

The Impact of Different Anthropometric Measures on Sustained Normotension, White Coat Hypertension, Masked Hypertension, and Sustained Hypertension in Patients with Type 2 Diabetes

Baris Afsar

Division of Nephrology, Department of Internal Medicine, Konya Numune State Hospital, Konya, Turkey

Background: Many studies have aimed to determine whether body mass index (BMI), waist circumference (WC), or waist to hip ratio (WHR) best predicts hypertension in diabetic patients, with conflicting results. However, no study has examined the specific relationship between these anthropometric parameters with sustained normotension (SNT), white coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT) based on office and ambulatory blood pressure (BP) measurements in these patients.

Methods: Patients with newly diagnosed type 2 diabetes underwent the following procedures: history taking, measurements of anthropometric parameters, office and ambulatory BP measurements, physical examination, laboratory analysis, and random and 24-hour urine analysis.

Results: In total, there were 65 dippers and 37 nondipper patients. None of the anthropometric parameters were different between the dippers and the nondippers. There were 25 patients with SNT, 32 with WCHT, seven with MHT, and 38 with SHT. A comparison of anthropometric parameters between these four groups of patients showed that WC ($P=0.016$) and WHR ($P=0.015$) were different among all groups. According to regression analysis, only BMI was independently related with MHT (odds ratio [OR], 1.373, $P=0.022$), whereas only WC has been associated with SHT (OR, 1.321, $P=0.041$).

Conclusion: Among anthropometric parameters, only WC and WHR were different in SNT, WCHT, MHT, and SHT in newly diagnosed patients with type 2 diabetes.

Keywords: Body mass index; Conicity index; Diabetes; Hypertension; Waist circumference

INTRODUCTION

Anthropometric indicators, including body mass index (BMI), waist circumference (WC), and waist to hip ratio (WHR), are widely used to predict increased chronic disease risk for con-

ditions such as hypertension and diabetes. In the literature, many studies have aimed to determine whether WC or WHR predict hypertension better than BMI, but their results have been conflicting [1]. Traditionally, increased BMI has been considered a risk factor for hypertension, diabetes, and coronary

Received: 21 May 2013, Accepted: 27 June 2013

Corresponding author: Baris Afsar

Division of Nephrology, Department of Internal Medicine, Konya Numune State Hospital, Ferhuniye Mah. Hastane Cad., Konya 42690, Turkey

Tel: +90-332-235-4500, Fax: +90-332-235-6786, E-mail: afsarbrs@yahoo.com

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heart disease [2]. However, the value of BMI in predicting cardiovascular risk has been challenged by the results of other studies [3,4]. Debate also exists regarding consideration of WHR as a risk factor for cardiovascular disease. Previous studies have suggested that WC alone may be a more useful and accurate tool than WHR to predict risk in adults [5]. In support of these findings, Kannel et al. [6] reported that the overall risk for cardiovascular events increased with the degree of central obesity, although none of the measures of central obesity was better than any others in predicting coronary disease. Another anthropometric parameter used to estimate abdominal and visceral fat is the conicity index (CI), which is an anthropometric estimate that models the relative accumulation of abdominal fat as the deviation of body shape from a cylindrical toward a double-cone shape (i.e., two cones with a common base at the waist level). CI is related to cardiovascular risk in the general population [7,8].

Recently, we showed that apart from other factors, patients with sustained hypertension (SHT) had increased BMI and WC compared to patients with white coat hypertension (WCHT), masked hypertension (MHT), or sustained normotension (SNT). However, in that study, no specific mention was given to anthropometrics, and patients with type 2 diabetes were excluded [9].

Thus, the current study was specifically developed to analyze the relationships between various anthropometric parameters with SNT, WCHT, MHT, CI, and dipping/nondipping status in newly diagnosed patients with type 2 diabetes.

