Sagittal abdominal diameter and waist circumference are equally good as identifiers of cardiometabolic risk

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Short running head: Measures of central obesity and metabolic syndrome markers

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Abbreviations: BMI, body mass index; CT, computed tomography; FFA, free fatty acids IDF, International Diabetes Federation; IL, interleukin; MRI, magnetic resonance imaging; ROC, Receiver Operating Characteristic; SAD, sagittal abdominal diameter; SAT, subcutaneous adipose tissue; TNF, tumor necrosis factor; VAT, visceral adipose tissue, WC, waist circumference.

Abstract

Background

Body mass index (BMI) and waist circumference (WC) are commonly used markers of cardiometabolic risk. However, sagittal abdominal diameter (SAD) has been proposed to be a better marker of intra-abdominal obesity compared to WC and might better associate with metabolic disturbances in high-risk populations. The objective of this study was to compare SAD, WC, and BMI as determinants of an adverse metabolic phenotype.

Method

Anthropometric and metabolic measures of 1516 overweight or obese individuals with features of the metabolic syndrome were included to examine differences between SAD, WC and BMI as measures of an adverse metabolic phenotype. Multiple linear regression and logistic regression models were used to investigate the association between SAD, WC, and BMI and markers of metabolic syndrome, insulin resistance, blood lipids, and low grade inflammation.

Results

Both SAD and WC correlated with BMI, but as BMI increased, SAD proportionately estimated higher abdominal adiposity compared to WC (slope = 0.0037 (0.0029; 0.0046), $p<0.0001$). We did not find major differences between SAD, WC and BMI in explained variance in models with the different markers of metabolic risk. Furthermore, we did not find differences between SAD and WC in the ability to identify individuals with metabolic syndrome according to the International Diabetes Federation (IDF) cut-offs, but a few differences from BMI were indicated but mostly before adjustments. Moreover, the differences between SAD and WC associations were not modified by sex or degree of adiposity, but identification of individuals with a metabolic phenotype was generally better in women.

Conclusion

These data indicate that SAD and WC are equally good indicators of an adverse metabolic phenotype. Thus, from a public health perspective choice of anthropometric measure may depend only on what is the most practical method in a given situation.

Introduction

Obesity is one of the most important risk factors for metabolic syndrome, cardiovascular disease (CVD) and type 2-diabetes (T2D). Body mass index (BMI) is often used to evaluate overweight and obesity, but BMI does not distinguish between lean and fat mass. Furthermore, BMI does not provide information on fat distribution, and therefore does not specifically reflect central obesity which is associated with an adverse metabolic phenotype and essential for the association between obesity and lifestyle disease (1).

When assessing abdominal obesity it is important to distinguish between subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) as VAT is the most metabolically adverse type of adipose tissue (1). Simple anthropometric indicators such as waist circumference (WC) and sagittal abdominal diameter (SAD) are used to examine abdominal obesity, and have both been shown to be better indicators measures of an adverse metabolic phenotype compared to BMI alone (2). WC is a commonly used measure of abdominal obesity, but SAD has been proposed to be a better marker for VAT and thus might better have improved predictive ability of metabolic disturbances (3,4).

SAD is measured as the height of the abdomen in a supine position, which increase with VAT accumulation as VAT is contained within the abdominal cavity, while SAT in the supine position will be distributed sideways, due to the force of gravity (5,6). Adjusting measures of WC and SAD for height (as in BMI) have been shown to improve prediction of cardiometabolic risk and thus is suggested to also improve the detection of adverse metabolic phenotypes (7).

Some studies have suggested that sex and degree of obesity might affect the predictive ability of SAD and WC measurements differently (8,9). One study found that SAD compared to WC was a stronger risk marker in women compared to men (8). This could be due to the sex specific fat distribution as women have a higher ratio of SAT to VAT mass, which can lead to formation of a so-called “abdominal apron” and make measurements of WC particularly tricky. Similarly, difficulties might also make SAD a better measure than WC at higher levels of adiposity.

The overall aim of this study was to investigate whether SAD, WC and BMI associate differently with metabolic syndrome and cardiometabolic risk, compromising markers of insulin resistance, dyslipidemia, low grade inflammation and blood pressure. We hypothesized that SAD is stronger associated with cardiometabolic health and a better measurement for identifying individuals with

metabolic syndrome markers above established cut-offs compared to WC and BMI. Furthermore, we hypothesise that height-adjustment of SAD and WC improves the association with adverse metabolic syndrome markers. Finally, we hypothesise that these associations depend on sex and that a stronger association for SAD compared to WC is most pronounced at higher BMIs (>35 kg/m^2). These hypotheses were examined with data from several cohorts of primarily overweight and obese individuals with an adverse metabolic phenotype.

