Noninvasive prediction of carotid artery atherosclerosis by multiple abdominal fat indices measured via ultrasonography

ULTRA SONO GRAPHY

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Purpose: The purpose of this study was to evaluate the efficiency of multiple abdominal fat indices as measured via ultrasonography for predicting the presence and severity of carotid artery atherosclerosis and to compare the predictive capacity of ultrasonographic measurements to that of anthropometric measurements.

Methods: A total of 92 patients were included in this study. All participants underwent clinical and laboratory assessments, and anthropometric measurements were obtained. Ultrasound examinations were performed to measure the values of all abdominal fat indices and the intima-media thickness, as well as to detect the presence of atherosclerotic plaques. Univariate and multivariate logistic regression analyses were performed.

Results: In the multivariate analysis, significant associations were detected between carotid artery atherosclerosis and posterior right perinephric fat thickness (PRPFT) (hazard ratio [HR], 15.23; P<0.001), preperitoneal fat thickness (PPFT) (HR, 4.31; P=0.003), visceral adipose tissue volume (VAT) (HR, 7.61; P<0.001), visceral fat thickness (VFT) (HR, 8.84; P<0.001), the ratio of VFT to subcutaneous fat thickness (VFT/SCFT) (HR, 9.39; P<0.001), and waist-to-height ratio (WHtR) (HR, 2.65; P=0.046). In the multivariate analysis, significant associations were also detected between carotid artery plaque and PRPFT (HR, 7.09; P<0.001), the abdominal wall fat index (AFI) (HR, 3.58; P=0.010), and VFT/SCFT (HR, 4.17; P=0.006).

Conclusion: Many abdominal fat indices as measured by ultrasound were found to be strong predictors of carotid artery atherosclerosis, including PRPFT, VFT/SCFT, VFT, VAT, PPFT, and WHtR. Moreover, PRPFT, VFT/SCFT, and AFI were identified as strong predictors of the presence of carotid artery plaque.

Keywords: Posterior perinephric fat; Abdominal fat thickness; Abdominal ultrasound; Anthropometric measurements; Carotid artery atherosclerosis

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Introduction

Atherosclerosis is a complex chronic disease [1] that is considered one of the most important preventable causes of ischemic stroke [2]. The first structural abnormality indicative of carotid artery atherosclerosis is an increase in intima-media thickness (IMT) [3]. Obesity has been shown to be one of the main factors contributing to atherosclerosis [4,5]. Moreover, visceral fat is regarded as an endocrine organ [6–8]. Like visceral fat, perirenal fat is metabolically active, and it has been demonstrated to be an independent predictor of cardiovascular disease risk [9–11].

The release of fatty acids and cytokines from adipose tissue into the circulation is the most widely accepted theory behind the association between abdominal fat and the development of carotid atherosclerosis [12].

Multiple indices of abdominal obesity exist, but which is the best discriminator of cardiovascular risk factors is still under debate [13]. Among anthropometric measurements, waist circumference (WC) has been found to be more strongly associated with subclinical atherosclerosis than is body mass index (BMI) [14–16]. However, WC showed a weaker association with carotid atherosclerosis than did visceral fat thickness (VFT) [17]. Among the various abdominal fat indices, the role of the posterior perinephric fat as a predictor of carotid atherosclerosis needs to be clarified.

The standard techniques used to quantify abdominal fat are computed tomography (CT) and magnetic resonance imaging (MRI) [18]. Nevertheless, these two modalities have major limitations and disadvantages, including cost, exposure to high doses of radiation, and technical concerns [19]. Several studies have compared the results obtained using CT or MRI to those obtained via ultrasound in the quantification of visceral fat, and they concluded that measurements obtained via ultrasonography were strongly correlated with those obtained via CT [18]. In addition, ultrasonography has been established as a noninvasive technique for the early detection of carotid atherosclerosis [3]. Several ultrasound measurements and ratios have been used as predictors of carotid atherosclerosis, but to the best of our knowledge, very few studies have examined the posterior perinephric fat as a predictor of this condition.

In the current study, we aimed to assess abdominal fat indices (as measured by ultrasonography) and anthropometric measurements as potential predictors of carotid atherosclerosis.

Materials and Methods

Study Design

This prospective study was approved by our institutional review board and the relevant committee of ethics (IRB no.: 129/2018), in accordance with the Declaration of Helsinki. All included participants provided written informed consent. We conducted this study between October 2018 and October 2019. It included 92 participants from the outpatient clinic of the internal medicine department of our institution, all of whom were referred for abdominal ultrasonography, were aged >18 years, agreed to participate in this study, and did not meet any exclusion criteria. Those criteria excluded participants with BMI >40 kg/m^2, with chronic debilitating diseases (advanced cardiac, renal, or hepatic diseases), who were taking antilipidemic drugs, or who had a history of abdominal or bariatric surgery.

Participant Assessment

All participants were clinically assessed, which included history-taking, physical examination, and blood pressure measurements using standard criteria. Serum blood glucose levels and the lipid profile were assessed for each participant.

Anthropometric Measurements

Weight and height were measured, and then BMI was calculated. Hip circumference (HC) was measured over the undergarments at the point of maximal gluteal protuberance. WC was measured in the standing position at the end of expiration, midway between the lower border of the last rib and the iliac crest. The waist-to-hip ratio (WHR) was calculated by dividing WC by HC (both in centimeters). The waist-to-height ratio (WHtR) was obtained by dividing WC by the height (both in centimeters). Measurements were obtained twice, and the average of the two measurements was used for the subsequent analyses.