METHODS

The current study was undertaken in the outpatient nephrology unit of a state hospital between 2009 and 2010. The study was in accordance with the Declaration of Helsinki, and informed consent was obtained from all participants before enrollment. The study population consisted of patients with newly diagnosed type 2 diabetes. The diagnosis of type 2 diabetes mellitus was based on two fasting plasma glucose levels (after at least 8 hours of fasting) using a cutoff point of 7.0 mmol/L [10]. Patients with secondary hypertension, coronary artery disease, cerebrovascular disease, chronic obstructive lung disease, hypothyroidism, hyperthyroidism, type 1 diabetes mellitus, rhythm problems, microscopic/macrosopic hematuria, urinary tract infection, or who were unwilling to participate were excluded. None of the patients reported alcohol intake. Patients with known essential hypertension and those who used antihypertensive medication were included. Participants presenting to

the outpatient clinic underwent a medical history examination, measurement of office blood pressure (BP), assessment of anthropometric parameters and calculations (including BMI, WC, WHR, and CI), physical examination, biochemical analysis, ambulatory blood pressure monitoring (ABPM), random urinalysis, and 24-hour urine specimen collection to determine creatinine clearance and 24-hour urinary protein and albumin excretion.

BMI was calculated as the ratio of weight (in kilograms) to height squared (in square meters). WC was measured with a nonmetallic, constant tension tape placed around the body at the midpoint between the highest point of the iliac crest and the lowest part of the costal margin in the mid-axillary line. Hip circumference was obtained using the femoral trochanters as references. WHR was determined by dividing WC (cm) by hip circumference (cm). CI was calculated as follows:

$$CI = WC / (0.109 \times \text{square root of weight/height})$$

where WC and height were measured in meters and weight was measured in kilograms.

Blood pressure measurements

Office BP measurements were performed using a mercury sphygmomanometer. An adequate-sized cuff (a standard cuff of 23×12 cm or a large cuff of 34×15 cm) according to arm circumference was applied around the patient's nondominant arm. The first and fifth phases of Korotkoff sounds were taken as the systolic and diastolic BP levels, respectively. The measurements were obtained after the patients had rested for 10 minutes in a sitting position, with the arm comfortably placed at the heart level. Two measurements were taken at 5-minute intervals. Each set of two measurements were averaged to produce the office systolic and diastolic BP levels. Ambulatory 24-hour BP monitoring was performed on each patient's nondominant arm using a SpaceLabs 90207 oscillometric monitor (SpaceLabs, Redmond, WA, USA). The accuracy of the device was checked against the standard auscultatory method to ensure that the difference in BP measurements between methods did not exceed +5 mm Hg. The device was set to obtain BP readings at 20-minute intervals during the day (07:00 AM to 11:00 PM) and at 30-minute intervals during the night (11:00 PM to 07:00 AM). Each ambulatory BP monitoring dataset was first automatically scanned to remove artifactual readings according to preselected editing criteria. All participants were instructed to rest or sleep between 11:00 PM and 7:00 AM (nighttime) and to continue their usual activities between 7:00 AM and 11:00 PM (daytime). Patients were asked to remain

still at the time of measurement and to note in a diary the occurrence of unusual events or poor sleep. Nocturnal dipping was defined as a reduction of >10% (when compared with the daytime values) in the systolic and/or diastolic BP levels at night.

Patients were further divided into the following four groups based on office and ABPM: STN, WCHT, masked MHT, and SHT. The definition of SNT, WCHT, MHT, and SHT were as follows, respectively: office systolic and diastolic BP <140/90 and mean daytime ABP <135/85, office systolic and diastolic BP \geq 140/90 and mean daytime ABP <135/85 mm Hg, office systolic and diastolic BP <140/90 and mean daytime ABP \geq 135/85 mm Hg, and office systolic and diastolic BP \geq 140/90 and mean daytime ABP time BP \geq 135/85 mm Hg [11].

Statistical analysis

All values are expressed as mean \pm standard deviation or as a percentage (%). Data were analyzed using the SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Data were checked for normality. A comparison of continuous parameters between the two groups was performed by Student *t* test or Mann-Whitney *U* test as appropriate. For the comparison of categorical variables, chi-square test or Fisher exact test was used. Parameter differences between the four groups were evaluated using the Kruskal Wallis test. For *post-hoc* analysis of nonnormally distributed variables, Bonferroni corrected Mann-Whitney *U* test was used. Lastly, serial multiple multivariate logistic regression analyses were performed to find independent factors related with SNT, WCHT, MHT, and SHT (as dependent parameters).

RESULTS

Initially, 133 patients were enrolled in the current study. Four patients with hypertension, two with coronary artery disease, one with cerebrovascular disease, two with chronic obstructive lung disease, two with hypothyroidism, one with hyperthyroidism, one with type 1 diabetes mellitus, two with atrial fibrillation and supraventricular tachycardia, one with microscopic hematuria, one with urinary tract infection, and 14 with an unwillingness to participate were excluded. The final patient population was composed of 102 participants with newly diagnosed type 2 diabetes. The demographic and laboratory parameters of the patients according to hypertension subgroups are shown in Table 1; 65 patients were dippers, and 37 patients were nondippers.