Methods

Study design

This study included cross-sectional baseline data from six human intervention trials: 3G, OPUS, DIOGENES, RIGHT, MyNewGut (MNG), and PROKA (10–15). The studies were registered at http://www.clinicaltrials.gov; 3G (NCT01719913 and NCT01731366); SHOPUS (NCT01195610); DIOGENES (NCT00390637); RIGHT (NCT02358122); MNG: (NCT02215343); PROKA (NCT01561131) and approved by the Research Ethics Committees of the Capital Region of Denmark in accordance with Helsinki Declaration 3G (H-2-2012-064 and H-2-2012-065); SHOPUS (H-3-2010-058); RIGHT (H-1-2014-062); MNG (H-4-2014-052); and PROKA (H-2-2011-145) or the local ethical committees in the respective countries (16).

Participants

Individuals included in the present study, were primarily overweight or obese (98%) at risk of the metabolic syndrome. We used the International Diabetes Federation (IDF) metabolic syndrome definitions (17). For impaired fasting glucose we used both the 5.6 mmol/L IDF cut-off and a 6.1 mmol/L cut-off.

Anthropometric, laboratory and analytical procedures

Body weight, height, WC and SAD were measured by standard anthropometric procedures. SAD was measured twice to the closest 0.1 cm using a Holtain-Kahn Abdominal Caliper (Holtain Ltd, Crymych, United Kingdom) and we used the mean of the two measurements. The subjects were in supine position when measured and were asked to bend their knees to a 45 degree angle and keep their feet flat on the examination table. SAD was measured as the distance between the highest point of the abdomen and the back as assessed by the distance between the two blades of the caliper

(by using a spirit level). The measurement was made at the end of a normal exhalation. WC was measured between the bottom of the ribs and the top of the hipbone. WC was measured twice to the nearest 0.5 cm using a non-elastic flexible measuring tape and the mean of the two measurements was used. All cohorts used a similar standard operating procedure for the anthropometric measurements.

Blood samples for all cohorts were drawn after overnight fasting. Standard clinical measurements of plasma glucose, insulin, total- , LDL- and HDL cholesterol, triglycerides, C-reactive protein (CRP), free fatty acids (FFA), and adiponectin were performed as well as measurements of serum inflammatory markers interleukin (IL)-6 and tumor necrosis factor (TNF)-α (Supplemental methods section). Blood pressure was measured using a digital blood pressure monitor (Supplemental methods section).

Statistical analysis

The statistical analyses were performed using R (v.3.5.1, R Core Team, Vienna, Austria) (18). Only baseline data from the studies were used in the analyses. Pearson correlation was used for evaluating the association between anthropometric measures. Simple linear regression of mean-centered data was used to evaluate any bias between measurements of SAD and WC across the BMI range, and reported as the slope. Multiple linear regression models were used to investigate the association between SAD, WC, and BMI and markers of metabolic syndrome, insulin resistance, blood lipids and measurements of low grade inflammation. Unadjusted analyses as well as analyses adjusted for age, sex, smoking and study were conducted. Similar analyses were done for the SAD-to-height and WC-to-height ratios. The ability of SAD, WC, and BMI to identify individuals with metabolic syndrome markers above the IDF cut-offs was evaluated by means of area under the receiver operating characteristics (ROC) curve using logistic regression models. Unadjusted analyses as well as analyses adjusted for age, sex, smoking and study were conducted

Results

The six cohorts provided a total of 1516 individuals (485 men and 1031 women) (Table 1). The participants had an average age of 42 years, and their BMI ranged from 21 to 52 kg/ m^2, WC ranged from 64-155 cm and SAD ranged from 15-39 cm.

The three anthropometric measures were highly correlated (r=0.82 for SAD and WC; r=0.74 for SAD and BMI; r=0.76 for WC and BMI). However, there was a systematic difference between the correlations for SAD and WC over the range of BMI range of 21-52 kg/m^2. As BMI increased there was a significant trend for SAD to measure proportionately higher abdominal adiposity compared to WC. This was highly significant for men, women, and men and women combined (**Figure 1**).

