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Ultrasonography for the evaluation of visceral fat and the metabolic syndrome

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Abstract

Association between abdominal obesity and cardiovascular disease has been related with visceral adiposity, through the predisposition of developing type 2 diabetes mellitus and metabolic syndrome (MS). Sonography is a simple and reliable method to measure both subcutaneous and visceral fat. To analyze the relationship of anthropometric measurements with abdominal adiposity measured by sonography and to analyze the utility of sonography in the prediction of insulin resistance (IR) and the other components of MS. Visceral fat measurements by sonography correlated better with components of MS than did subcutaneous fat measurements. Preperitoneal circumference (PC) was strongly correlated with all components of MS and with IR expressed as a homeostasis model assessment (HOMA) index for IR. PC was better than waist circumference (WC) in predicting triglyceride levels, apolipoprotein B levels, and HOMA index, but WC was better than PC in predicting high-density lipoprotein cholesterol levels. The area under the receiver operating characteristic curve was 0.699 for PC and 0.684 for WC, in subjects with body mass index 25 kg/m^2 or greater (P = .024 and .015, respectively). PC and WC showed good correlation with HOMA index (Spearman correlation coefficient = 0.306, P < .001 and .206, P < .001, respectively). Abdominal visceral fat is better correlated with MS than subcutaneous fat; sonography is a useful method to evaluate the abdominal fat; PC is the best sonography parameter correlated with components of MS, and in overweight and obese subjects, PC is better than WC at predicting components of the MS.

1. Introduction

Obesity, especially of abdominal distribution, is an international health problem that has been on the increase, especially in occidental countries, in recent years [1,2]. It has been clearly established that abdominal obesity is strongly associated with cardiovascular disease (CVD). The association between abdominal obesity and CVD has been related with visceral adiposity, through the predisposition of developing type 2 diabetes mellitus and metabolic syndrome (MS) [3,4]. The mechanism of this association has not been clearly established. However, adipose tissue with abdominal visceral distribution is very active in the production of several molecules such as tumor necrosis factor, resistin, plasminogen activator inhibitor 1, and interleukin 6, with potent proatherogenic and insulin resistance (IR) activities [5].

Along these lines, abdominal visceral adiposity measured by computed tomography scan or magnetic resonance imaging is well correlated with IR [6,7]. However, these procedures are, for the moment, reserved for research purposes.

The measurement of abdominal obesity through waist circumference (WC) has been established as a simple, inexpensive, and useful method for the diagnosis of abdominal obesity. For this reason, WC has been proposed

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as a key element for the diagnosis of MS. It has been proposed as a part of the routine general physical examination in clinical practice [8]. Moreover, WC is well correlated with visceral obesity, and in clinical studies, it has been associated with cardiovascular risk [9]. However, IR among subjects with elevated WC is highly variable, probably for a number of reasons, including genetic factors predisposing to IR and the lack of accuracy in the measurement of WC in subjects with a pendulous abdomen [10]. In addition, WC is highly correlated with both subcutaneous and visceral abdominal fat, the latter being much more closely related to IR than the former [11].

Sonography is a simple and reliable method for measuring both subcutaneous and visceral fat having been demonstrated to show a strong correlation with both adiposities measured with computed tomography scan [12]. The clinical use of abdominal sonography in the prediction of IR has not been previously compared with WC.

The purpose of this study was to analyze the relationship of anthropometric measurements, including WC, with abdominal adiposity measured by sonography, and to assess the value of sonography in the prediction of IR and other components of the MS.

2. Materials and methods

2.1. Subjects

We studied 177 volunteers, 68 men and 109 women, who underwent a routine medical examination. Exclusion criteria were age younger than 25 or older than 65 years, previous abdominal surgery, excessive alcohol consumption, current acute illness, and current use of drugs that modify lipid or glucose metabolism, including antidiabetic, antihypertensive, and hypolipidemic drugs, and estrogen replacement therapy. All subjects gave written informed consent. The local research committee approved the study.

Anthropometric measurements included age, sex, weight, height, body mass index (BMI), and WC. All measurements were made while the subjects were wearing a hospital gown with minimal underwear and no shoes. The weight was measured to the nearest 0.1 kg with a calibrated physician's office scale, and the height was measured to the nearest 1 mm with a wall-mounted stadiometer. Waist circumference was measured with a heavy-duty inelastic plastic fiber tape measure (Gulick II, Country Technology, Inc, Gays Mills, Wis) placed directly on the skin while the subject stood balanced on both feet, with the feet touching each other and both arms hanging freely. The measurement was taken immediately above the iliac crest and at end expiration [13]. Before taking a reading, specific attention was given to placing the tape perpendicular to the long axis of the body and horizontal to the floor. Blood pressure (OMRON M4-I, OMRON Matsusaka Co, Ltd, Matsusaka, Japan) was measured as recommended by the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure [14].