Abdominal Fat Thickness Measurements via Ultrasound

Examination was done by a single radiologist with 14 years of experience using constant settings and a high-resolution ultrasound system (Aplio 500, Toshiba, Tokyo, Japan). The participants were examined in the supine position with a 3.5-MHz convex array probe and a 10-MHz linear-array probe; all images were obtained at the end of expiration to avoid the effects of respiration, with light compression of the abdominal wall to avoid underestimation of the subcutaneous fat thickness (SCFT). The following measurements were made. First, posterior right perinephric fat thickness (PRPFT), the maximum fat thickness of the posterior right renal wall, was measured in the posterior right perinephric space [17]. In this study, we used PRPFT because it has been validated in previous research [20] (Fig. 1A). Next, SCFT was defined as the minimum fat thickness between the linea alba and the fat-skin interface, and it was measured between the umbilicus and the xiphoid process (Fig. 1B).

Preperitoneal fat thickness (PPFT) was measured as the maximum fat thickness between the linea alba and the upper surface of the liver (Fig. 2A). The next measurement was the maximum distance between the inner aspect of the rectus abdominis muscle and the posterior aortic wall; this measurement was made 1 cm above the umbilicus in a line perpendicular to the aorta [21] (Fig. 2B). The distance between the splenic vein and the inner aspect of the abdominal muscle was also measured [17] (Fig. 3A). Next, the abdominal wall fat index (AFI) was obtained by dividing the PPFT by the SCFT [19]. Visceral adipose tissue volume (VAT) was calculated using the following equation: VAT=9.008+1.191×(the distance between the splenic vein and the inner aspect of the abdominal muscle [in mm])+0.987×(the distance between the aortic posterior wall and the inner aspect of the abdominal muscle on the umbilicus [in mm])+3.644×(the thickness of the fat layer of the posterior right renal wall [in mm]) [22]. Three measurements were made, and the average was calculated; the intraobserver variability ranged from 1.2% to 1.6%. VFT was defined as the distance between the inner aspect of the rectus abdominis muscle and the anterior wall of the aorta, measured perpendicular to the aorta [22] (Fig. 3B). The final measurement obtained was the VFT/SCFT ratio.

Carotid Doppler Ultrasonography

Carotid Doppler ultrasound examinations were performed by the same radiologist using the same ultrasound system with a 10-MHz linear-array probe. The participants were examined in the supine

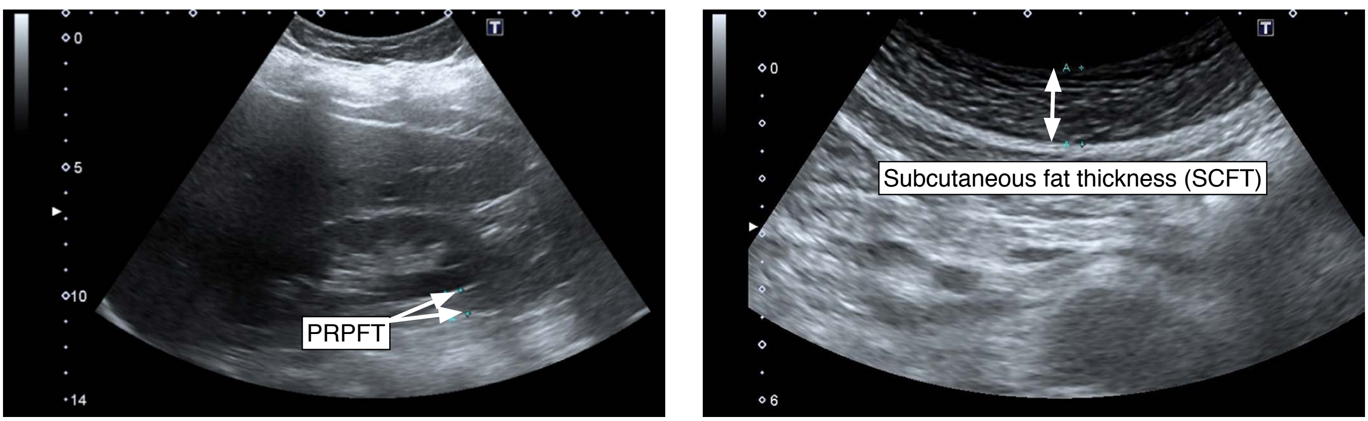

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Fig. 1. **Abdominal ultrasonography of a 58-year-old woman.**
A. The thickness of the posterior right perinephric fat, is approximately 9.5 mm. B. The minimum subcutaneous fat thickness is approximately 13.8 mm. PRPFT, posterior right perinephric fat thickness.

A B

Fig. 2. **Abdominal ultrasonography of a 62-year-old woman.**
A. The preperitoneal fat thickness is approximately 9.6 mm. B. The thickness from the posterior wall of the aorta to the inner surface of the abdominal muscle, is approximately 70.3 mm.

A B

Fig. 3. Abdominal ultrasonography of a 48-year-old man.
A. The fat thickness from the splenic vein to the inner surface of the abdominal muscle, measuring approximately 34.9 mm. B. Visceral fat thickness, which is the thickness from the anterior wall of the aorta to the inner surface of the abdominal muscle, measuring approximately 57.6 mm.

