

Sex differences for predicting metabolic syndrome by adipose dysfunction markers in institutionalized elderly

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Aims

Recent studies have emphasized that metabolic syndrome (MetS) was the most important modifiable risk factor for cardiovascular and cerebrovascular diseases in the institutionalized elderly. In addition, the occurrence of MetS was higher in those with longer age-adjusted institutionalization time. The present study was conducted to assess predictive value of markers of adipose tissue dysfunction for the early screening of MetS in this population.

Methods and results

Two hundred and eleven institutionalized older adults (132 women, aged 74.3 ± 7.3 years; 79 men, aged 71.5 ± 7.3 years) were enrolled in the current cross-sectional study. Lipid accumulation product (LAP), visceral adiposity index (VAI), body adiposity index (BAI), and triglycerides (TG)/high-density lipoprotein (HDL)-cholesterol ratio were determined. The receiver operating characteristic curve was calculated to compare the area under the curve of each index. The total prevalence of MetS was 23.8%. In female group, VAI and TG/HDL ratio presented moderate–high sensitivity (77.78% and 78.38%, respectively) and specificity (77.62% and 73.49%, respectively). In males group, LAP presented moderate–high sensitivity (75%) and specificity (76.9%).

Conclusion

Gender played a key role on the prediction of MetS by adipose dysfunction markers in institutionalized elderly. Accordingly, VAI and TG/HDL-cholesterol ratio showed the highest predictive value for MetS in female elderly. LAP was the strongest predictor of MetS in male elderly.

Keywords

Metabolic syndrome • Aged • Housing for the elderly • Visceral adipose index • Lipid accumulation product • Body adiposity index • Triglycerides/HDL-cholesterol ratio

Implications for practice

- Metabolic syndrome (MetS) is prevalent among Spanish institutionalized elderly.
- Sex played a key role on the prediction of MetS by adipose dysfunction markers.
- Visceral adiposity index and triglycerides/high-density lipoprotein ratio showed the highest predictive value for MetS in female group. Lipid accumulation product was the strongest predictor of MetS in male group.
- These indices may be of great interest in order to identify residents at particular risk for MetS and may contribute to save time and resources in clinical practice.

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Introduction

The prevalence of metabolic syndrome (MetS) in the adult population is high across Europe and its frequency is significantly increased with age.¹ In fact, several studies have reported MetS is highly prevalent in both community-dwelling and institutionalized elderly.^{2,3} In addition, the occurrence of MetS in institutionalized elderly was higher in those with longer age-adjusted institutionalization time.³ This finding was of particular interest given that cardiovascular disease in general⁴ and MetS in particular,⁵ have been associated with increased risk of frailty, the leading cause of disability and premature mortality in older age. Furthermore, MetS was associated with accelerated cognitive and functional decline in a population-based sample of very old men.⁶ Lastly, MetS has been also reported as the most important modifiable risk factor for cardiovascular and cerebrovascular diseases in aged adults.⁷

Although an early diagnosis of MetS is needed in different countries and cohorts,⁸ predicting the development of MetS is complex given its multifactorial nature.⁹ Recent studies have recommended to include routinely applicable indicators of visceral adiposity dysfunction, such as VAI (visceral adiposity index),¹⁰ LAP (lipid accumulation product),⁹ and BAI (body adiposity index)¹² for the screening of MetS at different life stages.^{13–15} However, no previous study has demonstrated the usefulness of these adiposity indices as predictors of MetS in institutionalized Spanish population. These findings would be of great interest in clinical practice for healthcare providers in nursing homes, providing an early identification of residents at particular risk for MetS that may finally save time and resources.

For the reasons already mentioned, the overall aim was to assess the role of several markers of adipose dysfunction to predict MetS in institutionalized elderly. Specific objectives were to determine sensitivity, specificity, the cut-off points and the area under the curve (AUC) for each potential predictor of MetS in this population group.