2.1.1. Biochemical measurements

Samples were obtained after at least 10 hours' fasting between 8 and 9 AM. Plasma glucose was determined by the glucose-oxidase method. Cholesterol content of lipoprotein fractions, serum triglycerides (TG), and uric acid were measured enzymatically. Apolipoprotein A-I (apo A-I), apolipoprotein B (apo B), and high-sensitivity C-reactive protein (hs-CRP) were measured by immunonephelometry. Low-density lipoprotein cholesterol (LDL-C) was calculated with the Friedewald formula. Insulin was measured with a commercial radioimmunoassay kit (Linco Research Inc, St Charles, Mo). As an indicator of IR, a homeostasis model assessment (HOMA) index for IR was used [15], which was calculated as follows:

$$\text{HOMA index} = [\text{fasting plasma glucose (mmol/L)} \times \text{fasting serum insulin } (\mu\text{U/mL})]/22.5$$

Sonography measurements were performed using a linear-array probe (Aloka SSD-900, Tokyo, Japan) (7.5 MHz and 42 mm) in supine position. It was kept perpendicular to the skin on the upper median abdomen, and longitudinal scan was done in the midpoint between the xiphoid appendix and the navel along the alba line with regard to the surface of the liver, to be almost parallel to the skin. Subcutaneous fat thickness (STh) and area (SA) were measured on the xiphoumbilical line in both longitudinal and transverse views. Measurements were taken 3 times directly from the screen using the electronic calipers at the inner edge of the skin and at the outer edge of the alba line and the fat-muscle interfaces for area. Preperitoneal fat thickness or visceral-fat thickness (VTh) and area (VA) were measured in the same sites and views (Fig. 1). In this case, measurements were taken at the inner edge of the alba line and at the peritoneal line for thickness and area. Then mean values were calculated. Preperitoneal circumference (PC) was calculated as $WC - (2\pi \times STh)$. This measurement assumes that WC is a circumference, hence after measuring WC and STh, the intra-abdominal radius and PC can be easily calculated with the formula cited previously. All the subjects were asked to hold their breath during the examination. Special care was taken to keep the probe just touching the skin to prevent compression of the fat layers. All measurements were performed by the same physician.

2.2. Statistical analysis

Statistical analysis was performed using the SPSS software package (version 11.0). Mean values, SD, and ranges of the anthropometric, biochemical, and sonographic measurements were calculated. The Spearman correlation test was applied to assess the association of sonographic measures and the rest of studied variables.

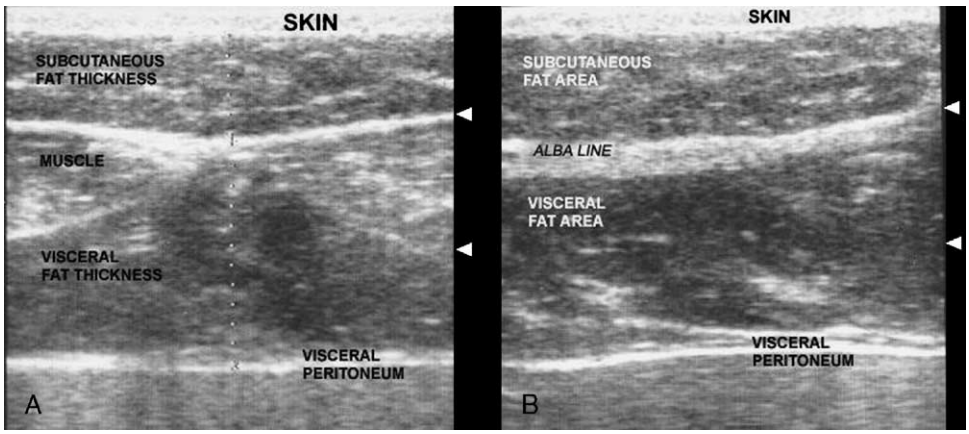

Fig. 1. Sonography scan of the upper abdominal wall on the xiphoumbilical line, showing the subcutaneous fat and preperitoneal fat layers. A, Transverse view. B, Longitudinal view.

