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Diagnostic Performance Of Lipid Accumulation Indices And Triglyceride And Glucose Index For Metabolic Syndrome In A Sample Of Peruvian Adult Population

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DIAGNOSTIC PERFORMANCE OF LIPID ACCUMULATION INDICES AND TRIGLYCERIDE AND GLUCOSE INDEX FOR METABOLIC SYNDROME IN A SAMPLE OF PERUVIAN ADULT POPULATION

RENDIMIENTO DIAGNÓSTICO DE LOS ÍNDICES DE ACUMULACIÓN LIPÍDICA Y EL ÍNDICE TRIGLICÉRIDOS Y GLUCOSA PARA SÍNDROME METABÓLICO EN UNA MUESTRA DE POBLADORES ADULTOS PERUANOS

Jesús E. Talavera [1,3], Jenny Raquel Torres-Malca [2]

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ABSTRACT

Objectives: To determine the diagnostic performance of the lipid accumulation product (LAP), visceral adiposity index (VAI), triglyceride and glucose index (TyG) and body mass index (BMI) for metabolic syndrome (MetS) in a sample of Peruvian adults. **Methods:** Study of diagnostic tests of the "National Survey on Nutritional, Biochemical, Socioeconomic, and Cultural Indicators related with Chronic Degenerative Diseases". An analysis of ROC curves (Receptor Operation) was made, and their respective area under the curve (AUC) obtaining the different parameters such as sensitivity (Sens) and specificity (Spe). It was stratified according to sex and according to age. To choose the cut-off point, the Youden index was used. **Results:** The LAP had the highest AUC in both men (AUC = 0.929; cut-off value = 59.85; Sens = 91.6 and Spe = 84.5) and for women (AUC = 0.950; cut-off value = 53, 06; Sens = 92.4 and Spe = 86.4). The second place, in the case of men, was occupied by the VAI (AUC = 0.905; cut-off value = 2.36; Sens = 91.6 and Spe = 79.7), while in the case of women it was the TyG (AUC = 0.914; cut-off value = 8.70; Sens = 87.4 and Spe = 87.3). The LAP index showed significant differences with VAI to predict MetS (p <0.05), while no differences were shown with TyG. **Conclusion:** The LAP index had the best diagnostic performance for MetS, both for men and women, regardless of age.

Keywords: Metabolic syndrome, triglycerides, glucose, product of lipid accumulation, body mass index (Source: MeSH NLM)

RESUMEN

Objetivos: Determinar el rendimiento diagnóstico del producto de acumulación de lípidos (LAP), índice de adiposidad visceral (VAI), índice de triglicéridos y glucosa (TyG) e índice de masa corporal (IMC) para síndrome metabólico (SMet) en una muestra de adultos peruanos. **Metodología:** Estudio de pruebas diagnósticas de la "Encuesta Nacional de Indicadores Nutricionales, Bioquímicos, Socioeconómicos y Culturales relacionados con las Enfermedades Crónicas-Degenerativas". Se hizo un análisis de curvas ROC (Operativa del Receptor), y su respectiva área bajo la curva (AUC) obteniendo los diferentes parámetros como sensibilidad (Sens) y especificidad (Esp). Se estratificó según sexo y según la edad. Para escoger el punto de corte se utilizó el índice de Youden. **Resultados:** El LAP tuvo el mayor AUC tanto en hombres (AUC = 0,929; valor de corte = 59,85; Sens = 91,6 y Esp = 84,5) como para mujeres (AUC = 0,950; valor de corte = 53,06; Sens = 92,4 y Esp = 86,4). El segundo lugar, en el caso de los hombres, lo ocupó el VAI (AUC = 0,905; valor de corte = 2,36; Sens = 91,6 y Esp = 79,7), mientras que en el caso de las mujeres lo fue el TyG (AUC = 0,914; valor de corte = 8,70; Sens = 87,4 y Esp = 87,3). El índice LAP mostró diferencias significativas con VAI para predecir SMet (p < 0,05), mientras que no se mostraron diferencias con TyG. **Conclusión:** El índice LAP tuvo el mejor rendimiento diagnóstico para SMet, tanto a hombres y mujeres, independiente de la edad.

