Design and validation of a novel estimator of visceral adipose tissue area and comparison to existing adiposity surrogates

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Abstract

Aims: Visceral adiposity measured by computed tomography (CT) as intra-abdominal fat area (IAFA) predicts metabolic diseases. Existing adiposity surrogates have not been systematically compared to a regression-based model derived in individuals of Japanese ancestry. We developed and validated a method to estimate IAFA in individuals of Japanese ancestry and compared it to existing adiposity surrogates.

Methods: We assessed age, BMI, waist circumference (WC), fasting lipids, glucose, smoking status, grip strength, mid-thigh circumference (MTC), humeral length, leg length, and IAFA by single-slice CT at the umbilicus for 622 Japanese Americans. We used stepwise linear regression to predict IAFA and termed the predicted value the Estimate of Visceral Adipose Tissue Area (EVA). For men, the final model included age, BMI, WC, high-density lipoprotein cholesterol (HDLc), glucose, and MTC; for women, age, BMI, WC, HDLc, low-density lipoprotein cholesterol, glucose, and MTC. We compared goodness-of-fit (R^2) from linear regression models and mean-squared errors (MSE) from k-fold cross-validation to compare the ability of EVA to estimate IAFA compared to an estimate by Despres et al., waist-to-height ratio, WC, deep

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abdominal adipose tissue index, BMI, lipid accumulation product, and visceral adiposity index (VAI). We classified low/high IAFA using area under receiver-operating characteristic curves (AUROC) for IAFA dichotomized at the 75th percentile.

Results: EVA gave the least MSE and greatest R^2 (men: 1244, 0.61; women: 581, 0.72). VAI gave the greatest MSE and smallest R^2 (mean 2888, 0.08; women 1734, 0.14).

Conclusions: EVA better predicts IAFA in Japanese-American men and women compared to existing surrogates for adiposity.

Keywords

visceral adiposity; body mass index; waist-to-height ratio; abdominal obesity; waist circumference; anthropometrics

1. INTRODUCTION

Excess visceral adipose tissue, quantified as intra-abdominal fat area (IAFA), is a major risk factor for metabolic disease in Japanese Americans[1-6]. Surrogate measures of visceral adiposity derived from anthropometric measures including body mass index (BMI) and waist circumference (WC) are routinely used[7] in both clinical practice and epidemiologic research, as direct measurement of IAFA is often prohibitively expensive or logistically difficult to obtain. Measures incorporating blood-based biomarkers have also been used to estimate IAFA, including the Lipid Accumulation Product[8] and the Visceral Adiposity Index[9].

When compared to White populations, Asians have more visceral fat[10,11] and a higher body fat percentage for a given BMI[12]. Adiposity surrogates derived in non-Asian populations might therefore perform poorly when applied to Japanese, Japanese-American, and other Asian populations[10]. We therefore examined whether an alternate adiposity surrogate might more closely parallel the quantity of IAFA among individuals of Japanese ancestry. We hypothesized that an adiposity surrogate incorporating widely available demographic information, anthropometric data, and blood-based biomarkers could predict computed tomography (CT)-measured IAFA better in Japanese Americans better than existing visceral adiposity surrogates. These include anthropometric measures such as BMI, WC, and WHtR; indices experimentally derived from clinical and anthropometric measurements such as the Deep Abdominal Adipose-Tissue index[13] and an index calculated by Després[14]; and indices derived from clinical, anthropometric and blood-based measurements such as the Visceral Adiposity Index[9] and the Lipid Accumulation Product[8].

