Original Article

JHSMR Journal of Health Science and Medical Research

Prevalence of Metabolic Syndrome and Its Prediction by Simple Adiposity Indices in Thai Adults

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Received 11 August 2020 ● Revised 28 September 2020 ● Accepted 9 October 2020 ● Published online 25 March 2021

Abstract:

Objective: Thai adults, have increased risk of being diagnosed with metabolic syndrome (MetS). Hence, early discrimination of MetS, with a simple and high accuracy index, appears necessary. However, the application of the discriminating ability of Lipid Accumulation Product (LAP), which is an emergent indicator of central lipid accumulation, to MetS among Thai people has not been investigated. This present study's purposes were to investigate the nationwide prevalence of MetS, and the ability of LAP in discriminating this disorder.

Material and Methods: Cross-sectional secondary data analysis was performed in 2018, using primary data from the Thai National Health Examination Survey, 2009. A total of 18,642 Thailanders ≥18 years were recruited. MetS was diagnosed by the National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP) and International Diabetes Federation (IDF).

Results: Overall, the prevalence of MetS-NCEP/ATP and MetS-IDF in Thai adults was 20.0% and 27.0%, respectively. LAP showed outstanding discriminating ability for MetS in both definitions (the cut-off point of 34.38 and 37.96 cm.mmol/L; area under the curve of 0.889 and 0.915 for NCEP/ATP and IDF, respectively). LAP performed the closest agreement in discriminating MetS-NCEP/ATP (κ=0.598, p-value<0.001) and MetS-IDF (κ=0.577, p-value<0.001). Logistic regression analysis exhibited a strong association of the LAP cut-off point with MetS, with the odds ratio being from 23.37 to 27.22 (p-value<0.001).

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J Health Sci Med Res .....
doi: 10.31584/jhsmr.2021791
www.jhsmr.org

Conclusion: These study results revealed that LAP was strongly associated with MetS, had an outstanding and reliable diagnostic accuracy for discriminating MetS in Thai adults, which might be helpful for early detection of MetS among vulnerable populations.

Keywords: adiposity index, cut-off point, metabolic syndrome, lipid accumulation product, Thai adults

Introduction

Metabolic syndrome (MetS) had contributed to the major causes of cardiovascular diseases, diabetes mellitus and even all-causes of mortality.[1-3] Therefore, the diagnosis and treatment of the underlying risk factors for MetS appear to be a crucial strategy for the minimization of all-cause mortality associated with MetS in the general population.[3] The prevalence of this disorder has continuously increased, and ranges between 24.0% to 32.6% by different definitions among Thai adults ≥35 years.[4] By tasking force on determining insulin resistance (IR), as a dominant cause of MetS, the World Health Organization (WHO) is an avant-garde to propose the MetS definition.[5] Over time, several diagnostic criteria have been introduced, and have disclosed that MetS is an abnormality of co-occurrence of several risk factors, including abdominal obesity, hypertension, dyslipidemia, dysinsulinemia and IR.[6] Currently, the diagnosis of MetS in the Thai population is based on The National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP), or International Diabetes Federation (IDF).[4] Consequently, individuals are diagnosed with MetS by undergoing five assessments of waist circumference (WC), blood pressure (BP), fasting blood glucose (FBG), serum triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C).[6] Therefore, it would be useful if there was a simpler, quicker and inexpensive indicator with high accuracy for early discriminating of MetS in the community.

Previous studies affirmed the strong association of body adiposity with obesity-related diseases.[7] Lipid accumulation product (LAP), first introduced by Kahn, is a novel index based on a combination of WC and TG. This index appeared to be an emergent indicator for assessing the central lipid accumulation.[8] Both components (WC and TG) tend to increase with age; thus, their values subjectively accumulate over time: having more detrimental influences on the metabolic system.[8] Numerous studies have been conducted to examine its diagnosis ability. LAP has been reported as being superior to other adiposity indicators, such as body mass index (BMI), WC, waist-to-hip ratio and waist-to-height ratio (WHtR), to predict MetS among Spanish[9], and Iranian populations.[10] Results for the area under the curve (AUC) of 0.91 and 0.901 for LAP in discriminating MetS has been documented in healthy Argentinian[11], and Taiwanese people ≥50 years.[12]

Thai adults, have an increased risk of being diagnosed with MetS, due to their greater abdominal and visceral adiposity than Caucasians with a similar BMI.[13] It has been suggested that central lipid distribution are distinct in different groups and ethnics; for instance, South Asians are more likely to accumulate additional fat in their abdomen and truncal part, which consequently possess greater WC, larger abdominal diameters, and thicker trunk skinfolds for a given weight in comparison with European individuals.[14] Meanwhile, Asians and Japanese American subjects tend to deposit more intra-abdominal fat or visceral fat during weight gaining.[14] Hence, early discrimination of MetS, with a simple and high accuracy index appears necessary. However, the application of the discriminating ability of LAP to MetS in the Thai population has not been investigated.

By re-analyzing the National Health Examination Survey 2009 (NHES-IV), this present study's objectives were to determine the prevalence of MetS in Thai adults ≥18 years and older. Furthermore, the study also assessed the MetS discriminatory ability of LAP, by employing numerous anthropometric and adiposity indices; including, traditional indices (BMI, WC, WHtR), non-traditional indices (cardiometabolic index (CMI) and the visceral adiposity index (VAI)).