Palabras clave: Síndrome metabólico, triglicéridos, glucosa, producto de la acumulación de lípidos, índice de masa corporal (Fuente DeCS BIREME)

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INTRODUCTION

Metabolic syndrome (SMet) is a clinical state that includes central obesity, hypertension, hyperglycemia, and dyslipidemia. The presence of SMet long term increases the risk of developing cardiovascular disease and diabetes mellitus [1,2].

The prevalence in the world of SMet varies. In China, around 32.4% is found [3], while in the United States it is 34.7 [4]. In Latin America, a systemic revision reported a prevalence of 24.9%, more frequent among women than men [5]. In Peru, a consensus does not exist [6], prevalence levels fluctuating between 20 to 47%[7,9].

Smet diagnosis is not complex, but we don't always have the five criteria at hand, even more so in low-income areas (10). For this reason, it is important to find simpler indicators to detect SMet. The ones that have shown a good diagnostic performance are triglyceride and glucose index (TyG)[11,14], and the lipid accumulation indices, such as lipid accumulation product (LAP) and visceral adiposity index (VAI). Body mass index (BMI) has also been studied[15,18].

These indicators have shown different cutting points and predictive capacity according to location where research took place[13,19,21]. For this reason, the objective of this study is to determine the diagnostic performance of LAP, VAI, TyG and BMI for SMet confirmed in a sample of adult Peruvian inhabitants.

METHODOLOGY

Experimental design

Diagnostic test studies. Data base analysis secondary to "National Survey on Nutritional, Biochemical, Socioeconomic, and Cultural Indicators related with Chronic Degenerative Diseases" (NSNBSCI), performed between the years 2004 – 2005 [22]. The purpose of this survey was to learn the prevalence of chronic diseases of metabolic origin, such as metabolic syndrome, lipid disorders, type 2 diabetes mellitus, and arterial hypertension.

Study population

The original study was carried out nationally, divided into five areas: Metropolitan Lima, the remainder of the Coast, Urban Mountains, Rural Mountains and Jungle. It was composed of everyone above or equal to 20 years of age, that resided in that location at the time of the survey.

The NSNBSCI had a multistage design. Clusters were selected in each level, by simple random sample, and within each one, blocks, houses, and people were selected. The sample unit was the housing of clusters, and the unit of analysis was the people with the beforementioned characteristics. Additional information about selection criteria, sample size and all variables that were taken have been published elsewhere[22].

In this study we included only the subjects who had the complete data on variables of interest, and whose laboratory or anthropometric values were within the biologically plausible lower limits.

Variables and measures

The main variable for the diagnosis was Smet. We considered SMet through the criteria of the National Education Program on Cholesterol Adult Treatment Panel III (ATPIII) Programa Nacional de Educación sobre el Colesterol Panel de Tratamiento de Adultos III (ATPIII) [23]. In the case of ATPIII, SMet is diagnosed by presenting three or more of the following alterations: abdominal obesity obtained with the abdominal circumference (AC) ≥ 88 cm for women or ≥ 102 cm for men; hypertriglyceridemia (triglycerides ≥ 150 mg/dl); hyperglycemia (fasting glucose ≥ 100 mg/dl or if they receive treatment to lower glucose levels); high blood pressure (systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or receive treatment to lower blood pressure levels); low HDL (HDL-cholesterol < 50 mg/dl in women or < 40 mg/dl in men).