2. MATERIALS/SUBJECTS & METHODS

2.1. Study design and setting

We measured demographic, metabolic and body composition variables in 622 Japanese-American men and women from the Japanese-American Community Diabetes Study (JACDS), a community-based cohort of second- and third-generation Japanese Americans of 100% Japanese ancestry who lived in King County, Washington State. These individuals

were representative of Japanese-American residents of the county in age, residential distribution and parental immigration pattern. JACDS was initially designed to investigate risk factors for and prevalence of type 2 diabetes among Japanese Americans. Individuals were recruited between 1983 and 1991. Selection and recruitment have been described previously[15]. Of an initial sample of 658 individuals, 36 were missing data on covariates, leaving an analytic sample of 622 participants. The study was approved by the University of Washington Human Subjects Division, and all participants provided written informed consent.

2.2. Data collection

Evaluations were done at the General Clinical Research Center at the University of Washington, Seattle. Information on age, sex, and current and former tobacco use was obtained by interview. Trained staff measured height, weight and WC. Weight was measured using a digital scale after shoes and outer clothing were removed. BMI was defined as weight in kg divided by height in meters squared. WC was measured twice using a flexible but non-stretchable tape measure and averaged. In male participants, the measurement was obtained at the midpoint between the iliac crest and the inferior border of the lowest rib. In female participants, the minimal circumference between iliac crest and lowest rib was used. WHtR was defined as waist circumference in cm divided by height in cm. Serum glucose, triglycerides (TG), high-density lipoprotein cholesterol (HDLc) and low-density lipoprotein cholesterol (LDLc) were measured in specimens taken after at least a 10-hour fast.

For comparison to our new index, we chose seven existing measures that have been used as IAFA surrogates. Measures included BMI, WC, and WHtR; indices experimentally derived from clinical and anthropometric measurements such as the Deep-Abdominal Adipose Tissue index[13] and an index calculated by Després[14]; and indices derived from clinical, anthropometric and blood-based measurements such as the Visceral Adiposity Index[9] and the Lipid Accumulation Product[8]. We calculated sex-specific values of each index for all participants. The Deep-Abdominal Adipose Tissue index was defined as $-382.9 + [1.09 \times$ weight (kg)] $+ [6.04 \times$ WC (cm)] $+ (-2.29 \times$ BMI) for men, and $-278 + [-0.86 \times$ weight (kg)] $+ [5.19 \times$ WC (cm)] for women[13]. The Després index was defined as $-225.39 + 2.125 \times$ age (years) $+ 2.843 \times$ WC (cm)[14]. Because the Després index was derived in a male cohort, we restricted the analysis of this index to the men in our dataset. The Visceral Adiposity Index was defined as {WC (cm)/(39.68 + [1.88 × BMI (kg/m2)]} × (triglycerides/1.03) × (1.31/HDL) for men, and {WC (cm)/(36.58 + [1.89 × BMI (kg/m2)]} × (triglycerides/0.81) × (1.52/HDL) for women[9], with both triglycerides and HDL specified in mmol/L. The Lipid Accumulation Product was defined as [(WC (cm) − 65) × TG (mmol/L)] in men, and [(WC (cm) − 58) × TG (mmol/L)] in women[8].

To estimate IAFA, single (1cm) CT-scan slices were obtained at the level of the umbilicus. Scans were analyzed for cross-sectional area of fat using automated density contour software. Areas corresponding to a density of −250 to −50 Hounsfield units were classified as adipose tissue[16]. IAFA was defined as fat within the confines of the transversalis fascia and reported in cm^2. Intra-observer variability for multiple measurements by a single observer of a single CT scan ranged from 0.2% to 1.4%.

2.3. Statistical analysis

We used number (%) and mean (standard deviation) for categorical and normally distributed continuous variables, respectively, to describe study population characteristics, both overall and stratified by sex. For TG, we reported median (inter-quartile range), as the distribution was skewed. To derive a novel adiposity estimate, we used backward stepwise linear regression to fit models using easy-to-obtain demographic, anthropometric, and blood-based measurements (age, BMI, WC, HDLc, LDLc, TG, fasting glucose, and smoking status) to predict IAFA. A p-value 0.05 allowed entry into the model, while a p-value of 0.1 or greater prompted removal. Because there was evidence of a multiplicative first-order interaction of sex with WC, we chose to perform analyses stratified by sex. We fit linear regression models looking for evidence of nonlinearity in associations of metabolic variables and body composition with IAFA using the Stata command *mfp.* We also performed model diagnostics to identify influential outliers and for evidence of violations of model assumptions[17]. We termed the new index the Estimate of Visceral Adipose Tissue Area (EVA). We dichotomized IAFA at the 75th percentile values and plotted receiver-operating characteristic (ROC) curves to estimate ability of EVA to categorize IAFA as below or above the 75th percentile.

