 1 shows the general characteristics of each group included in the study. Compared to the control group, the BMI, WC, and SBP of all groups with T2D were significantly higher than those of the controls. However, further comparisons between the new and old groups, regardless of glycemic control, revealed insignificant changes in BMI, WC, and SBP.

The bio-impedancemetry analysis revealed that the PBF, FM, and FM/FFM ratio of the participants newly diagnosed with T2D were significantly higher than those of the controls even if the HbA1C levels were controlled (Table 2). The FM was significantly higher in all diabetic groups than in the control group. The FM of the O&C group was significantly lower than that of the N&C group. That is, in patients with controlled HbA1C levels, the FM progressively decreased with time. However, this result was not observed in the N&U and O&U groups. Interestingly, in the groups with uncontrolled HbA1C levels, the FFM and TBW significantly decreased in the O&U group compared with the N&U group. Other comparisons of the FM/FFM ratio among the diabetic groups revealed no significant changes.

The biochemical analysis revealed that the HOMA-IR score, which is an indicator of insulin resistance, was significantly high in all diabetic groups than in the control group. Moreover, in the groups with uncontrolled glycemic status (N&U and O&U groups), the HOMA-IR scores significantly increased (Table 3). By contrast, in the groups with controlled glycemic status (N&C and O&C groups), the duration of T2D did not cause any significant change in the HOMA-IR score ($P=0.404$). Regarding lipid profile, all diabetic groups had significantly higher TG levels and lower HDL levels than the control group. Moreover, the N&U group had significantly higher triglyceride and lower HDL levels than the N&C group (Table 3).

Data about the presence of the MetS components among all the study groups are presented in Table 4. That is, all groups with T2D presented with central obesity based on WC values.

Table 1 General Characteristic Variables Among Study Groups

Groups	Age (Years)	T2D Duration (Years)	Height (cm)	Weight (kg)	BMI (kg/m ²)	WC (cm)	DBP (mmHg)	SBP (mmHg)
C	48.36±9.35	-----	165.24±8.70	72.14±17.52	26.34±5.80	89.76±11.61	75.92±7.36	116.28±9.14
N&C	45.71±8.20	0.46±0.15	166.20±10.26	87.94±15.40	31.83±4.55	107.96±10.65	81.36±7.95	132.64±11.88
N&U	51.96±9.49	0.44±0.16	166.53±10.14	91.06±9.35	33.10±4.53	108.53±8.65	80.47±12.10	128.71±15.21
O&C	50.80±6.55	5.87±0.64	162.88±10.08	79.29±14.36	30.57±5.12	105.28±12.47	86.92±25.75	130.52±25.09
O&U	31.12±6.21	5.73±0.55	160.86±14.05	83.51±21.41	30.72±6.18	104.12±11.34	78.40±9.29	129.68±15.32
P-value	0.000*	0.000*	0.597	0.000*	0.000*	0.000*	0.158	0.000*
Multiple Comparisons by Mann-Whitney Test	P-values							
C vs N&C	0.000*	0.000*	0.884	0.001*	0.000*	0.000*	0.011	0.000*
C vs N&U	0.000*	0.000*	0.590	0.000*	0.000*	0.000*	0.223	0.004*
C vs O&C	0.000*	0.000*	0.398	0.076	0.005*	0.000*	0.064	0.007*
C vs O&U	0.000*	0.000*	0.450	0.022*	0.007*	0.000*	0.228	0.002*
N&C vs N&U	0.199	0.727	0.797	0.131	0.450	0.858	0.817	0.187
O&C vs O&U	0.199	0.483	0.793	0.580	0.954	0.712	0.281	0.778
N&C vs O&C	0.055	0.000*	0.180	0.065	0.190	0.366	0.726	0.478
N&U vs O&U	0.046*	0.000*	0.293	0.010*	0.151	0.140	0.700	0.729

Notes: Data are presented as the mean ± SD. *Means significant difference ($p \leq 0.05$).

Abbreviations: BMI, body mass index; WC, waist circumference; N&C, newly diagnosed and controlled; N&U, newly diagnosed and uncontrolled; O&C, old and controlled cases; O&U, old and uncontrolled cases.