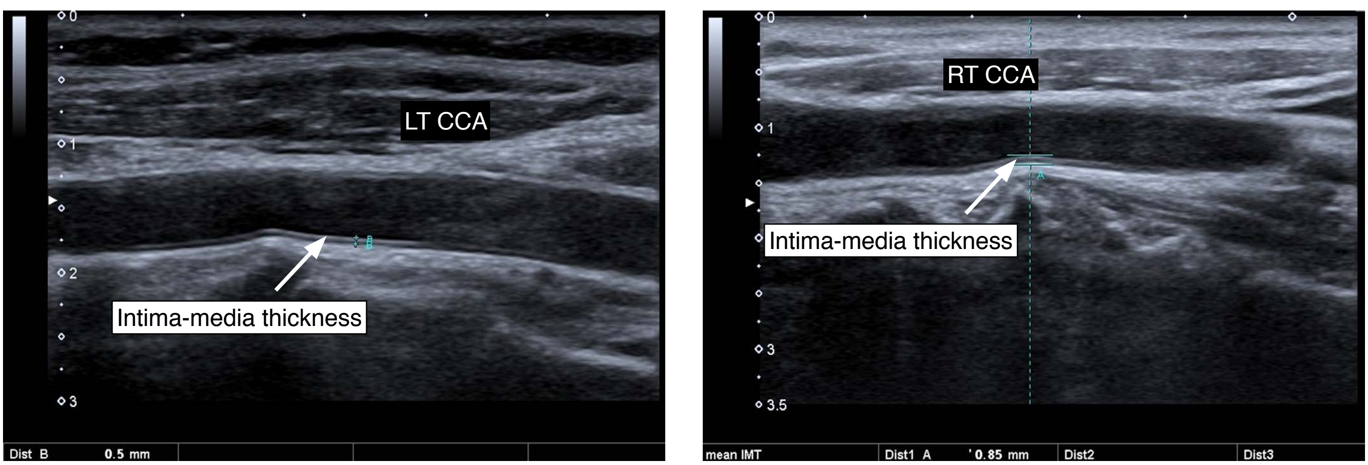

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Fig. 4. Ultrasonography of the left (LT CCA) and right common carotid arteries (RT CCA) of a 48-year-old man on a longitudinal scan showing the intima-media thickness.
The thickness is approximately 0.5 mm (A) and 0.85 mm (B).

position, with the head elevated and slightly directed toward the opposite side of the examined carotid artery. The examination began with the measurement of IMT. Measurements were repeated three times, at the thickest point over 10 mm of uniform length in the far wall of the bilateral common carotid arteries in the 20 mm before the carotid bulb, without any areas of focal thickening (that is, plaque-free areas) (Fig. 4). From the three measurements on each side, the average IMT was calculated according to the European Society of Hypertension and the European Society of Cardiology guidelines [23]. In these guidelines, an IMT >0.9 mm is considered abnormal (Fig. 4), and carotid plaque is defined as either an IMT ≥1.5 mm or a focal increase in thickness of 0.5 mm or 50% of the surrounding carotid IMT value (Fig. 5). The intraobserver variability ranged from 1.4% to 1.7%.

Statistical Analysis

Descriptive statistics were presented using either numbers and percentages or means and standard deviations, as appropriate. The comparison between IMT among the baseline characteristics of participants was conducted using the Fisher exact test or the independent t test, as appropriate. P-values <0.05 were considered to indicate statistical significance. A univariate and multivariate

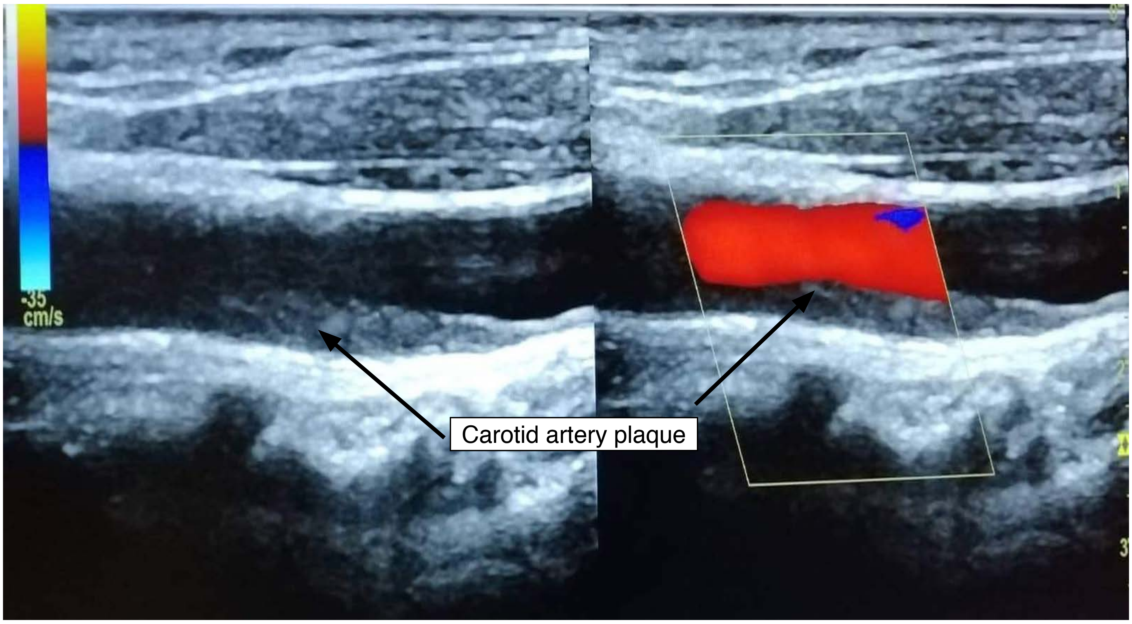

Fig. 5. **Color Doppler ultrasound of the right common carotid artery of a 62-year-old woman on a longitudinal scan.** The image on the right is a B-mode scan of the artery showing a large plaque partially obstructing the common carotid artery. The image on the left is a color Doppler scan showing blood flow within the artery and confirming the large size of the plaque.