Forty-seven participants had been using antihypertensive agents as follows: 17 angiotensin converting enzyme inhibitors, 16 angiotensin receptor blockers, four calcium channel blockers, five β blockers, two α blockers, 11 thiazide blockers, and three loop diuretics.

A comparison of laboratory, demographic and anthropometric parameters between dippers and nondippers showed that only potassium was higher (4.50 ± 0.47 vs. 4.32 ± 0.32 ; $P=0.048$) and the 24-hour urine albumin excretion rate was lower (37.4 ± 37.1 vs. 146.1 ± 245.6 ; $P=0.015$) in dippers when compared to nondippers. Other laboratory, demographic and anthropometric parameters were not different between dippers and nondippers (data not shown).

The current study included 25 patients with SNT, 32 with WCHT, seven with MHT, and 38 with SHT. A comparison of laboratory, demographic and anthropometric parameters between these four groups of patients showed that WC ($P=0.016$) (Fig. 1), WHR ($P=0.015$) (Fig. 2), and potassium ($P=0.045$) were different among the four groups. Post hoc analysis showed that WC was different only in patients with SNT and SHT (90.3 ± 8.4 vs. 97.6 ± 9.2 ; $P=0.012$). Other groups were not different with respect to WC. Post hoc analysis revealed that WHR was different only in patients with SNT and SHT (0.88 ± 0.059 vs. 0.91 ± 0.069 ; $P=0.008$). Other groups did not differ with respect to WHR. Lastly, post hoc analysis showed that potassium was different only in patients with SNT and SHT (4.64 ± 0.55 vs. 4.31 ± 0.35 ; $P=0.026$). The other groups were not varied with respect to potassium. The correlation coefficients between office BPs, ambulatory BPs and anthropometric parameters are shown in Table 2.

Serial multiple regression analyses were performed to determine independent factors including age, gender, smoking status, BMI, WC, WHR, CI, average fasting blood glucose, total cholesterol, triglyceride, uric acid, creatinine clearance, 24-hour urine protein excretion rate, and 24-hour urine albumin excretion rate with SNT, WCHT, MHT, and SHT (as dependent variables). As a result, none of the aforementioned factors was independently related with SNT and WCHT. Only BMI was independently associated with MHT (odds ratio [OR], 1.373; CI, 1.047 to 1.802; $P=0.022$). On the other hand, only WC was correlated with SHT (OR, 1.321; CI, 1.012 to 1.726; $P=0.041$).

DISCUSSION

The current study firstly examined the relationship between

Table 1. The Demographic and Laboratory Parameters of the 102 Patients with Newly Diagnosed Type 2 Diabetes according to Hypertension Subgroups