Table 2 Body Composition Parameters by Bio-Impedancemetry Analysis Among Study Groups

Groups	PBF (%)	Fat Mass (kg)	Fat-Free Mass (kg)	FM/FFM ratio	TBW (L)	BMR (kcal)
C	30.35±10.04	22.31±10.20	49.85±12.56	0.46±0.20	36.46±9.16	1522.12±357.02
N&C	38.50±8.68	34.10±10.63	53.94±11.10	0.65±0.23	39.49±8.12	1643.76±309.80
N&U	35.70±8.32	32.75±9.23	58.40±8.44	0.58±0.22	42.75±6.18	1760.53±228.39
O&C	34.76±9.14	28.32±9.67	52.61±10.85	0.55±0.23	38.52±7.95	1581.76±293.46
O&U	35.36±8.95	29.50±11.66	51.78±7.32	0.58±0.22	37.90±5.36	1561.04±206.08
P-value	0.096	0.001*	0.056	0.107	0.053	0.042*
Multiple Comparisons by Mann-Whitney Test	P-values					
C vs N&C	0.007*	0.000*	0.128	0.007*	0.123	0.107
C vs N&U	0.112	0.002*	0.008*	0.136	0.007*	0.007*
C vs O&C	0.162	0.036*	0.225	0.227	0.222	0.308
C vs O&U	0.128	0.026*	0.194	0.094	0.184	0.265
N&C vs N&U	0.265	0.573	0.115	0.393	0.112	0.115
O&C vs O&U	0.861	0.884	1.000	0.610	1.000	0.961
N&C vs O&C	0.135	0.045*	0.655	0.142	0.648	0.491
N&U vs O&U	0.959	0.205	0.017*	0.886	0.017*	0.011*

Note: *Means significant difference ($p \leq 0.05$).

Approximately 60%, 51.5%, 60%, and 59% of the participants in the N&C, N&U, O&C, and O&U groups, respectively, presented with central obesity. Both blood pressure and FBG had a similar distribution. The lipid, triglyceride, and HDL cholesterol levels were significantly higher in the N&U and O&U groups (groups with uncontrolled glycemic status,

regardless of disease duration). Interestingly, compared to the control group, the percentage of participants presenting with all the components of MetS was significantly higher in the groups with uncontrolled glycemic status (the N&U and O&U groups) than in those with controlled glycemic status.

Table 3 Biochemical Variables Among Study Groups

Groups	FBG (mg/dL)	HbA1c (%)	Insulin (mIU/mL)	HOMA-IR	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	TG (mg/dL)	Creatinine (μmol/l)
C	87.84±11.03	6.88±0.13	11.92±2.69	2.64±0.11	188.32±34.80	55.30±11.60	122.58±30.16	92.12±94.77	67.08±14.64
N&C	106.24±16.32	7.92±0.17	11.88±3.97	3.14±0.21	180.97±37.90	48.72±11.99	119.10±34.41	115.15±42.52	64.64±20.53
N&U	162.88±37.57	11.49±1.37	20.81±12.24	8.01±1.13	187.55±42.15	40.99±8.51	129.16±36.35	172.72±70.86	65.53±15.44
O&C	116.00±17.07	8.45±0.18	12.72±6.27	3.69±0.31	170.15±32.48	47.56±13.15	109.82±29.39	130.20±75.29	67.36±14.24
O&U	175.60±46.03	12.42±1.32	15.45±13.28	6.56±1.50	166.67±31.32	43.70±12.76	109.05±28.22	147.03±61.17	64.04±13.85
P-value	0.000	0.000	0.004	0.000	0.087	0.001	0.190	0.000	0.831
Multiple Comparisons by Mann-Whitney Test	P-values								
C vs N&C	0.000*	0.000*	0.165	0.034*	0.547	0.053	0.691	0.001*	0.362
C vs N&U	0.000*	0.000*	0.001*	0.000*	0.908	0.000*	0.530	0.000*	0.547
C vs O&C	0.000*	0.000*	0.177	0.013*	0.046*	0.021*	0.146	0.000*	0.985
C vs O&U	0.000*	0.000*	0.154	0.000*	0.012*	0.001*	0.171	0.000*	0.648
N&C vs N&U	0.000*	0.000*	0.001*	0.000*	0.788	0.046*	0.270	0.002*	0.691
O&C vs O&U	0.000*	0.000*	0.771	0.006*	0.720	0.151	0.839	0.091	0.467
N&C vs O&C	0.040*	0.010*	0.961	0.404	0.222	0.580	0.260	0.684	0.351
N&U vs O&U	0.405	0.061	0.028*	0.039*	0.084	0.758	0.042*	0.204	0.949