There were four variables considered to test their diagnostic performance (Table 1):

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Table 1. Predictive equations to calculate metabolic syndrome

Index	Equation	
BMI*	Weight (Kg) / height2 (meters)	
TyG**	Ln (TG [mg/dL] x fasting glucose (mg/dL)/2)	
VAI***	Men (AC/[39.68 + (1.88 x BMI)]) x (triglycerides/1.03) x (1.31/HDL-cholesterol)	Women (AC/[36.58 + (1.89 x BMI)]) x (triglycerides/0.81) x (1.52/HDL-cholesterol)
LAP****	Men (AC - 65) x TG	Women (AC - 58) x TG

*Body Mass Index, **Triglyceride and Glucose index, ***Visceral adiposity index, ****Lipid Accumulation Product

AC values lower than 65 and 58 cm in women and men were reassigned to 66 and 59 cm, in order to avoid invalid data. For VAI and LAP, TG and HDL in mmol/L were presented. The other variables included in the study were age (in years), body mass index (BMI), smoker state (if they have ever smoked "yes" or "no"), alcohol drinker (if they have ever had an alcoholic drink "yes" or "no"), and physical activity (do you practice physical activity outside of your work "yes" or "no").

In NSNBSCI, the anthropometric measures were obtained using a mobile wooden measure and a standing digital balance of Sohenle Brand with 120 kg capacity and specificity of 0.1 kg. Once the weight and height are obtained, we proceeded to calculate BMI applying the corresponding formula: Weight (kg) /Height2 (m). The waist perimeter was measured with a flexible measuring tape at the middle point between the lower edge of the ribs and the iliac crest, passing by the half centimeter closest to the navel. The blood pressure measures were performed using a Mac-Check-501 sphygmomanometer.

The subject was asked to have a minimum fasting of 8 hours to obtain the biochemical samples. The blood samples were taken through a vacuum system with a gel clot activator. We obtained the blood using Handzentrifuge manual centrifuges of 3000 RPM and cryovials that allowed the safe transfer and conservation of the samples. Glucose was obtained based on an enzymatic Trinder-GOD-PAD (glucose oxidase) method, and HDL-cholesterol was obtained through an enzymatic Trinder-Colorimetric method.

Statistical analysis

STATA v16.0 statistical software was used. For this analysis, we stratified according to sex. In the bivariate analysis, considering the SMet outcome, Chi square teste of independence was used for the categorical covariables, while the Mann Whitney U-test for the numerical covariables, since they did not present normal distribution, which was evaluated through bias, kurtosis, and histogram.

In order to evaluate the discriminative diagnostic performance, we used ROC curve analysis (Receiver Operating Characteristic) and its respective area under the curve (AUC) as statistical and graphic method. We calculated sensitivity (Sens), specificity (Spec), positive (PPV) and negative predictive value (NPV) and positive (LR+) and negative likelihood ratio (LR-). Youden's index was used to determine the optimal cut off point. The ROC curve was graphed according to sex and age younger and older equal to 65 years.

Ethical considerations

This is a secondary analysis of the database with free public access. At the same time, the base is codified, guaranteeing the confidentiality and anonymity of the participants. Therefore, the damage to these subject is minimal.

RESULTS

We worked with a total of 1936 men and 2055 women. Of the total, 24,33% presented SMet, as opposed to men which was only 5.53%. The average age of men with Smet was greater than the age of women. There were no differences between both sexes compared to having smoked before and presenting Smet. However, for women, we found an association between presenting Smet and having ever drank alcohol, but not in men. The rest of the comparisons, which were statistically significant, are found in Table 2.

Table 2. Table 2. Comparisons between clinical and biochemical characteristics according to sex and presence of Metabolic Syndrome. MetS: Metabolic Syndrome, TyG: Triglycerides and Glucose indices, LAP: Lipid Accumulation Products and VAI: Visceral Adipose Index