Methods

Design and population

The current cross-sectional observational study (COMeS study: **C**entral **O**besity and **M**etabolic **S**yndrome) was conducted at University of Málaga (Andalusia, Spain). A total of three non-profit nursing homes located in Málaga agreed to participate in the study.

Table 1 Characteristics of institutionalized elderly by gender and metabolic syndrome factors

Participants	Women		Men		Total	
	n	%	n	%	n	%
	132	62.9	78	37.1	210	100
	No MetS		MetS			
Blood pressure	142	(67.6%)	67	(31.9%)	209	99.5
Glucose	152	(72.4%)	55	(26.2%)	207	98.6
Triglycerides	159	(75.4%)	37	(17.6%)	196	93.3
HDL	96	(45.7%)	96	(45.7%)	192	91.9
MetS	158	(75.2%)	50	(23.8%)	208	99

Two hundred and eleven aged adults (132 women and 79 men) were enrolled in the study (Table 1). All participants were Caucasian, aged over 65 years, having functional autonomy, institutionalized and residing for more than 2 years in the same nursing home (inclusion criteria). The following exclusion criteria were considered: (i) refusal to participate; (ii) incomplete data for the diagnosis of MetS (i.e. difficult venous access); (iii) amputation and/or the use of prostheses in the lower limbs; (iv) hormone-replacement therapy in women; and (v) terminal illness.

Anthropometric assessment

The weight was measured, to the nearest 100 g, on a calibrated electronic scale SECA 813 (Hamburg, Germany). The height was measured to the nearest 0.1 cm using a stadiometer SECA 216 (Hamburg, Germany). The body mass index (BMI) in kg/m² was calculated. The circumferences were measured, with a precision of 0.1 cm, using a flexible steel tape calibrated in centimetres (Lufkin, model W606PM, Cooper Tools, México). The Gluteal (hip) girth was determined at the level of the greatest posterior protuberance of the buttocks and perpendicular to the long axis of the trunk. The waist circumference (WC) was measured at the level of the iliac crest and is measured perpendicular to the long axis of the trunk. Anthropometric measurements were obtained according to the recommendations of the International Society for Advancement in Kinanthropometry (ISAK)¹⁶ by a single, long-experienced, accredited level 3 anthropometrist.

Biochemical outcomes

Blood samples were drawn, after a 12-h overnight fast, from antecubital vein puncture and collected in heparinized tubes. The whole blood was centrifuged at 3000 rpm for 20 min in a clinical centrifuge. The fasting plasma glucose (GLU) and lipid profile [total cholesterol (CHOL); high-density lipoprotein-cholesterol (HDL); triglycerides (TG)] were measured by spectrophotometry (Advia 2400, Siemens HealthCare Diagnostics, USA).

Adipose function indices

- (1) BAI: body adiposity index¹². This index was calculated as follows:

$$BAI = [\text{hip circumference (cm)} / \text{Height (m)}]^{1.5} - 18$$

- (2) VAI: visceral adiposity index¹⁰. This index was calculated as follows:

$$\text{Women: } [\text{waist circumference} / 36.58 + (1.89 \text{ BMI})] \times [\text{TG} / 0.81] \times [1.52 / \text{HDL}]$$

$$\text{Men: } [\text{waist circumference} / 39.68 + (1.88 \text{ BMI})] \times [\text{TG} / 1.03] \times [1.31 / \text{HDL}]$$

Where the waist circumference is in cm, the BMI in kg/m², the TG and HDL in mmol/L.

- (3) LAP index (lipid accumulation product index).¹¹ This index was calculated as follows:

$$\text{Women: } (\text{waist circumference (cm)} - 58) \times \text{TG (mmol/L)}$$

$$\text{Men: } (\text{waist circumference (cm)} - 65) \times \text{TG (mmol/L)}$$

- (4) TG/HDL-Chol index: triglycerides/HDL-cholesterol.¹⁷

Blood pressure

Systolic and diastolic blood pressures were determined after 10-min rest period in the right arm with participants in a seated position, back supported and legs uncrossed in a quiet room after 10-min intervals, using an aneroid manometer (Riester, Disamed, Spain). The mean of the two measurements was used in the analyses.