Parameter	SNT (n=25)	WCHT (n=32)	MHT (n=7)	SHT (n=38)
Age, yr	45.8±12.8	50.4±7.0	48.7±10.1	49.6±7.7
Male/Female	7/18	13/19	3/4	16/22
Smoker/Nonsmoker	11/14	13/19	2/5	14/24
Dipper/Nondipper	18/7	17/15	6/1	24/14
Body mass index, kg/m ²	27.4±4.9	29.1±4.4	30.5±5.1	28.8±4.2
Waist circumference, cm	90.3±8.4	96.2±9.6	97.4±6.7	98.4±8.3
Hip circumference, cm	102.9±4.1	104.7±4.3	107.0±5.1	104.7±4.4
Waist to hip ratio	0.876±0.058	0.917±0.067	0.910±0.029	0.931±0.074
Conicity index	1.248±0.067	1.286±0.071	1.280±0.111	1.302±0.094
Office systolic blood pressure, mm Hg	130.9±7.5	153.9±12.2	133.3±5.2	155.6±15.0
Office diastolic blood pressure, mm Hg	81.9±4.9	98.8±8.6	83.0±4.8	102.9±7.7
Averaged fasting blood glucose, mmol/L	8.62±0.82	8.77±0.97	8.57±1.06	8.56±0.86
Hemoglobin, g/L	140.6±15.2	138.6±13.6	135.4±16.6	136.8±13.0
Albumin, g/L	43.1±4.0	44.8±4.6	44.6±4.4	43.9±3.8
Blood urea nitrogen, mmol/L	6.32±2.61	6.14±2.07	6.03±2.71	6.32±2.11
Creatinine, μmol/L	71.6±73.1	69.8±14.1	62.8±21.2	65.4±24.8
Sodium, mmol/L	139.6±3.5	141.0±4.4	141.7±1.9	139.9±3.2
Potassium, mmol/L	4.64±0.55	4.43±0.40	4.46±0.44	4.32±0.35
Calcium, mmol/L	2.30±0.10	2.31±0.08	2.26±0.09	2.30±0.13
Phosphorus, mmol/L	1.11±0.16	1.13±0.24	0.99±0.10	1.16±0.17
Uric acid, μmol/L	344.4±112.4	347.3±72.0	349.1±51.7	346.6±96.9
Total cholesterol, mmol/L	4.67±1.24	5.28±1.15	4.94±1.12	5.16±1.11
LDL-C, mmol/L	2.58±0.88	2.91±0.89	2.95±0.92	3.04±0.88
HDL-C, mmol/L	1.37±0.25	1.35±0.27	1.11±0.35	1.30±0.34
Triglyceride, mmol/L	1.63±0.87	1.66±0.66	1.65±0.77	1.84±0.77
Thyroid stimulating hormone, mU/L	1.40±0.63	1.45±1.09	1.32±0.41	1.83±1.15
hs-CRP, mg/L	4.60±2.94	3.97±2.79	6.63±3.32	4.37±3.30
Creatinine clearance, mL/min/1.73 m ²	86.4±43.5	84.9±26.8	74.2±7.9	82.7±30.4
24-Hour urine protein excretion rate, mg/day	131.2±77.7	141.9±90.0	157.8±173.3	249.5±326.9
24-Hour urine albumin excretion rate, mg/day	46.1±53.5	49.4±47.8	76.1±138.5	120.3±241.6

Values are expressed as mean±SD or number.

SNT, sustained normotension; WCHT, white coat hypertension; MHT, masked hypertension; SHT, sustained hypertension; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; hs-CRP, high sensitivity C-reactive protein.

BMI, WC, WHR, and CI with ABPM, dipping/nondipping status, SNT, WCHT, MHT, and SHT in newly diagnosed patients with type 2 diabetes. The novel findings included the following: 1) none of the anthropometric parameters were different between dippers and nondippers; 2) among anthropometric parameters only, WC and WHR were different between patients with SNT and SHT; 3) only BMI and only WC were independently associated with MHT and SHT, respectively.

In a very recent study, Zhou et al. [12] investigated the prevalence of MHT in type 2 diabetic patients. In contrast to the present study, their study included patients who were aware of their type 2 diabetes and were receiving medication. The authors found that among 856 patients, 48 (5.61%) of them were diagnosed with MHT. The authors did not identify any difference of BMI, WC, and WHR in patients with essential HT and MHT. In contrast, BMI, WC, and WHR were higher in MHT

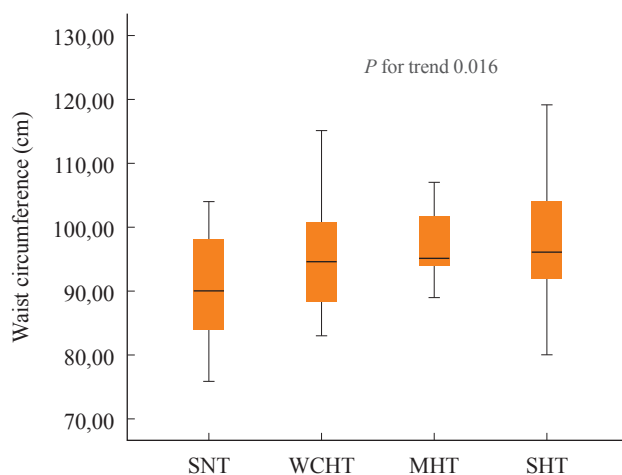


Fig. 1. The comparison of waist circumference among newly diagnosed type 2 diabetic patients with sustained normotension (SNT), white coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT).