Characteristics	Masculine (n = 1936)			Feminine (n = 2055)		
	MetS (-)	MetS (+)	P-value	MetS (-)	MetS (+)	P-value
Total (%)	1829 (84,47)	107 (5,53)		1555 (75,67)	500 (24,33)	
Age (years)	40 (30 - 55)	52 (39 - 64)	< 0,001	36 (27 - 46)	49 (40 - 58)	< 0,001
Body Mass Index (Kg/m2)	23,64 (21,70 - 26,26)	30,31 (27,83 - 33,18)	< 0,001	23,99 (21,71 - 26,32)	28,88 (26,32 - 31,72)	< 0,001
Smoking status (%)			0,231			0,861
No	205 (96,24)	8 (3,76)		818 (75,05)	272 (24,95)	
Yes	1624 (88,79)	99 (5,75)		619 (75,40)	202 (24,60)	
Alcohol drinking (%)			0,506			0,004
No	1796 (94,43)	106 (5,57)		1263 (74,21)	439 (25,79)	
Yes	33 (97,06)	1 (2,94)		174 (83,25)	35 (16,75)	
Physical Activity (%)			0,001			0,011
No	832 (96,41)	31 (3,59)		294 (80,33)	72 (19,67)	
Yes	997 (54,51)	76 (71,03)		1143 (73,98)	402 (26,02)	
Abdominal waist (cm)	87 (80,5 - 94)	105 (101,7 - 110)	< 0,001	84,7 (78,2 - 92)	97,75 (92,2)	< 0,001
Systolic blood pressure (mmHg)	110 (100 - 120)	130 (120 - 140)	< 0,001	108 (98 - 112)	120 (103 - 130)	< 0,001
Diastolic blood pressure (mmHg)	70 (60 - 80)	80 (70 - 90)	< 0,001	68 (60 - 70)	70 (66,5 - 80)	< 0,001
Glucose (mg/dl)	80 (75 - 86)	93 (85 - 109)	< 0,001	78 (73 - 84)	87 (80 - 97)	< 0,001
Triglycerides (mg/dl)	112 (81 - 157)	227 (173 - 313)	< 0,001	97 (75 - 126)	196 (244,5)	< 0,001
HDL - cholesterol (mg/dl)	42 (40 - 46)	39 (38 - 41)	< 0,001	43 (40 - 48)	42 (40 - 44)	< 0,001
MetS parameters						
LAP	25,32 (14,84 - 44,01)	99,15 (77,53 - 132,24)	< 0,001	29,32 (19,78 - 43,33)	88,01 (68,72 - 116,37)	< 0,001
VAI	1,84 (1,04 - 2,16)	3,45 (2,60 - 4,74)	< 0,001	1,88 (1,43 - 2,50)	4,07 (3,29 - 5,24)	< 0,001
TyG	8,40 (8,08 - 8,78)	9,30 (9,10 - 9,59)	< 0,001	8,23 (7,96 - 8,85)	9,07 (8,85 - 9,31)	< 0,001
MetS Components						
Central obesity (%)			< 0,001			< 0,001
No	1716 (98,45)	27 (1,55)		909 (98,27)	16 (1,73)	
Yes	113 (58,55)	80 (41,45)		528 (53,55)	458 (46,45)	
High blood pressure (%)			< 0,001	29 (1,86)	86 (17,00)	< 0,001
No	1727 (96,48)	63 (3,52)		1408 (78,35)	389 (21,65)	
Yes	102 (69,86)	44 (30,14)		29 (25,44)	85 (74,56)	
Hyperglycemia (%)			< 0,001			< 0,001
No	1762 (96,60)	62 (3,40)		1417 (79,12)	374 (20,88)	
Yes	67 (59,82)	45 (40,18)		20 (16,67)	100 (83,33)	
Hypertriglyceridemia (%)			< 0,001			< 0,001
No	1320 (99,70)	4 (0,30)		1288 (95,20)	65 (4,80)	
yes	509 (83,17)	103 (16,83)		149 (26,70)	409 (73,30)	
Low HDL - cholesterol (%)			< 0,001			< 0,001
No	1401 (97,49)	36 (2,51)		298 (99,00)	3 (1,00)	
Yes	428 (85,77)	71 (14,23)		1139 (70,75)	471 (29,25)	

Numeric values are presented in median and interquartile range

With relation to ROC analysis and AUC of the 4 indices tested for the identification of SMet, for both men and women, LAP had the highest AUC for men (AUC = 0.929; cut-off point = 59.85; Sens = 91.6 and Spec = 84.5) as for women (AUC = 0.950; cut-off point = 53.06; Sens = 92.4 and Spec = 86.4). In second place, for men, VAI index had the highest AUC (AUC = 0.905; cut-off point = 2.36; Sens = 91.6 and Spec = 79.7), while for women, it was TyG (AUC = 0.914; cut-off point = 8.70; Sens = 87.4 and Spec = 87.3). The LAP index showed significant differences with VAI to predict SMet (p < 0,05), while no differences were found with TyG. The rest of data are found in Table 3.