Other Spearman correlation was applied to assess the association of WC and PC and variables that express IR, such as fasting insulin levels, glucose/insulin ratio, McAuley method, Bennett index, quantitative insulin sensitivity check index, HOMA index, Raynaud index, and Hanson index [15-24]. *P* values of less than .05 were regarded as significant. Multivariate linear regression analysis was used to establish the independent contribution of sonography measurements to components of MS, and the same procedure was used to establish the independent contribution of WC or PC for prediction of components of MS in subjects with BMI 25 kg/m^2 or greater. Logarithmic transformation was used for variables with nonnormal distribution. Predictive model was assessed by the area under the receiver operating characteristic (ROC) curve for HOMA values less than 3.2 as normal insulin sensitivity [15], and values of $P \leq .05$ were considered statistically significant.

3. Results

The main anthropometric and biochemical data of subjects included in this study are presented in Table 1. Mean BMI was 25.3 ± 3.45 kg/m^2 (range 18.5-39.4 kg/m^2); 79 subjects (50 men and 29 women) had BMI greater than 25 kg/m^2, and obesity (BMI ≥30 kg/m^2) was present in 13 subjects (7.3%). Eleven women (10%) were postmenopausal. The prevalence of the MS as defined by the Adult Treatment Panel III criteria [10] was 13.6% (18 men and 6 women). Most subjects presented normal glucose plasma levels, although 3 subjects had more than 125 mg/dL, with the highest value being 127 mg/dL. Significant differences

Table 1
Clinical characteristics of subjects studied

Variable	Men (n = 68), mean ± SD	Women (n = 109), mean ± SD	*P* values	All (n = 177), mean ± SD	All (n = 177), range
Age (y)	39 ± 10	43 ± 9	.009	42 ± 10	23-61
BMI (kg/m^2)	27.2 ± 3.7	24.0 ± 2.6	.000	25.3 ± 3.4	18.5-39.4
WC (cm)	95.2 ± 10.3	82.9 ± 9.0	.000	87.6 ± 11.2	58-118
SBP (mm Hg)	125 ± 11	119 ± 15	.002	121 ± 14	90-164
DBP (mm Hg)	79 ± 9	77 ± 9	.069	78 ± 9	58-100
Cholesterol (mg/dL)	214 ± 46	210 ± 36	.674	212 ± 40	121-335
TG (mg/dL)	113 ± 115	59 ± 22.77	.000	79.63 ± 76.57	27-381
HDL-C (mg/dL)	48 ± 12	62 ± 13.63	.000	57.45 ± 14.73	27-100
LDL-C (mg/dL)	143 ± 43	135 ± 32.78	.175	138.49 ± 36.76	51-269
Apo A-I (mg/dL)	124 ± 20	136 ± 18	.000	132 ± 20	74-192
Apo B (mg/dL)	102 ± 32	88 ± 20	.008	94 ± 26	43-203
Glucose (mg/dL)	99 ± 14	97 ± 7	.377	98 ± 11	27-127
Insulin (μU/mL)	18.2 ± 7.1	15.1 ± 5.5	.002	16.2 ± 6.3	2.6-45.4
HOMA index	4.5 ± 2.2	3.7 ± 1.5	.007	4.0 ± 2.0	0.6-13
hs-CRP (mg/L)	2.4 ± 3.8	1.3 ± 1.6	.101	1.7 ± 2.7	0.0-21
STh (cm)	1.1 ± 1.4	1.2 ± 0.4	.000	1.2 ± 0.9	0.1-11.7
VTh (cm)	1.5 ± 0.5	0.9 ± 0.39	.000	1.1 ± 0.5	0.3-2.3
SA (cm^2)	9.5 ± 1.3	9.9 ± 0.91	.002	9.8 ± 1.1	2-12.4
VA (cm^2)	10.5 ± 1.4	9.6 ± 0.9	.000	9.9 ± 1.2	2.3-12.5
PC (cm)	88.0 ± 11.1	75.0 ± 7.9	.000	80.0 ± 11.2	35.5-113.2

Table 2
Spearman correlation between sonographic variables and age and anthropometric and biochemical variables