We compared performance of EVA to the seven previously described adiposity surrogates. Because mid-thigh circumference may be assessed less frequently than the other anthropometric measures that were collected, we also compared performance of EVA to a version of our model that did not include mid-thigh circumference, which we called EVA-R (reduced). We regressed IAFA on each adiposity surrogate in a univariate linear regression model. We compared R^2 values among the models and identified the model with the lowest Akaike Information Criterion (AIC). We validated results internally using k-fold cross-validation to compare mean-squared errors (MSE)[18]. For these analyses, data were partitioned into five subsamples repeatedly. Four sub-samples were combined as the training dataset and the last was left out as a validation dataset. Prediction errors (mean squared errors) were obtained on the left-out group. For each round this was repeated with each of the sub-samples used as the validation dataset. This was repeated 500 times. Errors were averaged, and 95% confidence intervals were calculated. Lastly, we compared performance of the seven visceral adiposity surrogates to EVA in discriminating low vs. high categories of IAFA. We used sex-specific 75th percentile cutpoints taken from the training dataset for all analyses (140 cm^2 [men] and 100cm^2 [women]). We compared the area under the ROC curves (AUROC) using chi-squared tests[19].

For AUROC comparisons, a p-value of <0.05 was considered statistically significant. MSE with non-overlapping 95% confidence intervals were considered statistically significantly different. Analyses were performed with Stata (version 15.0; StataCorp, College Station, TX).

3. RESULTS

Table 1 shows participant characteristics overall and stratified by sex. Coefficients and p-values from sex-specific linear regression models testing associations of metabolic risk factors with IAFA in the derivation cohort are shown in Table 2. All the variables shown in

Table 1 with the exception of IAFA and diabetes status were considered in the multivariable models described in Table 2. Using the stepwise methods described above, LDLc, triglycerides, smoking status, grip strength, humeral length and leg length were dropped from the model in men, leaving age, BMI, WC, HDLc, fasting glucose and mid-thigh circumference. In the model for women, triglycerides, smoking status, grip strength, humeral length, and leg length were dropped from the model, leaving age, BMI, WC, HDLc, LDLc, fasting glucose, and mid-thigh circumference. A test of regression assumptions found that for the model in women, the linear form of IAFA violated regression assumptions, while the square root transformation did not; however, nearly identical results were obtained with either the linear or square root transformation of IAFA as the dependent variable, so the linear version was used to permit easier interpretation of our findings. An examination of best fitting transformations of the independent variables using *mfp* revealed that the best fit was obtained with the linear versions of these covariates as shown in Table 2. Model diagnostics did not identify influential outliers, and there was no further evidence of violations of model assumptions. Sex-specific scatter plots of IAFA vs. fitted values of EVA for men and women are presented in Figure 1.In sensitivity analyses, we replaced BMI with height and weight as separate terms and BMI and waist circumference with weight and WHtR in our primary models. We also performed analyses including fasting insulin level as a covariate. The performance characteristics of the models obtained did not differ substantially from the primary models. Results comparing R^2 and AIC for linear regression models, MSE from k-fold cross-validation, and AUROC for prediction of IAFA above the 75th percentile comparing existing adiposity surrogates to EVA in prediction of IAFA are shown in Table 3. EVA exhibited the highest R^2 and lowest AIC in multiple regression models with continuous IAFA as the dependent variable for both sexes. It had significantly lower MSE for both men and women than all other models compared. For men, the AUROC for EVA in discriminating IAFA above the 75th percentile was significantly higher than all other measures compared, with the exception of the Després estimate (p=0.091). For women, the AUROC for EVA in discriminating IAFA above the 75th percentile was significantly higher than all other measures compared, with the exception of the EVA-R (p=0.771). In a "partial validation," we validated our limited model (the EVA-R) in a cohort of Japanese participants (n=1033 men, n=612 women), but we were unable to validate the full model because the validation cohort did not have measurements of mid-thigh circumference available. R^2 and AUROC were similar in the validation cohort. (Details of the methods and results for the partial validation are available in Supplementary Online Methods and Supplementary Table 1).