Figure 1 graphs AUC according to sex and age.

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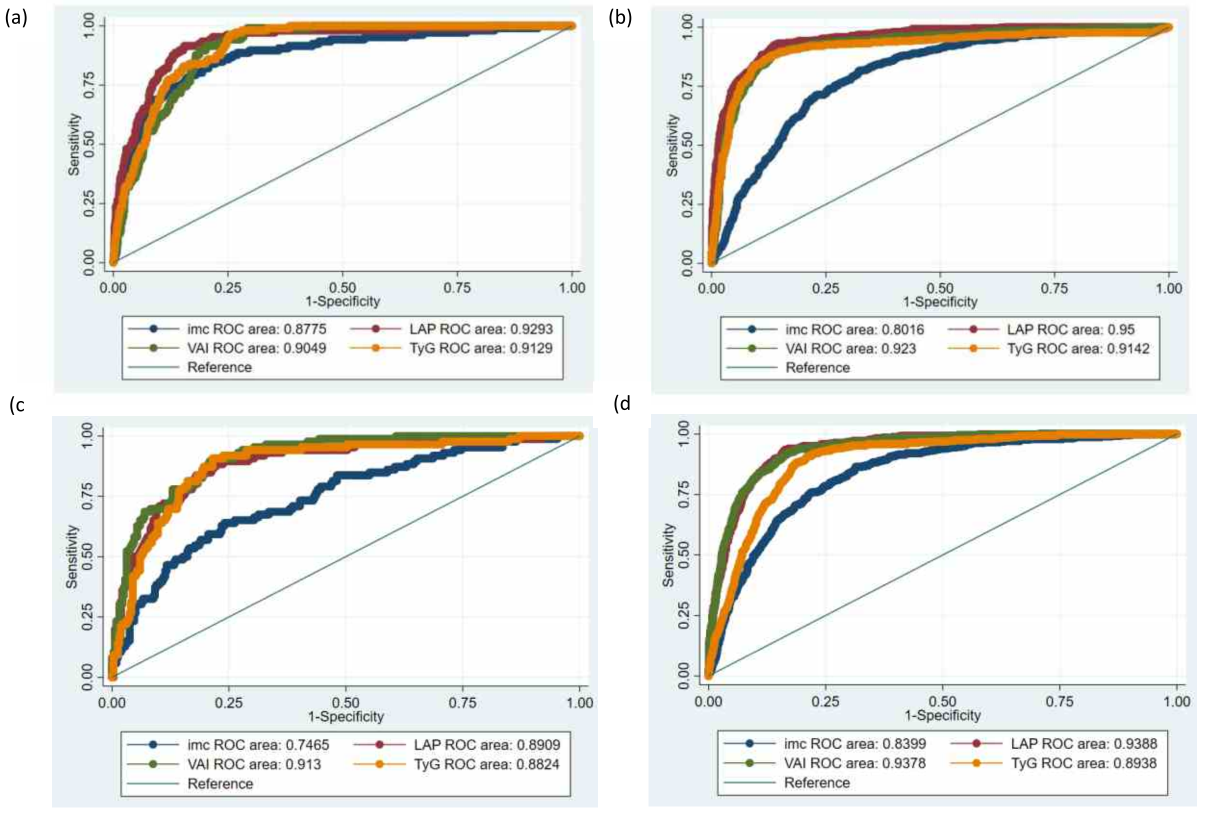

Figure 1. Diagnostic value comparison between triglyceride and glucose (TyG), Lipid accumulation product (LAP), and visceral adipose index (VAI) for metabolic syndrome in (a) men, (b) women, (c) under 65 years of age, and (d) over 65 years of age.

Table 3. Diagnostic values of TyG, LAP and VAI in men and women with metabolic syndrome.