Definition of metabolic syndrome

The definition of MetS was based on the criteria of the International Diabetes Federation (IDF). These criteria were a waist circumference of ≥ 94 cm for men and ≥ 80 cm for women plus two or more clinical features: (i) fasting plasma triglycerides ≥ 150 mg/dL or on specific medication; (ii) blood pressure of ≥ 130 systolic or ≥ 85 mm diastolic or previous diagnosis or on specific medication; (iii) HDL cholesterol < 40 mg/dL and < 50 mg/dL for men and women, respectively, or on specific medication; (iv) fasting plasma glucose > 100 mg/dL or previously diagnosed type 2 diabetes.¹⁸

Statistical analysis

A descriptive study was carried out to analyse the data. Continuous variables were presented as mean values \pm standard deviation (SD), while categorical variables were presented as frequencies. The Kolmogorov–Smirnov test was used to identify normal distribution of the data. A Student’s t-test was also conducted to compare anthropometric and biochemical parameters between male and female participants. Sensitivity (proportion of true positives, i.e. proportion of cases correctly identified as meeting the conditions of MetS according to IFD definition) and specificity (proportion of true negatives, i.e. proportion of non-cases correctly identified as not meeting MetS according to IFD definition) were calculated to assess the accuracy of standard biochemical markers as well as several novel metabolic indices (combining both anthropometric and lipid measures) in depicting MetS, creating receiver operating characteristic (ROC) curves.¹⁹ The AUC was used to determine the overall accuracy of each predictor ($AUC \geq 0.5$ was considered to have diagnostic value, the larger the area, the larger the value). The optimal cut-off point was selected by maximizing Youden’s J index, which is the difference between the true positive rate (sensitivity) and the false positive rate (1-specificity) in the ROC curve. Data analysis was conducted using MedCalc statistical software for Windows (v17.9.2, Ostende, Belgium). Statistical significance was defined as $P < 0.05$ for all analyses.

Ethical considerations

The present investigation conforms with the principles outlined in the Declaration of Helsinki (2013). All participants were informed about the aims, procedures, benefits and potential risks of the current study, and agreed to participate and signed an informed consent form. Furthermore, this protocol was approved by an Institutional Ethics Committee (report: EMEFYDE: 011-2015).

Results

Clinical and analytical characteristics of the sample population are presented in Table 1. The global prevalence of MetS, according to the IDF definition, was 23.8%.

When male and female institutionalized elderly were compared, significant differences were found in TG ($P = 0.0008$), CHOL ($P = 0.0007$), and HDL-cholesterol ($P = 0.0004$). In addition, significant differences were also found in BMI ($P = 0.02$), BAI ($P < 0.0001$), VAI ($P < 0.0001$), and LAP ($P < 0.0001$) (Table 2).

To the best of our knowledge, the present study was the first to provide the optimal cut-off points, sensitivity and specificity of several markers of visceral adiposity dysfunction to predict MetS in institutionalized elderly individuals in Spain.

In the female group, VAI ($AUC = 0.82$, $P < 0.001$), LAP ($AUC = 0.72$, $P < 0.001$), TG/HDL ratio ($AUC = 0.806$, $P < 0.001$), TG ($AUC = 0.696$, $P = 0.0003$), and CHOL ($AUC = 0.616$, $P = 0.04$) presented significant AUCs. Regarding the male group, BAI ($AUC = 0.702$, $P < 0.003$), VAI ($AUC = 0.705$, $P < 0.009$), LAP ($AUC = 0.797$, $P < 0.0001$), and GLU ($AUC = 0.714$, $P < 0.001$) presented significant AUCs. Results from the ROC curves analyses are shown in Table 3.