Variable	STh	SA	VTh	VA	PC
Age	0.113	0.142	−0.004	−0.036	0.19
Weight	0.096	0.119	0.684*	0.665*	0.791*
BMI	0.313*	0.342*	0.669*	0.675*	0.736*
WC	0.287*	0.333*	0.794*	0.768*	0.933*
SBP	0.108	0.155	0.381*	0.332*	0.351*
DBP	0.040	0.077	0.247*	0.235**	0.208***
Cholesterol	−0.104	−0.094	−0.037	−0.028	0.018
TG	−0.040	0.017	0.469*	0.435*	0.517*
HDL-C	−0.076	−0.105	−0.589*	−0.553*	−0.595*
LDL-C	−0.046	−0.032	0.093	0.090	0.141
Apo A-I	−0.143	−0.131	−0.448*	−0.425*	−0.447*
Apo B	−0.100	−0.089	0.251**	0.243**	0.277*
Glucose	0.085	0.116	0.343*	0.290*	0.327*
Insulin	0.096	0.158	0.390*	0.390*	0.400*
HOMA index	0.1050	0.165***	0.430*	0.411*	0.427*
hs-CRP	0.216**	0.217**	0.401*	0.357*	0.264*

Values express correlation coefficient.
* $P \leq .001$.
** $P \leq .01$.
*** $P \leq .05$.

between men and women were found in the following variables: age, BMI, WC, systolic blood pressure (SBP), TG, high-density lipoprotein cholesterol (HDL-C), apo A-I, apo B, insulin, HOMA index, STh, VTh, SA, VA, and PC (Table 1).

Table 2 shows the correlation of sonography measurements with age and anthropometric and biochemical variables. Subcutaneous fat measurements by sonography were correlated with BMI, WC, and hs-CRP, and visceral fat measurements were correlated with weight, BMI, WC, SBP, diastolic blood pressure (DBP), TG, HDL-C, apo A-I, apo B, glucose, insulin, hs-CRP levels, and HOMA index. PC was strongly correlated with all components of MS and with IR expressed as the HOMA index. WC was correlated with subcutaneous and visceral fat and with all components of MS (data not shown). hs-CRP was correlated with subcutaneous and visceral fat and with BMI (data not shown). The menopausal status did not significantly modify any correlation observed. Finally, Table 3 shows that both

Table 3
Spearman correlation between WCs and PCs and variables that express IR

Variable (reference)	Waist circumference	PC
Fasting insulin levels [16]	0.401*	0.400*
Glucose/insulin ratio [17]	−0.320*	−0.323*
McAuley method [18]	−0.401*	−0.475*
Bennett index [19]	−0.268**	−0.303**
QUICKI index [15,20]	−0.268**	−0.306**
HOMA index [15,21,22]	0.268**	0.306**
Raynaud index [23]	−0.401*	−0.400*
Hanson index [24]	−0.265*	−0.270*

Values express correlation coefficient. QUICKI index indicates quantitative insulin sensitivity check index.
* $P \leq .001$.
** $P \leq .05$.

Table 4
Multilinear regression to assess the contribution of WC and PC to the components of the metabolic syndrome in subjects with BMI 25 kg/m^2 or greater

MS components	WC			PC		
	β	SE β	P	β	SE β	P
SBP	0.209	0.227	.362	−0.108	0.183	.559
DBP	-3.07×10^{-2}	0.154	.842	-2.17×10^{-2}	0.124	.861
TG	-9.08×10^{-3}	0.008	.254	2.235×10^{-2}	0.008	.005
HDL-C	−0.655	0.178	.000	−0.101	0.147	.492
LDL-C	−1.479	1.560	.346	1.850	1.534	.230
Apo B	1.130×10^{-3}	0.002	.606	2.962×10^{-3}	0.010	.028
HOMA index	2.843×10^{-3}	0.003	.340	5.297×10^{-3}	0.002	.005

circumferences (WC and PC) correlated with the different variables that express IR.

3.1. Predictors of IR

To establish whether sonography measurements (STh, VTh, SA, VA, and PC) were good predictors of the major components of MS (SBP, DBP, TG, HDL-C, LDL-C, apo B, and HOMA index), a multilinear regression analysis was performed in subjects with BMI 25 kg/m^2 or greater. PC was the best predictor of all the measurements and related calculations. To determine whether PC was the best predictor of the major components of MS (SBP, DBP, TG, HDL-C, LDL-C, apo B, and HOMA index), a multilinear regression analysis was performed in the same subjects with WC and PC as independent variables (Table 4). PC was better than WC in predicting TG levels, apo B levels, and HOMA index. WC was better than PC in predicting HDL-C levels. PC significantly improved the prediction of the HOMA index even after inclusion of WC in the model. Regression analysis was not significant for SBP, DBP, or