regression analysis was also conducted to predict the effects of the risk factors and the degree of IMT; odds ratios along with 95% confidence intervals (95% CIs) were reported. Univariate and multivariate analyses were also carried out regarding the associations of the presence of a plaque or plaques with abdominal fat area thickness and anthropometric measurements. All statistical data analyses were performed using SPSS version 21 for Windows (IBM Corp., Armonk, NY, USA).

Results

In this prospective study, we enrolled 92 participants aged between 39 and 70 years (mean age, 57.72±7.32 years), with a male-to-female ratio of approximately 2.4 to 1. Table 1 presents the baseline characteristics of the study population. The difference between normal and atherosclerotic arteries was significant with regard to mean PRPFT (P<0.001), PPFT (P<0.001), VFT (P<0.001), VFT/SCFT (P<0.001), VAT (P<0.001), and SCFT (P=0.041), while it did not differ significantly with regard to AFI (Table 2). Of the anthropometric measurements, significant associations were detected between carotid artery atherosclerosis and both mean WC (P=0.046) and mean HC (P=0.009), while no significant associations were detected with other anthropometric measurements. Only a few indices showed significant associations with the presence of carotid artery plaque (Table 3). These associations were significant with regard to mean PRPFT (P<0.001), VFT/SCFT (P=0.004), and HC (P=0.026). No significant association was detected with any other abdominal or anthropometric index.

The results of univariate and multivariate regression analysis of possible indices predictive of carotid artery atherosclerosis were provided in Table 4. Regarding the abdominal fat indices, many variants showed a significant association with carotid artery atherosclerosis. For participants with SCFT >21.3 mm, the risk of carotid atherosclerosis was 3.27 times higher than among participants with SCFT ≤21.3 mm (crude odds ratio [OR], 3.27; 95% CI, 1.31 to 8.16; P=0.011), but after adjustment in the multivariate analysis, the risk did not differ significantly. Furthermore, among participants with PPFT >10.8 mm, the risk of carotid artery atherosclerosis was 4.45 times higher than among participants with PPFT ≤10.8 mm (crude OR, 4.45; 95% CI, 1.77 to 11.21; P=0.001); in the multivariate analysis, the risk decreased to 4.31 times higher (adjusted OR [AOR], 4.31; 95% CI, 1.67 to 11.12; P=0.003). Similarly, for participants with PRPFT >11.2 mm, the risk of carotid artery atherosclerosis was 16.62 times higher than among those with PRPFT ≤11.2 mm (crude OR, 16.62; 95% CI, 5.69 to 48.53; P<0.001); in the multivariate analysis, the risk decreased to 15.23 times higher (AOR, 15.23; 95% CI, 4.99 to 46.24; P<0.001).

In addition, the risk of carotid artery atherosclerosis was higher for individuals with the following abdominal fat measurements relative to their counterparts: VAT >176 mm^3 (crude OR, 8.26; 95% CI, 3.09 to 22.12; P<0.001; AOR, 7.61; 95% CI, 2.70 to 21.43; P<0.001), VFT >62.1 mm (crude OR, 9.98; 95% CI, 3.67 to 27.12; P<0.001;

Table 1. Baseline characteristics of participants according to sex

Variable	Total (n=92)	Male (n=64)	Female (n=28)	P-value[a]
Qualitative variables[b]				
Diabetes mellitus	40 (43.5)	25 (39.1)	15 (53.6)	0.254
Hypertension	55 (59.8)	35 (54.7)	20 (71.4)	0.168
Smoking	60 (65.2)	54 (84.4)	6 (21.4)	<0.001
Peripheral vascular disease	22 (23.9)	16 (25.0)	6 (21.4)	0.796
Quantitative variables[c]				
Age (year)	57.72±7.32	58.53±6.59	55.93±8.61	0.112
Total cholesterol (mg/dL)	223.41±45.72	220.82±43.91	229.41±49.91	0.412
TG (mg/dL)	132.31±30.91	130.73±31.92	135.91±28.93	0.463
LDL-C (mg/dL)	144.33±40.71	141.91±40.40	149.83±41.61	0.392
HDL-C (mg/dL)	46.30±7.56	46.91±7.23	44.72±8.17	0.186
Height (cm)	165.32±7.85	168.43±6.40	158.14±5.90	<0.001
Weight (kg)	81.83±11.94	81.93±12.61	81.63±10.62	0.917
BMI (kg/m^2)	29.91±3.65	28.82±3.43	32.51±2.67	<0.001
WC (cm)	104.94±10.74	103.22±10.93	108.92±9.32	0.019
HC (cm)	108.23±11.63	105.51±11.92	114.30±7.72	0.001
WHR	0.97±0.05	0.98±0.04	0.95±0.05	0.012
WHtR	0.64±0.06	0.61±0.06	0.69±0.04	<0.001
PRPFT (mm)	12.05±2.03	11.13±2.02	12.24±2.08	0.573
SCFT (mm)	21.91±5.03	20.92±4.73	24.42±4.96	0.002
PPFT (mm)	11.43±1.73	11.14±1.76	12.23±1.42	0.005
VFT (mm)	65.79±15.02	63.28±15.52	71.53±12.97	0.016
VFT/SCFT	3.02±0.47	3.04±0.46	2.99±0.49	0.721
AFI	0.57±0.12	0.59±0.12	0.55±0.11	0.235
VAT (mm^3)	179.21±27.36	176.72±28.12	184.99±25.23	0.184
Right IMT (mm)	0.96±0.15	0.97±0.15	0.92±0.16	0.211
Left IMT (mm)	0.97±0.15	0.98±0.14	0.93±0.17	0.169

Values are presented as number (%) or mean±SD.

TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; PRPFT, posterior right perinephric fat thickness; SCFT, subcutaneous fat thickness; PPFT, preperitoneal fat thickness; VFT, visceral fat thickness; VFT/SCFT, ratio of visceral fat thickness to subcutaneous fat thickness; AFI, abdominal wall fat index; VAT, visceral adipose tissue volume; IMT, intima-media thickness; SD, standard deviation.

[a]Significant at P<0.05 (two-tailed). [b]P-value was calculated using the Fisher exact test. [c]P-value was calculated using the independent t test.

AOR, 8.84; 95% CI, 3.18 to 24.61; P<0.001), and VFT/SCFT >2.9 (crude OR, 7.07; 95% CI, 2.54 to 19.73; P<0.001; AOR, 9.39; 95% CI, 2.97 to 29.72; P<0.001). Concerning the anthropometric measurements, participants with WHtR >0.615 had a risk of carotid artery atherosclerosis 3.34 times higher than those with WHtR ≤0.615 (crude OR, 3.34; 95% CI, 1.31 to 8.29; P=0.009). In the multivariate analysis, this risk decreased to 2.65 times higher (AOR, 2.65; 95% CI, 1.02 to 6.91; P=0.046). In contrast, participants whose HC was >105 cm, relative to their counterparts whose HC was ≤105 cm, showed a significant association in the univariate analysis, with a 2.9-fold increased risk of carotid artery atherosclerosis. However, after adjustment in the multivariate analysis, no significant association was detected (crude OR, 2.90; 95% CI, 1.18 to 7.11; P=0.020; AOR, 2.29; 95% CI, 0.89 to 5.86; P=0.082). Other anthropometric indices showed no significant associations in both univariate and multivariate analyses.

Additionally, the results of univariate and multivariate regression analysis of possible indices predictive of carotid artery plaques were provided in Table 5. Regarding the abdominal fat indices, participants with PRPFT >11.2 mm had a risk of carotid artery plaque that was 5.51 times higher than that of participants with PRPFT ≤11.2 mm (crude OR, 5.51; 95% CI, 2.15 to 14.22;

Table 2. Statistical association between abdominal fat indices and anthropometric indices with carotid artery atherosclerosis (n=92)

Factor	IMT ≤0.9 mm (n=31)	IMT >0.9 mm (n=61)	P-value[a)]
BMI (kg/m^2)	29.70±4.23	30.01±3.34	0.669
WC (cm)	101.82±13.73	106.52±8.55	0.046
HC (cm)	103.80±13.12	110.43±10.11	0.009
WHR	0.98±0.05	0.97±0.05	0.208
WHtR	0.62±0.08	0.64±0.05	0.061
PRPFT (mm)	10.38±1.82	12.91±1.55	<0.001
SCFT (mm)	20.51±6.42	22.72±4.01	0.041
PPFT (mm)	10.47±1.61	11.91±1.59	<0.001
VFT (mm)	55.28±15.91	71.14±11.74	<0.001
VFT/SCFT	2.78±0.62	3.15±0.29	<0.001
VAT (mm^3)	159.53±30.35	189.25±19.30	<0.001
AFI	0.58±0.13	0.57±0.11	0.885

Values are presented as mean±SD.

IMT, intima-media thickness; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; PRPFT, posterior right perinephric fat thickness; SCFT, subcutaneous fat thickness; PPFT, preperitoneal fat thickness; VFT, visceral fat thickness; VFT/SCFT, ratio of visceral fat thickness to subcutaneous fat thickness; VAT, visceral adipose tissue volume; AFI, abdominal wall fat index; SD, standard deviation.

[a)]Significant at P<0.05 (two-tailed). P-value was calculated using the independent t test.

Table 3. Statistical association between abdominal fat indices and anthropometric indices with carotid artery plaque (n=92)

Factor	Absence of plaque (n=42)	Presence of plaque (n=50)	P-value[a)]
BMI (kg/m^2)	30.14±3.98	29.71±3.36	0.577
WC (cm)	103.19±13.47	106.34±7.68	0.162
HC (cm)	105.24±12.49	110.61±10.23	0.026
WHR	0.98±0.05	0.96±0.05	0.119
WHtR	0.63±0.08	0.64±0.05	0.704
PRPFT (mm)	11.27±2.13	12.72±1.71	<0.001
SCFT (mm)	22.70±6.12	21.37±3.89	0.219
PPFT (mm)	11.22±1.69	11.59±1.76	0.307
VFT (mm)	64.54±18.93	66.85±11.27	0.471
VFT/SCFT	2.87±0.58	3.15±0.29	0.004
VAT (mm^3)	174.04±33.49	183.64±20.22	0.095
AFI	0.55±0.11	0.59±0.11	0.071

Values are presented as mean±SD.

BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; PRPFT, posterior right perinephric fat thickness; SCFT, subcutaneous fat thickness; PPFT, preperitoneal fat thickness; VFT, visceral fat thickness; VFT/SCFT, ratio of visceral fat thickness to subcutaneous fat thickness; VAT, visceral adipose tissue volume; AFI, abdominal wall fat index; SD, standard deviation.

[a)]Significant at P<0.05 (two-tailed). P-value was calculated using the independent t test.

P<0.001), and after adjustment in the multivariate analysis, this risk increased to 7.09 times higher (AOR, 7.09; 95% CI, 2.52 to 19.93; P<0.001). Additionally, participants with an AFI >0.519 were at 3.22 times higher risk for the presence of carotid artery plaque than participants with an AFI ≤0.519 (crude OR, 3.22; 95% CI, 1.31 to 7.95; P=0.011), and after adjustment in the multivariate analysis, the risk increased to 3.58 times higher (AOR, 3.58; 95% CI, 1.36 to 9.39; P=0.010). Similarly, participants whose VFT/SCFT was >2.9 were at a 4.18 times higher risk for the presence of carotid artery plaque than participants whose VFT/SCFT was ≤2.9 (crude OR, 4.18; 95% CI, 1.52 to 11.53; P=0.005); this OR was nearly unchanged by adjustment in the multivariate analysis (AOR, 4.17; 95% CI, 1.52 to 11.41; P=0.006). No other abdominal indices showed any significant associations with the presence of carotid artery plaque. Finally, none of the anthropometric indices showed any significant associations with the presence of carotid artery plaque.

Discussion

Many studies have shown that regional obesity is more closely associated with atherosclerosis than generalized obesity [24,25]. The harmful effect of abdominal obesity arises from metabolic activity. Free fatty acids are released into the hepatic circulation with subsequent stimulation of the release of apolipoprotein B-containing lipoproteins, increasing the plasma glucose level and reducing insulin sensitivity. A number of cytokines released by adipose tissue may also be involved in the development of atherosclerosis [12].

The present study demonstrated significant associations between carotid atherosclerosis and SCFT, PRPFT, VAT, PPFT, VFT, and VFT/SCFT. In contrast, the AFI showed a non-significant association with carotid artery atherosclerosis.

To further clarify and better assess the associations between the abdominal fat indices and carotid artery atherosclerosis, we performed univariate and multivariate analyses for all indices after choosing the best cutoff values via receiver operating curve (ROC) analysis. Regarding the abdominal fat indices, we detected that PPFT >10.8 mm, PRPFT >11.2 mm, VFT >62.1 mm, VFT/SCFT >2.9, and VAT >176 were associated with increased risk of carotid artery atherosclerosis relative to their counterparts in both the univariate and multivariate analyses. In contrast, SCFT and the AFI showed non-significant associations with the presence of carotid artery atherosclerosis. Moreover, the current study revealed that PRPFT and

Table 4. Univariate and multivariate analysis of ultrasonographic abdominal fat and anthropometric indices associated with carotid artery atherosclerosis (n=92)

Factor	No. (%)		Crude OR (95% CI)	P-value[a]	Adjusted OR[b] (95% CI)	P-value[a]
	IMT ≤0.9 (n=31)	IMT >0.9 (n=61)				
BMI level (kg/m^2)						
≤29.68	15 (48.4)	24 (39.3)	Ref		Ref	
>29.68	16 (51.6)	37 (60.7)	1.41 (0.60–3.46)	0.408	1.22 (0.49–3.64)	0.670
WC level (cm)						
≤103.0	15 (48.4)	23 (37.7)	Ref		Ref	
>103.0	16 (51.6)	38 (62.3)	1.55 (0.65–3.71)	0.327	1.39 (0.11–0.89)	0.482
HC level (cm)						
≤105.0	17 (54.8)	18 (29.5)	Ref		Ref	
>105.0	14 (45.2)	43 (70.5)	2.90 (1.18–7.11)	0.020	2.29 (0.89–5.86)	0.082
WHR level						
≤0.97	13 (44.8)	31 (51.7)	Ref		Ref	
>0.97	16 (55.2)	29 (48.3)	0.76 (0.31–1.85)	0.546	0.79 (0.31–2.04)	0.639
WHtR level						
≤0.615	17 (54.8)	16 (26.7)	Ref		Ref	
>0.615	14 (45.2)	44 (73.3)	3.34 (1.31–8.29)	0.009	2.65 (1.02–6.90)	0.046
PRPFT level (mm)						
≤11.2	23 (74.2)	9 (14.8)	Ref		Ref	
>11.2	8 (25.8)	52 (85.2)	16.62 (5.69–48.53)	<0.001	15.23 (4.99–46.24)	<0.001
SCFT level (mm)						
≤21.3	16 (51.6)	15 (24.6)	Ref		Ref	
>21.3	15 (48.4)	46 (75.4)	3.27 (1.31–8.16)	0.011	2.59 (0.99–6.81)	0.053
PPFT level (mm)						
≤10.8	19 (61.3)	16 (26.2)	Ref		Ref	
>10.8	12 (38.7)	45 (73.8)	4.45 (1.77–11.21)	0.001	4.31 (1.67–11.12)	0.003
VAT level (mm^3)						
≤176	20 (64.5)	11 (18.0)	Ref		Ref	
>176	11 (35.5)	50 (82.0)	8.26 (3.09–22.12)	<0.001	7.61 (2.70–21.43)	<0.001
AFI level						
≤0.519	13 (41.9)	18 (29.5)	Ref		Ref	
>0.519	18 (58.1)	43 (70.5)	1.72 (0.70–4.25)	0.235	2.84 (0.99–8.08)	0.051
VFT level (mm)						
≤62.1	22 (71.0)	12 (19.7)	Ref		Ref	
>62.1	9 (29.0)	49 (80.3)	9.98 (3.67–27.12)	<0.001	8.84 (3.18–24.61)	<0.001
VFT/SCFT						
≤2.9	16 (51.6)	8 (13.1)	Ref		Ref	
>2.9	15 (48.4)	53 (86.9)	7.07 (2.54–19.73)	<0.001	9.39 (2.97–29.72)	<0.001