For the female group, both VAI and TG/HDL ratio presented moderate-high Sensitivity/Specificity. In addition, LAP, TG, and

Table 2 Anthropometric and biochemical parameters of institutionalized elderly by gender

Variables	Women		Men		P-value
	n	Mean \pm SD	n	Mean \pm SD	
Age (years)	132	74.27 \pm 7.27	78	71.51 \pm 7.29	0.006
Weight (kg)	131	63.37 \pm 13	78	68.57 \pm 14	0.007
Height (cm)	129	151.8 \pm 6.94	78	162.5 \pm 8.39	<0.0001
BMI (kg/m ²)	129	27.52 \pm 5.47	78	26 \pm 5.15	0.02
Glucose (mg/dL)	131	96.63 \pm 44.8	76	92.7 \pm 25	0.92
Triglycerides (mg/dL)	124	118.7 \pm 47.5	70	100 \pm 51	0.0008
Cholesterol (mg/dL)	127	174.4 \pm 39.5	71	156.1 \pm 32.5	0.0007
HDL-Chol	122	49.76 \pm 14.3	71	43 \pm 10.3	0.0004
SBP (mmHg)	127	123.9 \pm 16.5	77	120.6 \pm 17.4	0.12
DBP (mmHg)	127	66.69 \pm 8.52	77	64.2 \pm 9.3	0.03
TG/HDL	122	2.641 \pm 1.5	70	2.45 \pm 1.64	0.17
LAP index	118	55.92 \pm 31.4	68	35.61 \pm 27.7	<0.0001
VAI	114	2.4 \pm 1.38	67	1.54 \pm 1.08	<0.0001
BAI	122	37.54 \pm 6.73	75	29.53 \pm 5.15	<0.0001

BAI, body adiposity index; BMI, body mass index expressed as kg/m²; CHOL, total cholesterol mg/dL; DBP, diastolic blood pressure mmHg; GLU, glucose mg/dL; HDL, high-density lipoprotein mg/dL; LAP, lipid accumulation product; MW, Mann–Whitney test for independent samples; SBP, systolic blood pressure expressed as mmHg; TG, triglycerides mg/dL; TG/HDL, triglycerides/HDL; VAI, Visceral adiposity index; Z, statistic Z.

Table 3 Areas under curve of biochemical indices in institutionalized elderly by gender for predicting MetS

Women	BAI	VAI	LAP	TG/HDL	TG	CHOL	GLU
AUC	0.566	0.821	0.72	0.806	0.696	0.616	0.554
SE	0.0587	0.0435	0.0528	0.0453	0.0548	0.0587	0.0613
95% CI	0.47–0.65	0.73–0.88	0.63–0.80	0.72–0.87	0.61–0.77	0.52–0.70	0.46–0.64
Z	1.13	7.383	4.176	6.746	3.578	1.983	0.882
P (area = 0.5)	0.2585	<0.0001	<0.0001	<0.0001	0.0003	0.0473	0.3776
Youden index J	0.2008	0.544	0.401	0.5187	0.344	0.2451	0.1862
Men							
AUC	0.702	0.705	0.797	0.664	0.589	0.505	0.714
SE	0.0951	0.078	0.0616	0.0883	0.0985	0.107	0.0849
95% CI	0.58–0.80	0.58–0.81	0.68–0.88	0.54–0.77	0.46–0.70	0.38–0.62	0.60–0.81
Z	2.12	2.622	4.816	1.859	0.904	0.046	2.515
P (area = 0.5)	0.034	0.0088	<0.0001	0.063	0.366	0.9633	0.0119
Youden index J	0.4247	0.4515	0.5179	0.3544	0.2299	0.178	0.3646

AUC, area under curve; BAI, body adiposity index; CHOL, total cholesterol; GLU, glucose; HDL, high-density lipoprotein; LAP, lipid accumulation product; TG/HDL, triglycerides/HDL TG, triglycerides; VAI, visceral adiposity index.