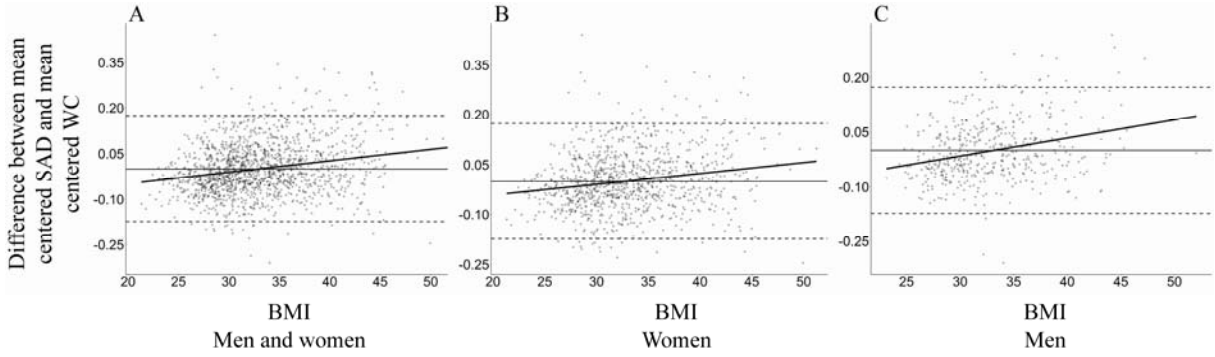

Figure 1 Difference between mean-centered sagittal abdominal diameter (SAD) and waist circumference (WC) across the body-mass index (BMI) range of the participants A) Men and women combined slope = 0.0037 (0.0029; 0.0046), p<0.0001, n=1516. B). Women: slope = 0.0032 (0.0022; 0.0043), p<0.0001, n=1031. C). Men: slope = 0.0049 (0.0035; 0.0064), p<0.0001, n=485.

Associations between anthropometric measures and cardiometabolic health

BMI, WC and SAD were associated with all markers of an adverse metabolic phenotype (Table 2). There were little difference between the measures in terms of R^2 values between SAD and WC, indicating that they explained the variation in cardiometabolic measures equally well (Table 2). Furthermore, there were no differences between the variance explained by SAD-to-height ratio and WC-to-height ratio (Supplemental table 1) and the variation explained by these measures did not from those of SAD and WC alone.

158 *The ability of anthropometric measurements to identify individuals with metabolic syndrome*
159 *markers above the IDF cut-offs*

160 We found that BMI, WC and SAD were overall fair in their ability to identify individuals with
161 metabolic syndrome markers above the IDF cut-offs after adjustments for age, sex, smoking and
162 study and there was no differences between BMI, WC and SAD in their ability to identify these
163 individuals (Table 3). However, in the unadjusted analysis WC and SAD performed slightly better
164 than BMI in identifying individuals with metabolic syndrome markers above the IDF cut-offs for
165 glucose >6.1 mmol/L, triglycerides, systolic and diastolic blood pressure, compared to BMI (Table
166 3). Using WC-to-height ratio and SAD-to-height ratio for identification of individuals with
167 metabolic syndrome markers above the IDF cut-offs did not show any differences between the two
168 (Supplementary table 2) or between these and SAD and WC alone.

169

170 *Differences between sexes and between BMI categories*

171 Contrary to the differences observed between the three anthropometric measures in the unadjusted
172 models in men and women combined, there were no differences between BMI, WC and SAD in
173 men or women alone (Supplementary table 3). However, we observed sex differences in the
174 measures ability of the measures to identify individuals with metabolic syndrome markers above the
175 IDF cut-offs. The prediction was generally better in women than in men especially for glucose >6.1
176 mmol/L, HDL and sBP in the unadjusted models and the prediction for sBP was still better for both
177 SAD and BMI after adjustment (Supplementary table 3).

178 As for the models for the entire population, WC and SAD had a better ability to identify individuals
179 with glucose >6.1 mmol/L, TAG, sBP, and dBP above the IDF cut-offs than BMI, but only in the
180 unadjusted models and only in those with a BMI <35 kg/m^2 (Supplementary table 4). For
181 individuals with a BMI >35 kg/m^2 a differences was only observed for glucose >5.6 mmol/L, where
182 BMI and WC showed better associations that SAD. We found no differences in the associations at
183 high and low BMI except for TAG, which had a higher AUROC at lower BMI even after
184 adjustment. Similar tendencies were observed in the unadjusted models for all metabolic syndrome
185 markers except HDL-cholesterol (Supplementary table 4).

Discussion

In the present study, we found distinct differences between SAD and WC over the BMI range, which may indicate differences in adipose distribution across BMI categories. However, we did not find that any of the anthropometric measures were superior in the association with cardiometabolic health markers or in identifying people/subjects? with metabolic syndrome markers above the IDF cut-offs. Moreover, we did not find that one anthropometric measurement were superior depending on sex or BMI category. Finally, adjusting SAD and WC for height did not improve the identification ability of the anthropometric measures.