IMT, intima-media thickness; OR, odds ratio; CI, confidence interval; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; PRPFT, posterior right perinephric fat thickness; SCFT, subcutaneous fat thickness; PPFT, preperitoneal fat thickness; VAT, visceral adipose tissue volume; AFI, abdominal wall fat index; VFT, visceral fat thickness; VFT/SCFT, ratio of visceral fat thickness to subcutaneous fat thickness.
[a]Significant at P<0.05 (two-tailed). [b]Adjusted for diabetes, smoking, and hypertension.

Table 5. Univariate and multivariate analysis of indices predicting carotid artery plaques

Factor	No. (%) Absence of plaque (n=42)	No. (%) Presence of plaque (n=50)	Crude OR (95% CI)	P-value[a)]	Adjusted OR[b)] (95% CI)	P-value[a)]
BMI level (kg/m^2)						
≤29.68	15 (35.7)	24 (48.0)	Ref		Ref	
>29.68	27 (64.3)	26 (52.0)	0.60 (0.26–1.39)	0.236	0.59 (0.25–1.41)	0.241
WC level (cm)						
≤103.0	21 (50.0)	17 (34.0)	Ref		Ref	
>103.0	21 (50.0)	33 (66.0)	1.94 (0.84–4.50)	0.122	2.04 (0.85–4.92)	0.111
HC level (cm)						
≤105.0	19 (45.2)	16 (32.0)	Ref		Ref	
>105.0	23 (54.8)	34 (68.0)	1.76 (0.75–4.11)	0.194	1.90 (0.78–4.67)	0.160
WHR level						
≤0.97	19 (45.2)	16 (32.0)	Ref		Ref	
>0.97	23 (54.8)	34 (68.0)	0.87 (0.38–2.00)	0.741	0.81 (0.34–1.92)	0.633
WHtR level						
≤0.615	18 (43.9)	15 (30.0)	Ref		Ref	
>0.615	23 (56.1)	35 (70.0)	1.83 (0.77–4.33)	0.172	0.51 (0.20–1.27)	0.147
PRPFT level (mm)						
≤11.2	23 (54.8)	9 (18.0)	Ref		Ref	
>11.2	19 (45.2)	41 (82.0)	5.51 (2.15–14.22)	<0.001	7.09 (2.52–19.93)	<0.001
SCFT level (mm)						
≤21.3	14 (33.3)	17 (34.0)	Ref		Ref	
>21.3	28 (66.7)	33 (66.0)	0.97 (0.41–2.31)	0.946	0.99 (0.39–2.49)	0.990
PPFT level (mm)						
≤10.8	18 (42.9)	17 (34.0)	Ref		Ref	
>10.8	24 (57.1)	33 (66.0)	1.46 (0.62–3.39)	0.384	1.47 (0.63–3.45)	0.372
VAT level (mm^3)						
≤176	18 (42.9)	13 (26.0)	Ref		Ref	
>176	24 (57.1)	37 (74.0)	2.13 (0.89–5.14)	0.091	2.36 (0.93–5.95)	0.070
AFI level						
≤0.519	20 (47.6)	11 (22.0)	Ref		Ref	
>0.519	22 (52.4)	39 (78.0)	3.22 (1.31–7.95)	0.011	3.58 (1.36–9.39)	0.010
VFT level (mm)						
≤62.1	19 (45.2)	15 (30.0)	Ref		Ref	
>62.1	23 (54.8)	35 (70.0)	1.93 (0.82–4.54)	0.134	2.06 (0.84–5.05)	0.113
VFT/SCFT						
≤2.9	17 (40.5)	7 (14.0)	Ref		Ref	
>2.9	25 (59.5)	43 (86.0)	4.18 (1.52–11.53)	0.005	4.17 (1.52–11.41)	0.006

OR, odds ratio; CI, confidence interval; BMI, body mass index; WC, waist circumference; HC, hip circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; PRPFT, posterior right perinephric fat thickness; SCFT, subcutaneous fat thickness; PPFT, preperitoneal fat thickness; VAT, visceral adipose tissue volume; AFI, abdominal wall fat index; VFT, visceral fat thickness; VFT/SCFT, ratio of visceral fat thickness to subcutaneous fat thickness.

[a)]Significant at $P<0.05$ (two-tailed). [b)]Adjusted for diabetes, smoking, and hypertension.

VFT/SCFT were significantly associated with the presence of carotid plaque. After selecting the best cutoff values using ROC analysis, we performed univariate and multivariate analyses. From the abdominal fat indices, we detected that PRPFT >11.2 mm, AFI >0.519 mm, and VFT/SCFT >2.9 were associated with increased risk of carotid artery plaque relative to their counterparts in both the univariate and multivariate analyses. In contrast, SCFT, PPFT, VAT, and VFT showed non-significant associations with the presence of carotid artery plaque.