Table 4 Optimal cut-off points, sensitivity (Sens), specificity (Spec), and positive likelihood ratio (+LR) for biochemical indices in institutionalized elderly for predicting MetS

Women	Cut-off	Sens	95% CI	Spec	95% CI	+LR	95% CI
BAI	>39.29	48.65	31.9–65.6	71.43	60.5–80.8	1.7	1.1–2.7
VAI	>2.41	77.78	60.8–89.9	76.62	65.6–85.5	3.33	2.1–5.2
LAP	>76.57	51.35	34.4–68.1	88.75	79.7–94.7	4.56	2.3–9.1
TG/HDL	>2.5	78.38	61.8–90.2	73.49	62.7–82.6	2.96	2.0–4.4
TG	>131	56.76	39.5–72.9	77.65	67.3–86.0	2.54	1.6–4.1
COL	≤161	54.05	36.9–70.5	70.45	59.8–79.7	1.83	1.2–2.8
GLU	>112	26.32	13.4–43.1	92.31	84.8–96.9	3.42	1.4–8.3
Men							
BAI	>28.55	90.91	58.7–99.8	51.56	38.7–64.2	1.88	1.4–2.6
VAI	>1.24	83.33	51.6–97.9	61.82	47.7–74.6	2.18	1.4–3.3
LAP	>38.69	75	42.8–94.5	76.79	63.6–87.0	3.23	1.8–5.8
TG/HDL	>2.12	72.73	39.0–94.0	62.71	49.1–75.0	1.95	1.2–3.2
TG	>137	33.33	9.9–65.1	89.66	78.8–96.1	3.22	1.1–9.7
COL	>160	50	21.1–78.9	67.8	54.4–79.4	1.55	0.8–3.1
GLU	>101	58.33	27.7–84.8	78.12	66.0–87.5	2.67	1.4–5.2

BAI, body adiposity index; CHOL, total cholesterol; GLU, glucose; HDL, high-density lipoprotein; LAP, lipid accumulation product; TG/HDL, triglycerides/HDL; TG, triglycerides; VAI, visceral adiposity index.

CHOL presented moderate-high specificity. The optimum cut-off points for VAI and TG/HDL ratio were 2.41 and 2.5, respectively.

For the male group, LAP presented moderate-high sensitivity (75%) and specificity (76.9%). BAI and VAI had greater sensitivity (90.91% and 83.33%, respectively) but lower specificity (51.56% and 61.82%, respectively). GLU had a low sensitivity (58%) and moderate-high specificity (78%). Lastly, the optimum cut-off point for LAP index was 38.69 (Table 4).

Discussion

There is emerging evidence that novel metabolic indices (LAP; VAI; BAI; etc.), combining both anthropometric and lipid measures, could be early, minimally invasive and simple markers for the screening of MetS.^{14,15} To the best of our knowledge, the present study was the first to provide the optimal cut-off points, sensitivity and specificity of several markers of visceral adiposity dysfunction to predict MetS in

institutionalized elderly individuals in Spain. Promising results on this topic have been previously published in Caucasian young-adults¹⁵ and middle-aged adults.¹⁴ Similar data have been also found in type 2 diabetes.²⁰ Previous authors also considered it could be a cost-effective screening strategy compared to imaging techniques, the gold standard technique to assess visceral adiposity, that may finally contribute to their widespread use in clinical practice.^{13,14,20}

In a more detailed way, the VAI index was firstly reported as a reliable indicator of visceral fat function associated with cardiometabolic risk.¹⁰ The current results suggested that the VAI index could be an optimal clinical marker for prediction of MetS in institutionalized elderly, showing moderate/strong AUC values (0.82 and 0.70 in females and males, respectively). Conversely, no gender differences in AUC values were reported by Gu et al.²¹ in Chinese community-dwelling elderly (AUC: 0.856 and 0.865 in females and males, respectively). In addition, it should be pointed out that HDL-C level, included in the equation to calculate the VAI index, was significantly associated with increased mortality among elderly individuals with MetS.²² Therefore, the VAI index should be given more consideration in the clinical practice in nursing homes.