4. DISCUSSION

We have developed and internally validated a novel adiposity surrogate, the Estimate of Visceral Adipose Tissue Area, to predict visceral adiposity in a Japanese-American cohort of men and women, and demonstrated that it performed better than existing adiposity surrogates incorporating clinical, anthropometric and laboratory measurements in this population. It relies on readily available clinical and laboratory measurements and can easily be calculated for men and women using the regression coefficients and constants in Table 2.

Whether EVA would be similarly accurate in other Asian and non-Asian populations is not known but possible and should be the subject of future research.

In this analysis, we compared anthropometric measures and indices that did and did not incorporate blood-based biomarkers in estimation of IAFA. The anthropometric measures and indices that did not incorporate blood-based biomarkers were the Despres index, WHtR, WC, the Deep-Abdominal Adipose Tissue index, and BMI. To our knowledge, discriminative ability of the Despres index and the Deep-Abdominal Adipose Tissue index for CT- or MRI-measured IAFA have not been previously validated in external cohorts. The ability of WHtR, WC, and BMI to estimate IAFA has been studied extensively, and trends in our results are generally consistent with previous studies[20,21]. In analyses stratified by both sex and age 60 years, Roriz et al. calculated AUROCs for WHtR in discrimination of IAFA $>130cm^2$ in a Latino sample[20] that were higher (0.90-0.91) than our AUROC for men and lower (0.81-0.87) than our AUROC for women, although the differences were not large. These discrepancies may be due to the different cutpoints that were chosen for high vs. low IAFA in the two analyses, especially among women, where their cutpoint was substantially higher (130 cm^2 vs. 100 cm^2).

Mid-thigh circumference was included in the model for men and women. In comparisons of models without and without mid-thigh circumference (EVA vs. EVA-R), MSE were lower in models including mid-thigh circumference for both men and women. The AUROC for EVA vs. EVA-R was significantly better for men (p=0.013) but not women (p=0.771). Despite this, both performed well in comparison to other measures tested; therefore, in datasets where mid-thigh circumference is not available, we believe use of the EVA-R could be considered. Regression equations for both versions are provided in Table 3. Unlike mid-thigh circumference, the other anthropometrics we tested (grip strength, humeral length, and leg length) did not meet criteria for inclusion. These results are consistent with previous analyses in this dataset. Mid-thigh circumference has previously been associated with lower odds of incident diabetes independent of age, sex and body fat depots, but mid-thigh subcutaneous fat area was not, suggesting that thigh muscle mass and not fat is the key component underlying the metabolic associations with thigh circumference [22]. Weaker grip strength is positively associated with diabetes only among the leanest individuals in this cohort[23].