To the best of our knowledge, few studies are available regarding the association between the posterior perinephric fat and carotid atherosclerosis in adults; our results align with results obtained by Liu et al. [11], who suggested that perirenal fat is a promising target for cardiovascular disease management. Moreover, Roever et al. [20] reported that PRPFT may be useful in identifying individuals with an elevated risk of developing atherosclerotic disease. Our findings are also in accordance with the results obtained by Rallidis et al. [17], who compared VAT and WC as predictors of subclinical atherosclerosis and concluded that only VAT was positively correlated with IMT and remained an independent predictor of carotid artery plaque after adjustment for cardiovascular risk factors. However, in contrast to our results, they found that WC could be used as a predictor of the presence of carotid plaque. Lear et al. [12] concluded that VAT was associated with carotid IMT in women and men, but after adjustment for risk factors, this relationship remained significant for men only.

With regard to VFT and VFT/SCFT, our results align with those obtained by Kim et al. [26]. Those researchers found a similar association between VFT and carotid IMT, both of which were measured via ultrasonography [26]. However, our findings do not agree with the results obtained by Jung et al. [18], who found that VFT and VFT/SCFT were not significantly correlated with IMT in women or men. Regarding the AFI, our results are in accordance with those obtained by Yamamoto et al. [27], who found that the AFI was not correlated with IMT. However, our findings contradict the results obtained by Kawamoto et al. [19], as they detected an association between IMT and the AFI, rather than maximum PPFT, in non-obese men. Kawamoto et al. [28] considered the AFI to be an independent risk factor for IMT in women.

Considerable disagreement exists regarding whether SCFT is a good predictor of carotid atherosclerosis. In contrast to our results, Jung et al. [18] demonstrated that SCFT was inversely associated with carotid IMT after adjustments for BMI and other traditional or non-traditional cardiovascular disease risk factors in men, but not in women. However, our results align with those of Radmard et al. [13], who concluded that subcutaneous fat measures were poor indicators of carotid IMT.

We detected a strong association between PPFT and carotid atherosclerosis, in accordance with findings obtained by Yamamoto et al. [27], who proposed that PPFT, as assessed via ultrasonography, may play a role in the progression of IMT in middle-aged non-obese men. Our results agree with those obtained by Kawamoto et al. [29], in which PPFT assessed via ultrasonography was found to be an important risk factor for carotid IMT, but they contradict findings obtained by Liu et al. [30] In that report, no significant association was detected in men; in the univariate analysis, borderline statistical significance was detected in women, but it disappeared after adjustment of the model.

In contrast, of the anthropometric measurements, only HC showed a strong association with carotid atherosclerosis. WC showed a weak association. After choosing the best cutoff value via ROC analysis, we performed univariate and multivariate analyses for all indices. Of all anthropometric indices, we detected that an HC >105 mm increased the risk of carotid artery atherosclerosis in the univariate analysis, but after adjustment in the multivariate analysis, this significance was lost. However, participants with WHtR >0.615 demonstrated increased risk of carotid artery atherosclerosis in both the univariate and multivariate analyses. Other anthropometric indices showed no significant associations.

Controversy persists regarding anthropometric indices as predictors of carotid atherosclerosis. Radmard et al. [13] reported that WHtR, BMI, and WHR were not good predictors for the presence of carotid atherosclerosis. Moreover, Lee et al. [31] revealed that BMI is a poor discriminator for cardiovascular risk factors, and Rallidis et al. [17] reported that BMI could not be used to predict the presence of carotid plaques. However, Hsieh and Yoshinaga [32] reported that WHtR was the tool with the best discrimination for detecting cardiovascular risk factor. Additionally, Rallidis et al. [17] reported that WC could be used as a predictor of carotid plaques only in the univariate analysis. De Michele et al. [4] concluded that WHR and BMI were significant predictors of carotid IMT.

In our study, we noticed a discrepancy between our results and previous findings; this could be partially due to the influence of ethnic differences on the intra-abdominal fat distribution.

The current study had some limitations. First, we included a relatively small number of patients, although we did include several abdominal fat and anthropometric indices and assessed their associations with carotid atherosclerosis. To the best of our knowledge, few papers have been published regarding associations between posterior perinephric fat thickness and carotid atherosclerosis. Furthermore, an important aspect of our research was the use of cutoff values to determine the risk for each index. Second, it is possible that our results may have been biased by the patient population, because the patients were referred randomly from outpatient internal medicine clinics. Several risk factors are associated with carotid atherosclerosis, and many of these factors show clinical overlap and could be present in the same patient. Third, MRI and CT are superior imaging modalities for the measurement of abdominal fat areas, but limited availability, high cost, and the hazards of ionizing radiation limit their usage. Therefore, we used ultrasonography in our assessment because of its accuracy relative to CT and MRI, availability, cost-effectiveness, and high safety profile. Finally, we only measured carotid IMT as a marker of carotid atherosclerosis. We did not assess other carotid atherosclerotic values, including pulse wave velocity and arterial elasticity.

In conclusion, posterior perinephric fat thickness as measured via ultrasound was found to be a strong predictor of carotid atherosclerosis, followed by VFT/SCFT, VFT, VAT, PPFT, and WHtR with regard to predictive capacity. Additionally, posterior perinephric fat thickness was identified as a strong predictor for carotid artery plaque, followed by VFT/SCFT and the AFI.

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Conflict of Interest

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

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