The LAP index has demonstrated a strong predictive accuracy for MetS in previous studies in both male and female adults.^{13,15,23} In this respect, LAP appeared to be better than both VAI and TG/HDL-C for predicting MetS in both female and male community-dwelling Chinese elderly.²¹ The current study has found that the LAP could be an optimal clinical marker for prediction of MetS in male institutionalized elderly (AUC: 0.797), having just a moderate AUC value (0.720) in the female group. In the latter two studies, MetS was defined according to IDF criteria so differences could be explained, at least in part, by different ethnicity²⁴ and living conditions (community-dwelling vs. institutionalized elderly). Stronger AUC values for identifying MetS have been previously reported in Spanish adults using NCEP-ATPIII criteria.²⁵

Available evidence suggests that the TG/HDL-C ratio has been successfully used in predicting the development of both MetS and insulin resistance.^{26,27} In the current study, the TG/HDL-C ratio showed the highest AUC value for MetS in the female group (AUC 0.80) with a cut-off point of 2.5. Higher AUC values (0.85) were previously reported in female young adults (AUC: 0.85) and adolescents (AUC: 0.89).^{28,29} Conversely, TG/HDL-C ratio showed the lowest AUC value in the male group (AUC: 0.60).

The current study has also found that the BAI index had the lowest discriminatory ability for MetS compared to the rest three markers in institutionalized elderly. In this line, the AUC value for BAI was low and not significant in the female group (AUC: 0.56). Similarly, Guo et al.¹³ reported the poor utility of BAI for the screening of MetS in community-dwelling Chinese elderly. Better AUC values for MetS were reported in Spanish adolescents and university students.^{30,31}

Lastly, it is worth emphasizing that gender played a key role on the prediction of MetS by adipose dysfunction markers (VAI, LAP, and BAI) in institutionalized elderly. This finding is consistent with previous studies.^{21,32,33}

For the reasons already mentioned, the current study provides clinically relevant information regarding the usefulness of several adiposity dysfunction markers that may contribute to an early screening of MetS in institutionalized elderly. This is of great interest in clinical

practice because of its prevalence and severe consequences in this population group.^{5,6} In fact, based on 20 prospective cohort studies, MetS was associated with a higher risk of all-cause mortality [relative risk, 1.23; 95% confidence interval (1.15–1.32)].²²

This study had some strengths. It is the first report that provides gender-specific thresholds for various adipose dysfunction markers to predict MetS, defined by IDF criteria, in institutionalized elderly in Spain. It should be pointed out that the IDF diagnostic criteria are the most widely used for both, clinical practice and research, in Spain. The use of standardized procedures for the anthropometric and biochemical determinations minimized measurement bias. In a more detailed way, the anthropometric data were obtained by level-3 ISAK (International Society for the Advancement of Kinanthropometry) accredited technicians. Lastly, participants were recruited from a well-defined population, which represented a single ethnic group (Caucasian), older than 65 years and institutionalized in nursing homes.

Several limitations to the study are also recognized. The sample size is small and would benefit from a larger population. In addition, it was a cross-sectional cohort of institutionalized elderly and the results might not apply to the community-dwelling elderly. Further multicentre studies, with larger sample sizes, are required to confirm the predictive value of VAI, LAP and TG/HDL-C ratio in identifying MetS in institutionalized elderly.

Conclusion

It was concluded that sex played a key role on the prediction of MetS by adipose dysfunction markers in institutionalized elderly. In this line, VAI and TG/HDL-C ratio showed the highest predictive value for MetS in female elderly. In contrast, LAP was the strongest predictor of MetS in male elderly. Consequently, these adipose dysfunction indices would be recommended for use in clinical settings for the early detection and follow-up of MetS in the institutionalized elderly.

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