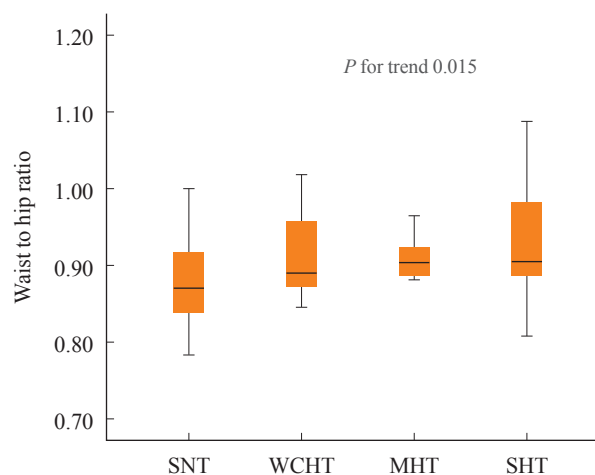


Fig. 2. A comparison of the waist to hip ratio among newly diagnosed type 2 diabetic patients with sustained normotension (SNT), white coat hypertension (WCHT), masked hypertension (MHT), and sustained hypertension (SHT).

Table 2. The Correlation Coefficients between Office Blood Pressures (BPs), Ambulatory BPs, and Anthropometric Parameters in 102 Newly Diagnosed Patients with Type 2 Diabetes

	BMI	WC	WHR	CI
Office SBP	0.156	0.205 ^a	0.255 ^b	0.081
Office DBP	0.142	0.338 ^b	0.296 ^b	0.288 ^b
Average ambulatory daytime				
SBP	0.162	0.355 ^c	0.397 ^c	0.356 ^c
DBP	0.055	0.189	0.262 ^b	0.168
Average ambulatory nighttime				
SBP	0.189	0.414 ^c	0.457 ^c	0.409 ^c
DBP	0.031	0.221 ^a	0.274 ^b	0.261 ^b
Average ambulatory 24-hour				
SBP	0.163	0.368 ^c	0.411 ^c	0.369 ^c
DBP	0.063	0.209 ^a	0.275 ^b	0.190
Mean ambulatory arterial BP				
Daytime	0.090	0.266 ^b	0.345 ^c	0.282 ^b
Nighttime	0.129	0.368 ^c	0.413 ^c	0.389 ^c
24-Hour	0.100	0.303 ^b	0.379 ^c	0.327 ^b
Mean ambulatory heart rate				
Daytime	0.200 ^a	0.062	0.049	-0.126
Nighttime	0.262 ^b	0.125	0.160	-0.124
24-Hour	0.219 ^a	0.095	0.093	-0.107

BMI, body mass index; WC, waist circumference; WHR, waist to hip ratio; CI, conicity index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

^a $P < 0.05$; ^b $P < 0.01$; ^c $P < 0.0001$.

patients compared to normotensive patients. Using logistic regression analysis, they found that BMI, WHR but not WC, a 6 to 15 year disease course of diabetes, smoking, and alcoholism were independently related with MHT [12]. The present study further extended these findings while also analyzing the other anthropometric factors, such as CI related with WCHT, MHT, and SHT in patients not receiving any medication for diabetes. The current study demonstrated that only WC and WHR were different between patients with SNT, WCHT, MHT, and SHT. These findings are hard to explain given the fact that anthropometric parameters were closely related with each other. The exact pathophysiologic mechanisms regarding these factors are unknown, but one can speculate that the prognostic importance of abdominal fat accumulation is more important than general obesity assessments by BMI [2]. However, it is even more difficult to explain why only WC was related with SHT, although CI and WHR are also measures of abdominal fat like WC. One explanation for these findings may be that CI might not be an accurate measure of obesity. It has been speculated that calculated values such as CI may not be as appropriate for assessing obesity as direct measurements [13].

WC is a superior indicator because it requires only one measurement, and it is a better indicator of visceral fat and cardiovascular risk when compared to WHR [14-16]. Indeed, a seven-year longitudinal study showed that the change in WC was a better correlate of the change in visceral adipose tissue observed over this period than the change in WHR [17]. It was also concluded that misleading information may be caused by

simultaneous increases in waist and hip measurements, which result in the WHR being stable over time despite considerable accumulation of visceral adipose tissue [18]. Thus, all of these factors may explain the lack of relationship between WHR and CI with SHT.