The addition of blood-based biomarkers might be expected to improve model fit, given the associations between IAFA and multiple metabolic measurements[4-6]. We evaluated two existing indices that included blood-based biomarkers: the Lipid Accumulation Product and the Visceral Adiposity Index. Both performed relatively poorly in estimation of IAFA in our cohort. It is important to note that neither index was designed for this purpose, although both have been used as surrogates for IAFA[24,25]. In previous studies, the association of both the Lipid Accumulation Product and the Visceral Adiposity Index with IAFA are variable[20,21,26,27], but different analytic methods make direct comparisons somewhat difficult. In their Latino sample, Roriz et al. calculated AUROC for the Lipid Accumulation Product and the Visceral Adiposity Index that were quantitatively similar to the AUROC we obtained for these surrogates: Lipid Accumulation Product 0.81-0.88 in men and 0.78-0.80 in women; Visceral Adiposity Index 0.73-0.83 in men and 0.65-0.71 in women[20]. In an

Australian study of 39 men and women with nonalcoholic fatty liver disease, Visceral Adiposity Index was modestly correlated with IAFA on MRI (r=0.39) [21]. In our Japanese-American population, the correlation of Visceral Adiposity Index with IAFA was 0.29 for men and 0.38 for women. In a study of 99 overweight post-menopausal Canadian women enrolled in a weight reduction randomized controlled trial, baseline Visceral Adiposity Index was less well correlated with CT-measured IAFA than it was among the Japanese-American women in our dataset (r=0.28)[27]. A ROC analysis of the ability of the Visceral Adiposity Index to classify these study participants into the lowest or highest tertile of CT-measured IAFA demonstrated an AUROC of 0.61 that was of significantly lower magnitude than the AUROCs for BMI (0.84) or WC (0.86)[27]. In a study of 180 premenopausal Korean women with polycystic ovary syndrome, the Visceral Adiposity Index displayed an AUROC of 0.88 in the prediction of CT-measured VAT >100 cm[26], which was considerably greater than corresponding values in our cohort, or in the analysis by Roriz et al. Notably, the Korean cohort had a relatively narrow age range.

The relatively poor performance of the Lipid Accumulation Product and the Visceral Adiposity Index in our cohort, as well as the better performance of Visceral Adiposity Index in a cohort of younger female Koreans with a relatively narrow age range may be explained by a single unifying phenomenon. In our analysis, the two measures with the best overall performance characteristics (EVA and the Després estimate) both include age as a covariate, suggesting a potential mechanism for some of the underlying differences in the relative performance of these measures. In 1991, Després et al. used all-possible-regressions selection methods to arrive at an adiposity surrogate to predict IAFA in men that incorporated age and WC[14]. Similarly, in an analysis that used stepwise regression to generate sex- and race-stratified equations for IAFA prediction in Europeans, South Asians and African Caribbeans, age was included in the models that were derived for every population group[28]. Older age is a recognized determinant of visceral adiposity[29], potentially due to metabolic changes in visceral fat depots[30]. A prospective study of this Japanese-American population demonstrated that weight gain at older ages was more likely to accumulate fat in the visceral depot[31]. Age may therefore be a key feature associated with visceral fat deposition, which merits consideration for inclusion in surrogate measures of this depot. The other adiposity surrogates that we tested did not directly account for age.

This study has several strengths. Chief among them, we used a cohort of Japanese-American participants with well-characterized measurements of anthropometric and metabolic features. Secondly, the novel index that we developed was validated using robust statistical methods. Lastly, the small number of readily available covariates that were used in the model allows generalizability to external datasets and routine clinical use. There are also some limitations. First, measurements of IAFA were derived from single CT-scan slices; however, although the strength of the relationship varies somewhat depending on the location of the CT slice[32], a high correlation has been demonstrated between a single CT slice and direct measurement of visceral fat volume, which limits the potential for bias[33]. We did not assess the contribution of menopausal status on IAFA in women. In addition, the performance characteristics of EVA in non-Asian populations is unknown and requires further study. Lastly, we were not able to validate the full model in an external dataset. We did validate the EVA-R in an external cohort. In addition, to validate the full model, we used

k-fold cross-validation to simulate an independent dataset in an effort to decrease overfitting and give a reasonable assessment of the new model's performance.