Masculine	AUC* (IC 95%)	Cut-off point	Sens %* (CI 95%)	Spec % *(CI 95%)	PPV%* (Ci95%)	NPV %* (CI 95%)	LR+ %* (CI 95%)	LR- %* (CI 95%)	IY*
VAI**	0,905 (0,886 - 0,923)	2,36	91,6 (84,6 - 96,1)	79,7 (77,7 - 81,5)	20,9 (17,3 - 24,1)	99,4 (98,9 - 99,7)	4,50 (4,04 - 5,01)	0,10 (0,57 - 0,19)	0,713
LAP**	0,929 (0,907 - 0,952)	59,85	91,6 (84,6 - 96,1)	84,5 (82,8 - 86,2)	25,7 (21,4 - 30,4)	99,4 (98,8 - 99,7)	5,92 (5,24 - 6,68)	0,09 (0,05 - 0,18)	0,761
TyG**	0,913 (0,894 - 0,923)	8,77	96,3 (90,7 - 99,0)	74,3 (72,2 - 76,3)	18 (14,9 - 21,4)	99,7 (99,3 - 99,9)	3,75 (3,44 - 4,08)	0,05 (0,02 - 0,13)	0,708
IMC**	0,878 (0,842 - 0,913)	26,96	83,2 (74,7 - 89,7)	79,1 (77,1 - 80,9)	18,9 (15,4 - 22,7)	98,8 (98,1 - 99,3)	3,97 (3,51 - 4,49)	0,21 (0,14 - 0,32)	0.631
Feminine									
VAI**	0,923 (0,909 - 0,937)	2,92	87,6 (84,4 - 90,4)	86,6 (84,8 - 88,2)	67,7 (63,9 - 71,3)	95,6 (94,4 - 96,6)	6,52 (5,72 - 7,43)	0,14 (0,11 - 0,18)	0,748
LAP**	0,950 (0,940 - 0,960)	53,06	92.4 (89,7 - 94,6)	86,4 (84,6 - 88,1)	68,6 (65,0 - 72,1)	97,3 (96,2 - 98,0)	6,81 (5,99 - 7,74)	0,09 (0,06 - 0,12)	0,788
TyG**	0,914 (0,897 - 0,931)	8,70	87,4 (84,2 - 90,2)	87,3 (85,5 - 88,9)	68,8 (65,1 - 72,4)	95,6 (94,4 - 96,6)	6,86 (6,00 - 7,85)	0,14 (0,12 - 0,18)	0,751
BMI**	0,801 (0,781 - 0,822)	25,75	81,6 (77,9 - 84,9)	67,5 (65,1 69,8)	44,6 (41,4 - 47,9)	91,9 (90,2 - 93,5)	2,51 (2,31 - 2,70)	0,27 (0,23 - 0,33)	0,021

*AUC: area under the curve, Sens: sensitivity, Spec: specificity, PPV: positive predictive value, NPV: negative predictive value, LR+: Positive likelihood ratio, LR-: Negative likelihood ratio and YI: Youden's Index
CI 95%: Confidence interval at 95%
** VAI: visceral adipose index, LAP: lipid accumulation product, TyG: triglyceride and glucose index and BMI: body mass index

DISCUSSION

Principle findings

With the objective of finding a better indicator to predict SMet, this study evaluated BMI, LAP< VAI, TyG indices in a sample of adult Peruvian inhabitants. In general, we found that LAP, followed by TyG, were practical parameters to identify SMet, for both men and women and independent of age.

Comparison with other studies

LAP was mentioned first by Khan [24], where it was considered an excessive marker of lipid accumulation in adults, and very useful for predicting SMet [25]. In the current manuscript, LAP was considered the best indicator for predicting SMet, for their AUC as for their sensitivity and specificity values. These results coincide with some others found in literature. The study by Chiang and Koo [19] found that LAP was a better SMet predictor than VAI and TyG in Thai adults older than 50 years of age, with a cut-off point of 31.6 and with a sensitivity of 88% and 60% for men and women, respectively. In another study carried out by Spaniards[26] they found the same regarding LAP with cut-off points of 51.82 and 48.09 with sensitivity of 81 % and 78 % for men and women, respectively. In the work by Kyung-A y Young-Joo [16]., LAP values were the best predictors of SMet.