Note: *Means significant difference ($p \leq 0.05$).

Table 4 Components of MetS in Study Groups and Their Analysis by Using Chi Square Test

Variables	% Within Variable			% Within Variable			% Within Variable			% Within Variable		
	C	N&C	P value	C	N&U	P value	C	O&C	P value	C	O&U	P value
WC			0.005*			0.005*			0.005*			0.017*
No	90.0	10.0		100.0	0.0		90.0	10.0		81.8	18.2	
Yes	40.0	60.0		48.5	51.5		40.0	60.0		41.0	59.0	
HTN			0.000*			0.023*			0.000*			0.001*
No	82.6	17.4		73.1	26.9		82.6	17.4		73.1	26.9	
Yes	22.2	77.8		37.5	62.5		22.2	77.8		25.0	75.0	
FBG			0.000*			0.000*			0.000*			0.000*
No	100.0	0.0		100.0	0.0		100.0	0.0		100.0	0.0	
Yes	7.4	92.6		10.5	89.5		7.4	92.6		7.4	92.6	
HDL			0.248			0.014*			0.382			0.024*
No	56.7	43.3		77.3	22.7		54.8	45.2		65.4	34.6	
Yes	40.0	60.0		40.0	60.0		42.1	57.9		33.3	66.7	
TG			0.066			0.000*			0.221			0.008*
No	56.1	43.9		79.3	20.7		53.5	46.5		60.5	39.5	
Yes	22.2	77.8		15.4	84.6		28.6	71.4		16.7	83.3	

Notes: 1) WC: waist circumference (yes if ≥ 94 cm for men or ≥ 80 cm for women); 2) HTN: hypertension (yes if systolic blood pressure/diastolic blood pressure $\geq 130/85$ mmHg or under pharmacological treatment); 3) FBG: fasting blood glucose (yes if ≥ 100 mg/dL); 4) HDL: high density lipoprotein cholesterol yes if <40 mg/dL in men or <50 mg/dL in women or under specific treatment); 5) TG: triglycerides (yes if ≥ 150 mg/dL or under specific medication). *Means significant difference ($p \leq 0.05$).

Abbreviations: WC, waist circumference; FBG, fasting blood glucose; HDL, High-density lipoprotein; TG, Triglyceride; BP, blood pressure.

The correlations between HbA1C levels as well as WC, FBG level, and the other components of MetS are presented in Table 5. In the control group, the HbA1C level was significantly correlated to WC and TG levels ($r=0.483$ and 0.464 ,

respectively, $P<0.05$). However, no other parameters were significantly correlated in any other group. In addition, we performed a binary logistic regression analysis to identify the independent risk factors associated with the presence or

Table 5 Correlation of HbA1C Level with Metabolic Syndrome Components Among Different Studied Groups

		C	N&C	N&U	O&C	O&U
Waist circumference	r	0.483	-0.021	-0.069	-0.218	0.131
	sig	0.015*	0.922	0.793	0.295	0.534
FBG	r	0.370	0.637	0.289	0.210	0.528
	sig	0.068	0.001**	0.260	0.313	0.007**
HDL	r	-0.136	0.149	-0.364	0.111	-0.063
	sig	0.516	0.477	0.151	0.598	0.765
TG	r	0.464	-0.086	0.388	0.079	0.110
	sig	0.019*	0.681	0.124	0.708	0.602
SBP	r	0.233	0.176	-0.085	-0.138	0.134
	sig	0.263	0.400	0.746	0.645	0.522
DBP	r	0.101	-0.010	0.077	-0.189	-0.178
	sig	0.632	0.637	0.769	0.365	0.394

Notes: Analysis by Spearman correlation coefficient; *means significant difference ($p \leq 0.05$); **means significant difference ($p < 0.01$).