Earlier studies comparing SAD and WC show conflicting results and only examine a few risk markers at a time whereas our study measures multiple cardiometabolic risk markers giving a more complete metabolic overview. Similar to other studies our study show no difference between SAD and WC as markers of cardiometabolic health (19,20). One study in 826 elderly Dutch men and women report differences in correlations with markers of insulin resistance, dyslipidemia, and blood pressure between SAD or WC both above and below the age of 65 years of age but no consistently with respect to which was the better (19). However, other studies have shown that SAD is a superior anthropometric measure compared to WC and BMI (2,21,22) although some studies only show a minor benefit of SAD compared to WC (2,22). One study showed that SAD was a better predictor of insulin resistance compared to WC in high-risk group of 59 moderately obese men (21), whereas a study including 885 men and women only found that SAD was marginally better correlated with total and LDL-cholesterol, blood pressure and serum glucose and insulin (22). The latter is in line with results from a study with 4032 participants which showed small improvements in identifying elevated cardiometabolic risk in men with SAD compared to WC, but no difference women (2)

For hard endpoints such as CVD, SAD has been shown to be a better predictor than WC (4,9). One study showed that SAD >25 cm was the only anthropometric measurement associated with major CVD events in patients with T2D (4). Similary, a different study showed that SAD was the only measure that significantly predicted CVD in men, but not in women (9). This study also showed that SAD could predict CVD after adjustments for traditional biomarkers such as total- and HDL cholesterol and systolic blood pressure. This indicates that SAD might have predictive ability

beyond established biomarkers of CVD. In the present study we tried to address this by including additional biomarkers linked to abdominal obesity, CVD and T2D including inflammatory cytokines. However, we did not find that SAD and WC were differentially associated with inflammatory markers.

The proposed mechanism behind the association of abdominal obesity and an adverse cardiometabolic profile is that increased adipose tissue mass and adipocyte size, leads to amplification in pro-inflammatory response of adipose tissue and raise FFA release into circulation (23,24). The increase of FFA and pro-inflammatory cytokines in circulation may increase the fat accumulation in skeletal muscle and liver which may lead to insulin resistance and related cardiometabolic abnormalities (23,24). Especially VAT is associated with increased cytokine production and FFA release into circulation. In the present study, we included inflammatory cytokines in order to elucidate whether SAD was really, a better predictor of adverse metabolic cytokine production associated with increased VAT. We did not find that SAD and WC were differentially associated with inflammatory markers and thus cannot shed any light on whether this could explain the before mentioned superior predictive ability of SAD on top of established risk markers.

The discrepancies in results between studies might also be because of age, ethnicity, sex, phenotype or methodological differences. One of the methodological differences that might lead to discrepancies in the results is the choice measurement sites and the optimal point of measuring SAD is still debated (3). We used the highest point of the abdomen, which differ from the protocol described in the US National Health and Nutrition Examination Survey (NHANES). This might result in lower correlation with cardiometabolic measures (3,25,26) and could prevent us from observing differences between SAD and WC. However, if minor differences in measurement point can affect the associations drastically, its clinical utility may be limited. Furthermore, it has been argued that assessment of WC requires less tools and is more practical compared to SAD, which might limit the use of SAD as a clinical screening tool. However, similarly to others(2) we find that difference is negligible. SAD has also shown to have a high intraclass correlation in both lean and obese individuals, while the intraclass correlation was lower in obese compared to lean individuals when measuring WC (27). This could indicate that SAD is more reliable when measuring individuals of different weight categories and that SAD is better than WC in individuals with high

amounts of abdominal fat, especially SAT. SAD may therefore be more reliable when measuring individuals of different weight categories with low variation and might also be less sensitive to the investigator performing the measurement compared to WC.

One limitation of the present study is the cross-sectional design using biomarkers which is a weaker design compared to studies with a prospective design and hard endpoints such as T2D, CVD and mortality. Such studies are highly warranted. Furthermore, the present study used individuals, which were primarily overweight and obese (98%), whereas other studies that used both normal weight and overweight individuals (7,8). This limits our generalizability to normal weight populations. However, our study used a clinically relevant population group, which are at risk of developing T2D and CVD, and thus a clear relevance for establishing a highly predictable anthropometric measure. The current study has measured many different cardiometabolic outcomes including markers of insulin resistance, dyslipidemia, low grade inflammation and blood pressure. As previous studies have not included all these markers, this study provides a good view of overall cardiometabolic health. Furthermore, the sample size in the present study is appropriate to examine the research questions posed.

Conclusions

In conclusion, the data from 6 cohorts of high-risk individuals showed that neither SAD, WC nor BMI seems to be superior as an indicator of an adverse metabolic phenotype or in their ability to identify individuals with metabolic syndrome markers above the IDF cut-offs regardsless of sex and BMI category. Thus choosing the most practical anthropometric measure might be the best solution from a public health perspective.

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Author contributions

MVL, MK, AA, TML, CR and GM were involved in conception and design of the study. MVL, LK, SV, SKK, OP, LL, TML, WS, AA and MK were involved in the collection of data and biological samples. CR, GM and MVL did the statistical analysis. MVL and GM drafted the

manuscript. All authors were involved in the interpretation of the data and all authors read, revised and approved the final manuscript.