In conclusion, accurate estimation of IAFA is of special importance in individuals of Asian ancestry, as they may have a higher body fat percentage for a given BMI[10-12] and are at greater risk to develop diabetes at any given body-mass index[34]. Measures incorporating age may provide better estimates of IAFA in individuals of Japanese ancestry and potentially in other Asian and perhaps non-Asian populations as well. Further testing in other populations would demonstrate its potential value to achieve this aim.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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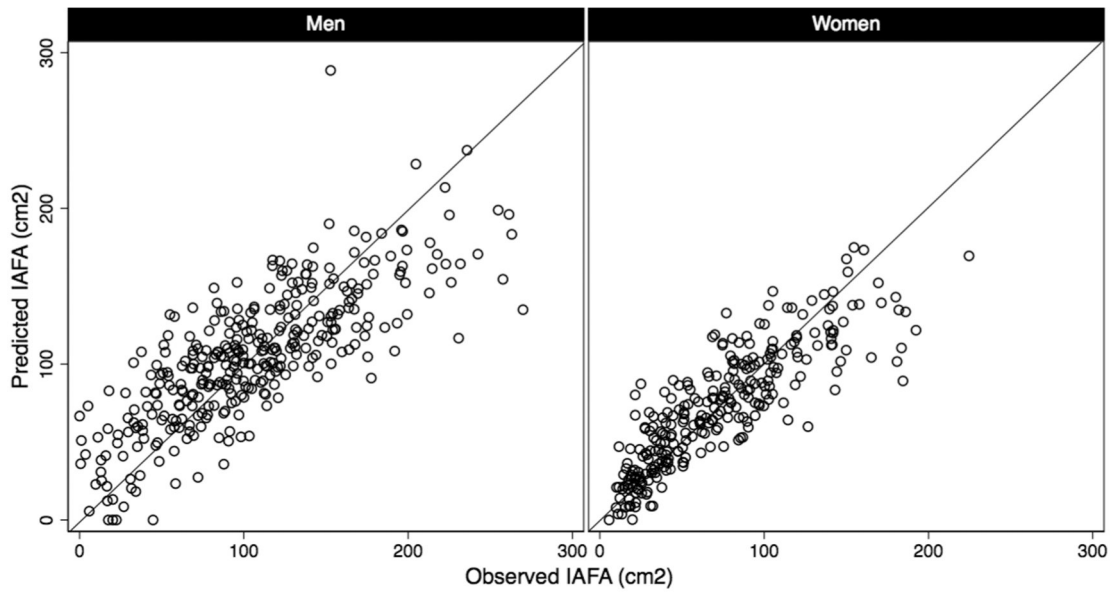
Figure 1.
Sex-stratified scatter plots of intra-abdominal fat area (cm^2) vs. fitted values (cm^2) of EVA for men and women.

Table 1.

Baseline characteristics of Japanese American Community Diabetes Study participants with complete data on all covariates

	Overall n = 622	Men n = 344	Women n = 278	p-value[*]
Mean age, years (SD)	53.7 (11.8)	54.2(11.4)	53.1 (12.4)	0.25
Sex, % male (n)	55(344)	—	—	—
Mean body mass index, kg/m² (SD)	24.5 (3.3)	25.5 (3.0)	23.2 (3.2)	<0.0001
Mean waist circumference, cm (SD)	83.3 (10.5)	88.8 (8.2)	76.5 (9.0)	<0.0001
Mean HDL cholesterol, mg/dL (SD)	57(17)	50 (13)	65 (16)	<0.0001
Mean LDL cholesterol, mg/dL (SD)	141(37)	146 (38)	135 (34)	0.0002
Median triglyceride level, mg/dL (IQR)	118 (79-167)	133 (95-207)	95 (67-135)	<0.0001
Mean fasting glucose, mg/dL (SD)	106 (37)	114 (43)	97 (25)	<0.0001
Smoking status				<0.0001
Current smoker, % (n)	13 (80)	15 (50)	11 (30)	
Former smoker, % (n)	42 (261)	58 (198)	23 (63)	
Mean grip strength, lbs (SD)	49.9 (14.0)	59.1 (10.7)	37.6(6.5)	<0.0001
Mean mid-thigh circumference, cm (SD)	49.2 (4.5)	50.1 (4.2)	48.1 (4.7)	<0.0001
Mean humeral length, cm (SD)	29.0 (2.2)	30.2(1.9)	27.4(1.6)	<0.0001
Mean leg length, cm (SD)	81.2 (6.8)	86.0(4.3)	75.3 (3.9)	<0.0001
Diabetes at baseline, % yes (n)	20(122)	24 (84)	14 (38)	0.004
Mean intraabdominal fat area, cm² (SD)	90.6 (53.3)	105.3 (55.3)	72.4 (44.7)	<0.0001