Abbreviations: FBG, fasting blood glucose; HDL, High-density lipoprotein; TG, Triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure.

absence MetS (Table 6, left side). Among all the selected independent factors, only age increased the likelihood of MetS diagnosis by 7% (OR= 1.07; 95% CI=1.004–1.149; $P < 0.05$), and other variables, such as sex, regular physical activity, adherence to diet regimen, disease duration, and glycemic control, were not significantly associated. The efficacy of a similar independent variable model in predicting changes in the FM/FFM ratio was also assessed. Age, sex, adherence to diet regimen, and T2D duration revealed lower odds ratios (ORs) of increased FM/FFM ratio (Table 6, right side). Furthermore, the ORs for adherence to diet regimen and T2D duration were negative, which indicates that the tested variable had a protective role.

Discussion

This study aimed to assess the roles of disease duration and glycemic control in T2D-associated changes in body composition and the components of MetS. Previously, the prevalence of MetS was found to be high in patients with T2D regardless of the method used to diagnose MetS.²¹ As expected, the patients with T2D had significant increases in FBG, insulin, and HbA1C levels and HOMA-IR scores compared to nondiabetic individuals in the control group. Similarly, patients with T2D had significantly higher body fat percentage, fat mass, lipid profile, and SBP. In the control group, a significant positive correlation was observed between HbA1C levels and the components of MetS, such as WC and FBG level. However, in the diabetic groups, this correlation was not significant.

Interestingly, via logistic regression analysis, no significant difference was observed between disease duration and glycemic control in the prediction of complete MetS diagnosis in patients with T2D. However, all the components of MetS were significantly higher in the groups with uncontrolled glycemic status than in the controls using the chi-square test (Table 4). A previous report has shown that shorter diabetes duration, lower FBG, HbA1C, and triglyceride/total cholesterol levels, and insulin treatment were the significant predictors of MetS based on the COX regression analysis. They hypothesized that a lower HbA1C level indicates higher insulin levels with a higher risk of insulin resistance.²⁷ Another study of a large Chinese cohort with T2D²⁸ had a different finding. That is, individuals with long duration of diabetes (≥ 5 years), poor glycemic control, and sedentary lifestyle were more likely to have full MetS according to multivariate logistic regression analysis.

Based on previous study results, disease duration contributes to changes in body composition as indicated by FM/FFM ratio, rather than glycemic control. Meanwhile, poorer glycemic control and partially the duration of time with T2D can, no doubt, often contribute to increased WC and the development of hypertension and/or dyslipidemia. Notably, each component of MetS may present individually before the criteria for T2D is met. Indeed, each component of MetS has an individual causal contribution to the risk of T2D and vice versa.^{29,30} Regardless, patients with T2D and MetS who have a higher waist circumference, SBP, DBP, and triglyceride

Table 6 Multiple Logistic Regression Analysis of a Model of Independent Variables as Determinants of MetS Development and the Value of FM/FFM Ratio

	Metabolic Syndrome			FM/FFM Ratio		
	Odd Ratio	95% CI	P-Value	Odd Ratio	95% CI	P-Value
Age	1.07	1.004 to 1.149	0.039	0.18	0.000 to 0.007	0.041
Sex	1.59	0.537 to 4.707	0.402	0.7	0.272 to 0.387	0.000
Regular Physical activity	0.56	0.170 to 1.842	0.340	0.01	-0.053 to 0.066	0.832
Adherence to diet regimen	2.19	0.688 to 6.987	0.185	-0.14	-0.120 to -0.003	0.040
HbA1c level (%)	1.57	0.904 to 2.720	0.110	0.07	-0.019 to 0.032	0.630
Glycemic Control (categories)	8.78	0.912 to 84.63	0.060	-0.03	-0.129 to 0.100	0.802
T2D duration (Years)	1.04	0.189 to 5.761	0.962	-0.53	-0.068 to -0.019	0.001
T2D duration (categories)	2.81	0.000 to 25,197.3	0.824	0.53	0.047 to 0.263	0.005

concentrations and lower HDL levels may require more urgent treatment strategies than those with only one of the components of MetS due to a higher risk of cardiovascular disease.³⁰