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Table 1 Characteristics of the participants at baseline (n = 1516)

Variables	n	3G	n	SHOPUS	n	DIOGENES	n	RIGHT	n	MNG	n	PROKA	n	Across studies
Age (years)	117	48.70 ± 11.25^{a}	181	42.10 ± 13.08^{b}	902	41.14 ± 6.26^{b,c}	73	50.85 ± 9.26^{c}	29	43.97 ± 11.53^{a,b}	214	40.03 ± 10.68^{b}	1516	42.20 ± 9.17
Men % (M/F)	117	39.3 (46/71)^{a}	181	31.0 (53/128)^{a}	902	33.4 (301/601)^{a,b}	73	43.8 (32/41)^{b}	29	28.0 (8/21)^{a}	214	39.5 (45/169)^{a}	1516	32.0 (485/1031)
Weight (kg)	117	85.9 ± 13.0^{a}	181	89.9± 17.1^{a}	902	99.6 ± 17.4^{b}	73	83.5 ± 9.1^{a}	29	88.0 ± 13.7^{a}	214	96.6 ± 13.6^{b}	1516	96.0 ± 17.0
Sagittal abdominal diameter (cm)	117	22.9 ± 2.9^{c,d}	181	23.0 ± 3.2^{c}	902	25.2 ± 3.8^{a}	73	21.5 ± 2.1^{d}	29	22.0 ± 2.5^{c,d}	214	24.0 ± 2.5^{b}	1516	24.4 ± 3.6
Waist circumference (cm)	117	100.0 ± 9.0^{b,c}	181	100.1 ± 12.4^{b,c}	902	107.5 ± 13.0^{a}	73	96.0 ± 8.0^{c}	29	96.5 ± 8.8^{c}	214	103.2 ± 10.6^{b}	1516	104.70 ± 12.60
Body-mass index (kg/m^{2})	117	28.7 ± 3.5^{a}	181	30.3 ± 4.9^{c}	902	34.5 ± 4.8^{b}	73	27.8 ± 1.9^{a}	29	30.1± 3.1^{a,c}	214	33.2 ± 3.3^{d}	1516	33.0 ± 5.0
Smoking, % (no/yes)	117	7 (109/8)^{a}	181	22 (136/39)^{b}	851	28 (616/235)^{b}	73	0 (73/0)^{b}	29	0 (29/0)^{a}	214	0 (214/0)^{c}	1459	19 (1177/282)
Fasting insulin (pmol/L)	114	65.0 ± 32.1^{a}	181	75.4 ± 45.3	799	83.4 ± 72.1^{b}	73	74.2 ± 39.4	28	43.6 ± 30.3^{a}	210	74.6 ± 44.5	1405	78.3 ± 61.2
Fasting glucose (mmol/L)	117	5.7 ± 0.6^{c}	181	5.3 ± 0.5^{b}	817	5.0 ± 0.7^{a}	73	5.9 ± 0.6^{c}	28	5.5 ± 0.4^{b}	210	5.7 ± 0.7^{c}	1426	5.3 ± 0.7
2-h glucose (mmol/L)		-	181	5.6 ± 1.4^{a}	794	6.7 ± 2.2^{b}		-		-		-	975	6.5 ± 2.1
HOMA-IR	114	2.4 ± 1.3^{b,c}	181	2.5 ± 1.6^{c}	798	3.2 ± 2.9^{a}	73	2.8 ± 1.6^{a,c}	28	1.0 ± 0.7^{b}	210	1.9 ± 1.4^{b,c}	1404	2.8 ± 2.4
Matsuda index		-	180	5.7 ± 3.0^{a}	783	5.3 ± 3.3^{b}		-		-		-	963	5.4 ± 3.2
TNF-α (pg/mL)	117	1.8 ± 2.2^{a}	181	1.2 ± 2.2^{b}		-		-		-		-	298	1.4 ± 2.2
IL-6 (pg/mL)	116	1.7 ± 1.6^{a}	180	1.3 ± 0.9^{b}		-	73	2.1 ± 1.6^{c}		-		-	369	1.6 ± 1.3
CRP (mg/L)	117	1.5 ± 1.8^{a}	181	2.6 ± 2.3^{c}	744	3.3 ± 2.3^{d}	72	1.8 ± 1.6^{a,c}	26	2.0 ± 2.0^{a,c}		-	1113	2.9 ± 2.3
Adiponectin (µg/mL)		-		-	832	9.1 ± 4.3		-		-		-	832	9.1 ± 4.3
Total cholesterol (mmol/L)	117	5.3 ± 1.0^{c}	180	4.6 ± 0.9^{b}	832	4.9 ±1.0^{a}	73	5.2 ± 0.9^{a,c}	28	5.0 ± 0.9	210	5.3 ± 0.9^{c}	1440	5.0 ± 1.0
HDL cholesterol (mmol/L)	117	1.3 ± 0.3^{b}	180	1.2 ± 0.3^{a}	834	1.2 ± 0.3^{a}	73	1.4 ± 0.3^{b}	28	1.4 ± 0.4^{b}	210	1.4 ± 0.4^{b}	1442	1.2 ± 0.3
LDL cholesterol (mmol/L)	117	3.1 ± 0.7	180	3.0 ± 0.8	828	3.1 ± 0.9	73	3.3 ± 0.8	28	3.1 ± 0.9	210	3.2 ± 0.8	1430	3.1 ± 0.8
Triglycerides (mmol/L)	117	1.3 ± 0.6^{b,c}	180	1.2 ± 0.6^{b}	822	1.4 ± 0.7^{c}	73	1.2 ± 0.6^{b}	28	2.8 ± 1.1^{a}	210	1.4 ± 0.8^{c}	1430	1.4 ± 0.7
FFA (mmol/L)	117	0.48 ± 0.16^{a}	159	-	735	0.65 ± 0.32^{b}		-		-	211	0.46 ± 0.16^{c}	1063	0.6 ± 03
Systolic blood pressure (mmHg)	117	129 ± 13^{a}	181	122 ± 14^{b}	885	125 ± 15^{a,b}	73	129 ± 17^{a}	29	120 ± 15^{b,c}	214	118 ± 11^{c}	1499	124.0 ± 14.5
Diastolic blood pressure (mmHg)	117	81 ± 9^{a}	181	81 ± 10^{a}	885	77 ± 11^{b}	73	85 ± 12^{a}	29	78 ± 10^{b,c}	214	76 ± 9^{c}	1499	78.3 ± 10.8