Abbreviations: SD (standard deviation), HDL (high-density lipoprotein), LDL (low-density lipoprotein)

[*] p-value for t-test (continuous) or Chi-squared test (categorical) comparing distributions for men and women

Table 2.

Coefficients from sex-specific multiple regression models testing associations of metabolic risk factors with intraabdominal fat area (cm^2)

	Men n = 344		Women n = 278	
	β	p-value	β	p-value
Age, years	0.80	<0.001	1.07	<0.001
Body mass index, kg/m^2	3.06	0.05	3.73	0.003
Waist circumference, cm	3.96	<0.001	1.96	<0.001
HDL cholesterol, mg/dL	−0.54	0.001	−0.40	<0.001
LDL cholesterol, mg/dL	—	—	0.01	0.041
Triglyceride level, mg/dL	—	—	—	—
Fasting glucose level, mg/dL	0.10	0.03	0.14	0.023
Smoking status	—	—	—	—
Grip strength, lbs	—	—	—	—
Mid-thigh circumference, cm	−2.92	<0.001	−1.29	0.016
Humeral length, cm	—	—	—	—
Leg length, cm	—	—	—	—
Constant term	−205.91	<0.001	−160.02	<0.001

On first-order multiplicative interaction testing, there was a significant interaction of waist circumference with sex in the full model (β= −1.98, p=0.003; male=1, female=2). We therefore chose to present sex-stratified results.

We built reverse stepwise prediction models using all covariates above. P-value for entry was set at 0.05. P-value for removal was set at 0.1.

Abbreviations: HDL (high-density lipoprotein), LDL (low-density lipoprotein)

Table 3.

Model R² from linear regression models predicting continuous intraabdominal fat area, mean squared errors from k-fold cross validation, and AUROC and 95% confidence intervals for prediction of high (above 75th percentile) vs. low visceral adiposity category, comparing a novel estimate of visceral adipose tissue area (EVA) to selected existing visceral adiposity surrogates

	Men n = 344							Women n = 278						
	R²	AIC	MSE[a]	95% CI	AUROC[b]	95% CI	p-value	R²	AIC	MSE[a]	95% CI	AUROC[b]	95% CI	p-value
EVA[c]	0.61	3421	1244	1243 - 1246	0.90	0.86 - 0.93	—	0.72	2554	582	581 - 583	0.94	0.92 - 0.96	—
EVA without mid-thigh circumference[d]	0.59	3433	1267	1265 - 1268	0.88	0.84 - 0.92	**0.013**	0.72	2558	589	588 - 590	0.94	0.92 - 0.97	0.771
Després estimate[e]	0.50	3501	1544	1543 - 1545	0.85	0.80 - 0.89	**0.004**	—	—	—	—	—	—	—
WHtR	0.48	3515	1613	1611 - 1614	0.86	0.82 - 0.90	0.091	0.58	2664	852	852 - 853	0.88	0.84 - 0.92	**<0.0001**
WC, cm	0.48	3513	1603	1602 - 1605	0.84	0.80 - 0.88	**0.009**	0.56	2678	898	897 - 898	0.88	0.84 - 0.92	**0.003**
DAAT index[f]	0.46	3529	1680	1678 - 1681	0.82	0.77 - 0.87	**0.001**	0.58	2665	857	856 - 858	0.88	0.84 - 0.92	**0.0003**
BMI, kg/m²	0.36	3584	1968	1966 - 1970	0.82	0.76 - 0.87	**0.003**	0.40	2762	1215	1214 - 1216	0.84	0.79 - 0.89	**<0.0001**
LAP[g]	0.17	3674	2607	2602 - 2612	0.81	0.75 - 0.86	**0.0002**	0.22	2834	1793	1785 - 17801	0.86	0.81 - 0.90	**<0.0001**
VAI[h]	0.08	3710	2888	2882 - 2893	0.73	0.68 - 0.80	**<0.0001**	0.14	2861	1734	1733 - 1736	0.78	0.72 - 0.84	**<0.0001**