In terms of body composition parameters, patients newly diagnosed with T2D had higher WC, BMI, PBF, FM, and FM/FFM ratio. A previous report has shown that the incidence of T2D is associated with higher BMI and WC.³¹ The risk of exacerbating T2D and the development of MetS was also correlated to disturbances in body composition. Wang et al³² have reported that the skeletal muscle mass-to-visceral fat area (SMM/VFA) ratio was significantly lower in the population with T2D and MetS. Furthermore, the SMM/VFA ratio could be used to predict T2D and MetS with high sensitivity and specificity. Consistent with our results, Solanki et al³³ have found that individuals with T2D had significantly higher PBF, FM, visceral fat, and subcutaneous fat than nondiabetic controls. Moreover, both quantitative and qualitative increases in fat mass were observed. The augmented FM, particularly the visceral part, triggers several mechanisms that result in the development of MetS, such as the development of insulin resistance, disturbed adipokine production, and visceral fat-enhanced gluconeogenesis.³⁴ Kim and Park³⁵ have reported that the incidence of MetS among Korean individuals with high fat/low muscle mass was 1.9 times higher than those with low fat/low muscle mass.

Our study found that when the disease duration is longer, there is a higher risk of insulin resistance, as indicated by the HOMA-IR score, and non-control of HbA1c level hastens the process of insulin resistance. Both the N&U vs N&C and O&U vs O&C groups had significantly higher HOMA-IR scores ($p < 0.001$ and < 0.01 ,

respectively). Carrillo-Larco et al³⁶ have concluded that the HOMA-IR score can be used to assess T2D patients. However, the ability of HbA1c levels was significantly better (more area under the curve). The participants with a higher HOMA-IR score had distinctive disturbances in about 30 metabolites, including glucose, specific amino acids, lipids, and other organic acids, compared with those with a lower HOMA-IR score.³⁷ Insulin resistance induces the development of cardiovascular morbidity via several mechanisms, which are as follows: a) hyperglycemia-induced oxidative stress, inflammation, and endothelial cell damage,³⁸ b) altered systemic lipid metabolism with consequent dyslipidemia,³⁹ c) alteration of insulin signal transduction in myocardial cells,⁴⁰ d) and dysregulation of substrate metabolism and altered supply of substrates to the myocardium.⁴¹

The current study had some limitations that might affect the interpretation of data. Although power calculations were conducted during the sample size calculation, the surprising insignificant difference between disease duration and glycemic control in the prediction of MetS might not be observed in a larger sample size. In particular, glycemic control has a P value of 0.06, which is extremely close to the significant value. In addition, although metabolic health may naturally worsen with age, notably, there is a significant difference in age between the T2D groups and the healthy control group included in this study.

Conclusions

Patients with early T2D had a significantly higher FM/FFM ratio. Moreover, disease duration rather than glycemic control causes further changes in the disease course. The development of MetS in patients with T2D might be

strongly associated with age rather than glycemic control or T2D duration. Indeed, further characterization of T2D contributes to the development of strategies that can prevent, detect, and treat poor cardio-metabolic health in the population with T2D.

Abbreviations

DBP, Diastolic blood pressure; HbA1C, Hemoglobin A1C; HOMA-IR, Homeostasis model assessment-insulin resistance; HDL, High-density lipoprotein; MetS, Metabolic syndrome; T2D, Type 2 diabetes; SBP, Systolic blood pressure.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics and Consent Statement

The study protocol was approved by the ethics committee of the College of Applied Medical Sciences, King Saud University (at all sites; approval letter no: CAMS 30/3536).

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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