Data shown as mean ± SD. ^{a,b,c} Values with different superscripts letters indicate statistically significant differences between studies, assessed by analysis of variance or chi-square tests, $p<.05$. Abbreviations: CRP, C-reactive protein; FFA, Free fatty acids; HOMA-IR, Homeostatic model assessment for insulin resistance; IL-6, Interleukin 6, TNF- α, Tumor necrosis factor alpha.

Table 2 Associations between SAD, WC, BMI and markers of cardiometabolic health

	n	SAD (cm)			WC (cm)			BMI (kg/m2)		
		Slope (CI)	*p*-value	R^2	Slope (CI)	*p*-value	R^2	Slope (CI)	*p*-value	R^2
Fasting insulin (pmol/L)										
Unadjusted	1405	14.6 (12.7, 16.5)	<0.001	0.139	16.8 (14.9, 18.7)	<0.001	0.180	15.0 (11.1, 14.9)	<0.001	0.110
Adjusted	1354	14.7 (12.5, 16.9)	<0.001	0.173	17.7 (15.5, 19.9)	<0.001	0.213	14.8 (12.6, 17.0)	<0.001	0.173
Fasting glucose (mmol/L)										
Unadjusted	1426	0.04 (0.007, 0.1)	0.019	0.004	0.1 (0.1, 0.1)	<0.001	0.014	-0.02 (-0.1, 0.01)	0.180	0.001
Adjusted	1376	0.09 (0.06, 0.1)	<0.001	0.252	0.1 (0.1, 0.2)	<0.001	0.263	0.1 (0.1, 0.1)	<0.001	0.256
2-h glucose (mmol/L)										
Unadjusted	975	0.3 (0.2, 0.4)	<0.001	0.023	0.2 (0.1, 0.3)	<0.001	0.016	0.3 (0.2, 0.4)	<0.001	0.026
Adjusted	925	0.3 (0.2, 0.4)	<0.001	0.083	0.2 (0.1, 0.4)	<0.001	0.077	0.2 (0.1, 0.4)	<0.001	0.077
HOMA-IR										
Unadjusted	1404	0.6 (0.5, 0.7)	<0.001	0.151	0.7 (0.6, 0.8)	<0.001	0.198	0.5 (0.4, 0.6)	<0.001	0.110
Adjusted	1353	0.5 (0.5, 0.6)	<0.001	0.247	0.7 (0.6, 0.7)	<0.001	0.285	0.6 (0.5, 0.6)	<0.001	0.248
Matsuda index										
Unadjusted	963	-0.9 (1.1, -0.8)	<0.001	0.121	-1.1 (-1.3, -1.0)	<0.001	0.181	-0.8 (-0.9, -0.6)	<0.001	0.081
Adjusted	913	-0.8 (-1.01, -0.7)	<0.001	0.140	-1.1 (-1.3, -0.9)	<0.001	0.191	-0.8 (-1.0, -0.6)	<0.001	0.137
TNF-α (pg/mL)										
Unadjusted	298	0.1 (0.001, 0.2)	0.047	0.013	0.1 (0.001, 0.2)	0.048	0.013	0.1 (-0.02, 0.1)	0.123	0.008
Adjusted	292	0.1 (-0.002, 0.2)	0.043	0.221	0.1 (-0.002, 0.2)	0.056	0.220	0.1 (0.04, 0.2)	0.003	0.233
IL-6 (pg/mL)										
Unadjusted	369	0.2 (0.1, 0.3)	<0.001	0.048	0.2 (0.1, 0.3)	<0.001	0.036	0.2 (0.1, 0.3)	<0.001	0.054
Adjusted	364	0.3 (0.2, 0.4)	<0.001	0.237	0.3 (0.2, 0.4)	<0.001	0.217	0.3 (0.2, 0.4)	<0.001	0.247
CRP (mg/L)										
Unadjusted	1087	0.8 (0.7, 1.0) [a]	<0.001	0.093	0.8 (0.6, 0.9) [a]	<0.001	0.126	1.3 (1.1, 1.4) [b]	<0.001	0.178
Adjusted	1039	0.8 (0.6, 1.0)	<0.001	0.191	0.9 (0.7, 1.0)	<0.001	0.205	0.9 (0.8, 1.1)	<0.001	0.221
Adiponectin (µg/mL)										
Unadjusted	832	-0.7 (-0.9, -0.4) [a]	<0.001	0.027	-0.9 (-1.1, -0.6) [a]	0.001	0.043	-0.3 (-0.6, 0.1) [b]	0.098	0.003
Adjusted	787	-0.3(-0.6, -0.1)	0.017	0.092	-0.5 (-0.8, -0.2)	0.001	0.099	-0.2 (-0.5, 0.1)	0.142	0.072
Total cholesterol (mmol/L)										
Unadjusted	1440	0.1 (0.04, 0.1)	<0.001	0.009	0.1 (-0.003, 0.1)	0.066	0.002	0.03 (-0.03, 0.1)	0.323	0.001
Adjusted	1389	0.1 (0.04, 0.2)	<0.001	0.097	0.04 (-0.02, 0.1)	0.127	0.090	0.04 (-0.01, 0.1)	0.139	0.091
HDL cholesterol (mmol/L)										
Unadjusted	1442	-0.09 (-0.1, -0.1)	<0.001	0.066	-0.1 (-0.1, -0.1)	<0.001	0.111	-0.1 (-0.1, -0.04)	<0.001	0.030
Adjusted	1391	-0.04 (-0.1, -0.03)	<0.001	0.216	-0.1 (-0.1, -0.1)	<0.001	0.237	-0.1 (-0.1, -0.03)	<0.001	0.221
LDL cholesterol (mmol/L)										