Abbreviations: AIC (Akaike information criterion), AUROC (area under the receiver-operating characteristics curve), CI (confidence interval), EVA (estimate of visceral adiposity), WHtR (waist-to-height ratio), WC (waist circumference), DAAT index (deep abdominal adipose tissue index), BMI (body-mass index), LAP (lipid accumulation product), VAI (visceral adiposity index).

[a] For k-fold cross validation, data were partitioned into 5 training sets, repeated 500 times

[b] The 75th percentile of visceral adiposity was 140 cm2 for men and 100 cm2 for women; p-value compared to AUROC for VAE with fasting insulin

[c] EVA (men) = [0.80 × age (years)] + [3.06 × BMI (kg/m2)] + [3.96 × WC (cm)] – [0.54 × HDL-cholesterol (mg/dL)] + [0.10 × fasting glucose (mg/dL)] – [2.92 × mid-thigh circumference (cm)] – 205.91; EVA (women) = [1.07 × age (years)] + [3.73 × BMI (kg/m2)] + [1.96 × WC (cm)] – [0.40 × HDL-cholesterol (mg/dL)] + [0.01 × LDL-cholesterol (mg/dL)] + [0.14 × fasting glucose (md/dL)] – [1.29 × mid-thigh circimference (cm)] – 160.02

[d] without mid-thigh circumference: EVA-C (men) = [1.28 × age (years)] + [4.12 × WC (cm)] – [0.53 × HDL-cholesterol (mg/dL)] + [0.14 × fasting glucose (mg/dL)] – 319.50; EVA-C (women) = [1.26 × age (years)] + [1.89 × BMI (kg/m2)] + [2.16 × WC (cm)] – [0.43 × HDL-cholesterol (mg/dL)] + [0.11 × LDL-cholesterol (mg/dL)] + [0.18 × fasting glucose (mg/dL)] – 207.22

[e] Després estimate: calculated using coefficients derived by Després et al. (1991) in 110 men: IAFA =−225.39 + 2.125 × age(years) +2.843 × WC(cm); it was derived in a male cohort, so we chose not to calculate values for women

[f] Deep abdominal adipose tissue (DAAT) index: calculated using coefficients derived by Brundavani et al. (2006). Men = −382.9 + [1.09 × weight -(kg)] + [6.04 × WC-(cm)] + (−2.29 × BMI), women = −278 + [−0.86 × weight -(kg)] + [5.19 × WC-(cm)]

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[g]Lipid accumulation product (LAP): men [(WC (cm)-65) × TG (mmol)], women [(WC (cm)-58) × TG (mmol)], in the manner of Kahn H. et al. (2005)

[h]Visceral adiposity index (VAI): calculated using coefficents derived by Amato et al. (2010): VAI = (WC/(39.68+(1.88*BMI)))*(triglycerides/1.03)*(1.31/HDL) for men, and (WC/(36.58+(1.89*BMI)))*(triglycerides/0.81)*(1.52/HDL) for women, with both triglycerides and HDL specified in mmol/L