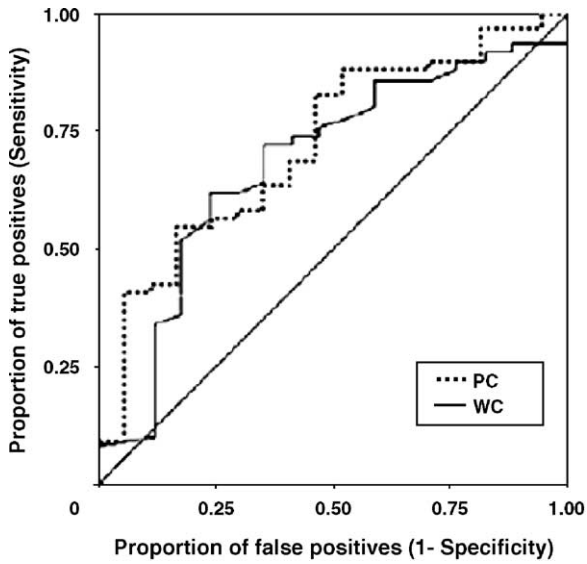

Fig. 2. ROC curves in subjects with BMI 25 kg/m^2 or greater for PC and for WC; areas under the curves were 0.699 (P = .024) and 0.684 (P = .015), respectively.

LDL-C levels (Table 4). The calculated area under the ROC curve was 0.699 for PC and 0.684 for WC, considering HOMA values less than 3.2 as normal insulin sensitivity [15] in subjects with BMI 25 kg/m^2 or greater (asymptotic significance, $P = .024$ and .015, respectively) (Fig. 2).

4. Discussion

IR is a complex metabolic disturbance in which many factors are involved [25]. In this study, we have confirmed that abdominal fat is a major determinant of IR, and abdominal sonography is an easy and reliable method to assess abdominal fat, as has been previously reported [26-28]. In addition, our study demonstrates for the first time that a simple, widely available, and inexpensive technique, such as sonography, correlated better with IR and other obesity-related metabolic disturbances than WC measurement.

Our results show that factors associated with IR and MS, that is, hyperglycemia, hypertriglyceridemia, hypertension, and low HDL-C, are strongly linked with visceral fat and only marginally with subcutaneous adiposity evaluated by sonography. This has recently been observed in diabetic patients in whom visceral fat measured by sonography also correlated with the risk of CVD [29]. In agreement with our results, it has been recently shown that abdominal liposuction of large volumes of subcutaneous adipose tissue does not significantly improve the metabolic abnormalities associated with obesity [30]. In our study, we found a high correlation between the amount of preperitoneal fat and the components of the MS, suggesting a common etiopathogenic link among them.

An interesting finding of our study is the relationship among hs-CRP with BMI and both subcutaneous and visceral fat, supporting the observation that hs-CRP blood levels are well correlated with general adiposity, in agreement with previous results [31].

Noting that WC is actually expressing subcutaneous and visceral fat, and that only visceral fat is related with MS, 1 of our objectives was to investigate whether sonographic measurement of visceral fat would improve the prediction of IR and MS from WC. In spite of our sample being made up of volunteers, most with normal weight and normal abdominal fat, our results show that sonographic measurements are better predictors than WC for the HOMA index, TG, and apo B levels, especially in obese or overweight subjects, for whom the prediction is more important. These results suggest that sonography would be very useful in obese subjects who present larger variations of the distribution of the subcutaneous and visceral fat depositions than do lean individuals.

The best sonographic parameter associated with IR, expressed as HOMA index and the components of the MS, was PC; in this context, we have also shown that in subjects with BMI 25 kg/m^2 or greater, PC had greater area under the ROC curve than WC with respect to HOMA values (<3.2 or ≥ 3.2) (Fig. 2). Thus, this indirect evaluation of visceral fat excluding subcutaneous fat is even better than the direct visceral measurements themselves. This is probably caused by the heterogeneous distribution of intra-abdominal visceral fat, and most likely, only the measurement of the whole amount of intra-abdominal fat by multislice magnetic resonance imaging could improve the PC [32].

In conclusion, abdominal visceral fat correlated better with the components of the MS than subcutaneous fat. Sonography is a useful method for evaluating abdominal fat. PC is the best sonographic parameter correlated with components of the MS. In overweight and obese subjects, PC is better than WC in predicting components of the MS.

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