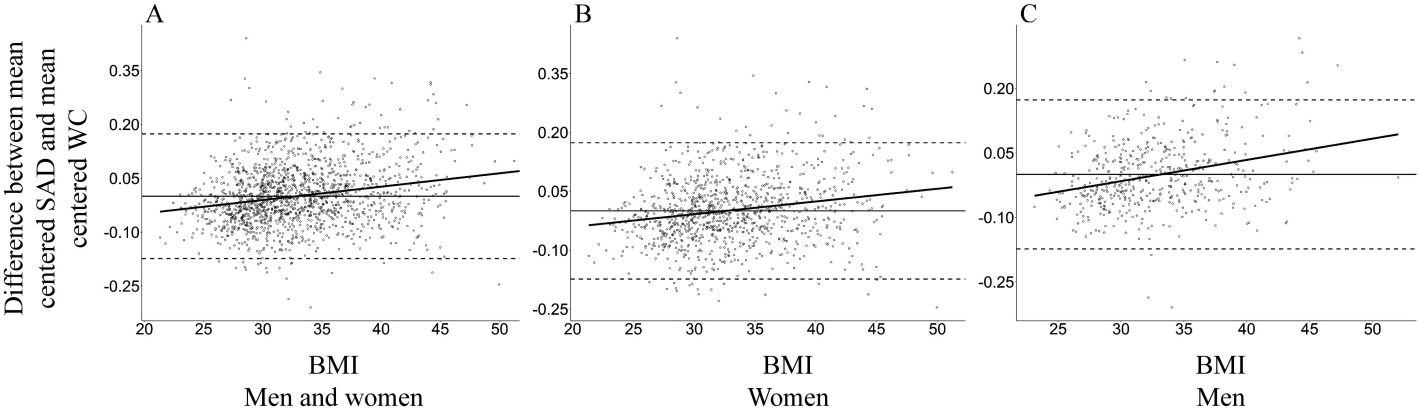
Unadjusted	1436	0.1 (0.1, 0.2)	<0.001	0.018	0.09 (0.1, 0.1)	<0.001	0.012	0.06 (0.01, 0.1)	0.014	0.004
Adjusted	1386	0.1 (0.1, 0.1)	<0.001	0.064	0.07 (0.02, 0.1)	0.003	0.058	0.06 (0.01, 0.1)	0.015	0.058
Triglycerides (mmol/L)										
Unadjusted	1430	0.2 (0.1, 0.2)	<0.001	0.072	0.1 (0.2, 0.2)	<0.001	0.061	0.1 (0.1, 0.1)	<0.001	0.024
Adjusted	1380	0.1 (0.1, 0.2)	<0.001	0.185	0.1 (0.1, 0.1)	<0.001	0.173	0.1 (0.1, 0.1)	<0.001	0.166
FFA (mmol/L)										
Unadjusted	1063	0.03 (0.02, 0.04)	<0.001	0.018	0.01 (0.00, 0.03)	0.058	0.003	0.5 (0.04, 0.07)	<0.001	0.048
Adjusted	1022	0.04 (0.02, 0.05)	<0.001	0.203	0.04 (0.02, 0.05)	<0.001	0.189	0.04 (0.02, 0.05)	<0.001	0.199
Systolic blood pressure (mmHg)										
Unadjusted	1499	3.8 (3.1, 4.5) [a]	<0.001	0.072	3.9 (3.2, 4.6) [a]	<0.001	0.073	1.9 (1.3, 2.6) [b]	<0.001	0.017
Adjusted	1445	2.9 (2.2, 3.6)	<0.001	0.209	2.5 (1.7, 3.2)	<0.001	0.199	2.6 (1.9, 3.4)	<0.001	0.203
Diastolic blood pressure (mmHg)										
Unadjusted	1499	2.8 (2.8, 3.3) [a]	<0.001	0.068	2.1 (1.6, 2.6) [a]	<0.001	0.038	0.9 (0.4, 1.4) [b]	<0.001	0.007
Adjusted	1445	3.5 (2.9, 4.0)	<0.001	0.188	2.4 (1.8, 3.0)	<0.001	0.142	2.3 (1.8, 2.9)	<0.001	0.143