Why has WC been the only anthropometric parameter found to be related to SHT? Currently, the answer is not known; however, previous studies have also demonstrated varied impacts of different anthropometric parameters on HT. Cassani et al. [19] investigated the relationship between various anthropometric variables with hypertension. The authors demonstrated that except for WHR, all anthropometric variables were positively correlated with systolic and diastolic BP; however, only WC was found to be independently related with HT [19].

A 5-year prospective study from Greece demonstrated that among various anthropometric measurements that showed a significant association with hypertension incidence, WC was the best predictor. The authors suggested that this finding may lead to new pathophysiological mechanisms for the development of hypertension [20]. Another study performed in patients older than 60 years of age found that WC impacts HT independently of BMI, showing both an independent and an added impact in males and females as demonstrated in the multivariable analysis [21]. It has also been suggested that WC is the only marker of adiposity associated with ABPM [22].

The cause of previous and present findings regarding the WC and SHT are not known currently, but speculations can be made. Abdominal obesity represents a key component of the metabolic syndrome. The crucial components that may link abdominal obesity to other features of the metabolic syndrome and end-organ damage are presumably the presence of insulin resistance and elevated insulin levels, increased inflammation with macrophage infiltration in fat tissues with concomitant release of proinflammatory cytokines, and endothelial dysfunction, which all may lead to SHT. Hormones and cytokines that are produced from adipocytes, which are collectively called adipokines, have pleiotropic effects on multiple tissues, leading to a fine tuning of fuel utilization, energy homeostasis, and cardiovascular function, all of which can impact HT [20]. Visceral fat has recently been shown to produce more angiotensinogen and interleukin-6 but less leptin as compared to subcutaneous fat [23]. This increased production of angiotensinogen leads to the activation of the rennin-angiotensin system, causing vasoconstriction and reabsorption of sodium, while the formation of inflammatory markers has been related to the incidence of arterial hypertension independently of other risk

factors. For these reasons, abdominal fat distribution has been suggested to be associated with hypertension, even independently of BMI [24]. Lastly, it was also possible that clinical characteristics and etiological differences are present among patients with WCHT, MHT and SHT. Therefore, different anthropometric parameters may play different pathologic roles in these various conditions.

In the current study, only MHT was found to be related with BMI. Previously, MH was found to be associated with BMI in nondiabetic patients [25]. Wang et al. [26] investigated the anthropometric and lifestyle factors associated with WCHT, MHT and SHT in a Chinese population. The authors demonstrated that MHT increased as BMI increased [26]. Trudel et al. [27] also found that the prevalence of MHT increased in both males and females as BMI increased. In type 2 diabetic patients, Zhou et al. [12] reported that BMI was the most powerful determinant of MH. However, WHR was also a predictor of MHT [12]. In contrast, only BMI but not other anthropometric parameters were independently related with MHT in the current study. Interestingly, it was shown that in severely obese participants, WCHT was more prevalent than MHT, while in overweight and moderately obese youths, the MHT prevalence was more than two times that of WCHT [28]. In the present study, the mean BMI was 28.7 ± 4.5 , and only 12 patients had a BMI greater than 35. Thus, it should be investigated whether a moderate BMI exerts a specific pathophysiological impact on MHT that other anthropometric parameters do not. It was also possible that the discrete findings of the current and previous studies may be related to patient characteristics, methods of the patient selection process and medications. More studies will be needed to highlight the mechanisms underlying these discrete results.

The present study has to be interpreted within the context of its potential limitations. First, our cross-sectional study did not allow us to study the reproducibility of the classifications according to office BP and ABMP. Secondly, since the study was not interventional and experimental, cause and effect relationships cannot be suggested. Another limitation was the lack of gold standards, such as computed tomography and magnetic resonance imaging, for assessing central fat distribution. However, these methods are costly, expose patients to radiation (with computed tomography) [13]. Lastly the number of patients in our study was relatively low. The study population was composed of special patients with newly diagnosed type 2 diabetes without comorbidities. Therefore, the potential effects of medications and comorbidities were ruled out.

In conclusion, among the anthropometric parameters tested, only WC and WHR were different in SNT, WCHT, MHT, and SHT in newly diagnosed patients with type 2 diabetes. Upon regression analysis, only BMI was associated with MHT and only WC was related with SHT. It is possible that different anthropometric parameters may produce distinct impacts on the development of MHT and SHT. More studies are needed to highlight the underlying mechanisms regarding the anthropometrics and hypertension subtypes in patients with type 2 diabetes.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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