The difference with the cut-off points with the current manuscript could be due to ethnic and biomarker frequency differences that make up LAP and SMet. In the study of 522 healthy Argentinians, by Tellechea [27], the LAP cut-off point 53.63 demonstrated the greatest precise diagnosis for SMet, with a sensitivity of 0.83 and specificity of 0.83. In a study in Brazil, although the cut-off points were different, we must take into account that they used criteria different than ATPIII[20].

VAI is an important indicator related in an important manner with Smet [28]. In this study, LAP occupied second place as a diagnostic predictor of SMet in men, and third in women, behind TyG. This differs from other research works. In a study of Iranian population of 35-65 year-olds, Baveicy et al [21] found that VAI had a greater predictive value for SMet than other biomarkers. The same found in the study by Stefanescu et al [29]., who worked with Peruvian inhabitants, residents of Callao. However, LAP was not considered among its variables, and it was only a localized population. The same was found with respect to VAI in the study by Motamed et al[30]. The ethnic and dietary reasons may be involved. Regarding TyG, no differences were found with AUC. However, LAP sensitivity and specificity values are better balanced than those of TyG, being more useful the first as a diagnostic test.

Nevertheless, we must consider its role in SMet. Although TyG was studied at first as a predictor of RI[31], later studies have considered it as an SMet marker. In the study by Kyung-A and Young-Joo [16], TyG values increased as SMet component numbers increased. Aslan Çin et al [11]. and Anggonari [13] highlight its SMet diagnostic value in adolescents. On the other hand, the cut-off point for this study differed for men (8.77) as for women (8.70), which differ from other works such as Li et al [32], who gave a cut-off point of 8.81; or in the study by Moon [14]., who reported a cut-off of 8.45. Reasons why TyG index may not be the best indicator for SMet are that, although it includes glucose and triglycerides, it does not include AC, which some authors consider it as the most important SMet marker[33].

Regarding BMI, it demonstrated the least SMet diagnostic capacity for both sexes. A metanalysis by Lee et al [34]. reported that BMI was the worst discriminator to predict diabetes, hypertension, or dyslipidemia. Herrera et al. also reported that BMI was the least precise measure for coronary disease risk [35]. In a study by Thai-Hua[17], other indices, such as VAI surpassed BMI in predicting metabolic syndrome.

Result interpretations

Among all the different scenarios that could lead us to SMet, one of the most important is visceral adiposity. In several studies, it has been demonstrated that visceral adipose tissue has a greater rate of lipolysis and a greater production of adipocytokines, such as interleukin-6, the inhibitor of plasminogen-1 activator and tissue macrophage activation, which is more related with cardiometabolic risks in comparison to subcutaneous adipose tissue[36,37].

At the same time, a release of free fatty acids may cause the accumulation off at intraorganically, such as liver and pancreas. The latter produces, ultimately, a state of insulin resistance, increasing the hepatic production of glucose, reduction of hepatic insulin clearance, increase in abdominal waist, increase of circulating triglycerides, and, finally, all which lead to SMet[38].

Study limitations

Some limitations should be considered. First, this is a cross-sectional study, which means we cannot evaluate the association of these variables with SMet in a longitudinal form. Second, the database was not collected for the purpose of this study. Furthermore, the survey was carried out in the years 2004-2005, which is possible the abdominal circumference of a similar current population may be different. However, it is important to consider that it offers us a first glimpse of diagnostic performance of variables that have been

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tested. Third, while the participants are Peruvians from different regions of the country, it is probable that it is not completely representative, but given the characteristics that they may share in common, some inference may be made.

CONCLUSIONS

The LAP index had the greatest SMet diagnostic performance, for men and women, independent of age, with optimal cut-off points of 59.85 and 53.06, respectively. The LAP index is easy to use and does not require expensive laboratory tests, making it an easy-to-use index in primary care compared to VAI that requires AC, TG, BMI and HDL cholesterol for its calculation. If the current results are confirmed in future research, LAP should be included as an SMet predictor primary health care.

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