Data shown as estimated slope and confidence interval (CI) from multiple linear regression models. The adjusted models included age, gender, smoking and study.[a,b] Values with different superscripts letters indicate statistically significant differences between studies assessed by chi-squared test, $p < 0.05$. Abbreviations: CRP, C-reactive protein; FFA, Free fatty acids; HOMA-IR, Homeostatic model assessment for insulin resistance; IL-6, Interleukin 6; SAD, sagittal abdominal diameter; TNF- α, Tumor necrosis factor alpha; WC, waist circumference.

Table 3 SAD, WC, and BMI as identifiers of individuals with metabolic syndrome markers above the IDF cut-offs measured as area under the receiver operating characteristics curve (AUROC) (n=1516).

	SAD (cm)	**WC** (cm)	**BMI** (kg/m^2)
Glucose (>5.6 mmol/L)			
Unadjusted	0.53 (0.50, 0.57)	0.56 (0.52, 0.59)	0.53 (0.50, 0.56)
Adjusted	0.79 (0.77, 0.82)	0.80 (0.77, 0.83)	0.80 (0.77, 0.82)
Glucose (>6.1 mmol/L)			
Unadjusted	0.60 (0.55, 0.64)[a,b]	0.61 (0.57, 0.65)[a]	0.52 (0.47, 0.56)[b]
Adjusted	0.78 (0.74, 0.82)	0.78 (0.75, 0.82)	0.78 (0.74, 0.82)
Triglycerides (>1.7 mmol/L)			
Unadjusted	0.63 (0.60, 0.67)[a]	0.62 (0.58, 0.65)[a,b]	0.56 (0.52, 0.59)[b]
Adjusted	0.72 (0.69, 0.76)	0.71 (0.68, 0.74)	0.71 (0.67, 0.74)
HDL cholesterol (< 1.03 (men) or <1.29 (women) mmol/L)			
Unadjusted	0.59 (0.56, 0.62)	0.60 (0.57, 0.63)	0.58 (0.55, 0.61)
Adjusted	0.65 (0.62, 0.68)	0.66 (0.63, 0.69)	0.64 (0.61, 0.67)
Systolic blood pressure (> 130 mmHg)			
Unadjusted	0.63 (0.60, 0.66)[a]	0.62 (0.59, 0.65)[a]	0.55 (0.52, 0.58)[b]
Adjusted	0.74 (0.72, 0.77)	0.73 (0.71, 0.76)	0.73 (0.71, 0.76)
Diastolic blood pressure (>85 mmHg)			
Unadjusted	0.62 (0.59, 0.65)[a]	0.59 (0.56, 0.62)[a,b]	0.53 (0.50, 0.57)[b]
Adjusted	0.72 (0.69, 0.76)	0.70 (0.67, 0.73)	0.70 (0.67, 0.73)

Data shown as estimated AUROC and 95% confidence interval using logistic regression models. The adjusted models included age, gender, smoking and study. Values with different superscripts letters indicate statistically significant differences between anthropometric measurements assessed by overlapping confidence intervals.


A
B
C
Difference between mean centered SAD and mean centered WC
0.35
0.20
0.05
-0.10
-0.25
20
25
30
35
40
45
50
BMI
Men and women
Women
Men