Material and Methods

Study design and population: This present study analysed the database from NHES-IV. NHES-IV; ethical approval was performed by the Ethical Review Committee for Research in Human Subjects, Ministry of Public Health of Thailand. The design is described in the previous publication.[15] Multistage probability cluster sampling technique was applied, and its sampling units were divided into four steps. Step one, 5 provinces in each of the 4 main regions (north, northeast, central, and south and Bangkok); step two, 2-3 districts in each selected province; step three, 13-14 electoral units (EU) or villages in each district; and step four, individuals among six age groups of each gender from each EU or village. A complete set of demographic and biochemistry variables were collected from all eligible subjects; with pregnancy being an exclusion factor. Finally, 18,642 Thai's 18 years: 8,910 males and 9,732 females, were analysed. Since the present study is a restrospective secondary data analysis conducted in 2018, a request for exemption of informed consent for this study was submitted and approved by Institutional Review Board. The study protocol was approved by the Institutional Review Board of Mahidol University, Thailand (Protocol number MU-CIRB 2018/106.2105).

Data collection: A prior report described NHES-IV data collection procedures in detail.[15] Key variables included demographic data; for example: age, education background, habitant's area; smoking and alcohol usage; medical history and physical activity patterns. Sitting BP was measured using an automatic monitor. Anthropometrical characteristics regarding body weight, height, WC, hip circumference (HC) were collected. Body weight and height was measured using a calibrated digital scale and stadiometer, using standard procerdures. HC was measured at the height of the greater trochanter to the nearest 0.1cm around the thighs, and WC was measured at a horizontal plane midway between the iliac crest and lower rib margin in centimeters to the nearest 0.1 cm. Biochemical data were analyzed by fasting venous blood samples, which were collected in the morning from participants after 12-hours of fasting. TG was analyzed using the enzymatic colorimetric method; HDL-C, low-density lipoprotein cholesterol level (LDL-C) were analyzed by homogeneous enzymatic colorimetric methods; FBG were analyzed by the hexokinase enzyme method. All glucose and lipid parameters were carried out using the Hitachi 917 biochemistry analyzing machine (Roche Diagnostics, Basel, Switzerland).

Definitions: Individuals were diagnosed as having MetS when they meet the criteria by definitions of NCEP/ATP and/or IDF. The NCEP/ATP defined that MetS individuals are a person who has ≥3 metabolic abnormalities (BP≥130/85 mmHg, WC>90/80 cm for males/females, TG≥150 mg/dL, FPG≥100 mg/dL, HDL-C<40/50 mg/dL for males/females.[6] According to the IDF criteria, people are diagnosed with MetS when they have an essential component of central obesity; with WC≥90/80 cm for males and females, respectively, together with having ≥2 metabolic abnormalities (BP≥130/85 mmHg, TG≥150 mg/dL, FPG ≥100 mg/dL, HDL-C<40/50 mg/dL for males/famales.[6]

Formulas: BMI was calculated by Quetelet's formula, as body weight (kg) divided by height squared (m^2); WHtR was calculated by dividing WC (cm) with height (cm); LAP was calculated: [WC (cm) - 65] × [TG (mM)] for males, [WC (cm) - 58] × [TG (mM)] for females;[8] Cardiometabolic

index (CMI) was calculated: TG/HDL-C × WHtR.[16] VAI was calculated as follows, males: VAI = {WC (cm)/ [39.68 + (1.88 × BMI)]} × (TG/1.03) × (1.31/HDL-C); females: VAI = {WC (cm)/ [39.58 + (1.89 × BMI)]} × (TG/0.81) × (1.52/HDL-C); wherein TG and HDL-C values were expressed in mM.[17]

Statistical analysis: Complex survey analysis, including clustering, stratification and weighting, was employed to take into account the probability sampling design. Descriptive statistics were reported as age-adjusted arithmetic mean, with a 95% confidence interval (95% CI). Demographical and biochemical parameters, between subjects having MetS and not having MetS, were compared using Mann–Whitney U test or chi-squared test appropriately. Chi-squared test was used to examine the differences in MetS prevalence. The overall p for a trend of MetS prevalence was analyzed by Mantel-Haenszel chi-square test. We used the cohen's kappa correlation coefficient to assess the agreement between WHtR, LAP and CMI and the references (NCEP/ATP and IDF). The interpretation suggested by Landis and Koch was used as follows: poor-to-fair agreement ($\kappa \leq 0.40$), moderate agreement (κ of 0.41-0.60), substantial agreement (κ of 0.61-0.80) and excellent agreement (κ of 0.81-1.0). Multiple logistic regression examined the association of WHtR, LAP and CMI, with the presence of MetS expressed by odds ratios (ORs), as categorized into per 1 standard deviation (S.D.) increment of the variable, and the cut-off point. Receiver-operating characteristic (ROC) curves evaluated the discriminating ability of adiposity indices to MetS. We determined an optimal cut-off value for ROC analysis to maximize Youden's index (J). The J can be defined as: maximum = sensitivity + specificity–1.[18] The comparison of AUC, for each indicator, were made via the recommendation of Hanley and McNeil.[19] Values for each AUC could be ranged from 0 to 1, with a value of 1 indicating perfect diagnostic accuracy, and one with 0.5 having no discrimination power. Sensitivity (Sen), specificity (Spe), positive predictive value (PPV) and negative predictive value (NPV), for different indices' cut-off points, in discriminating MetS were calculated and expressed by percentages; with a 95% CI. IBM-SPSS Statistic for Windows, v 24.0 (IBM Corp., Armonk, New York, The United States of America) were applied for all statistical analyses: a CI of 95% was adopted for all tests. Two-sided p-value<0.050 was considered statistically significant.

Results

Characteristics for the 18,642 subjects, with 8,910 males (47.8%) and 9,732 females (52.2%), are presented in Table 1. Regardless of gender, Thai adults having MetS were significantly older; lived abundantly in urban areas; appeared to be lower educated and conduced less physical activities; had higher body weights, HC and BP. Despite having lower smoking and alcohol consumption, they appeared to have less favorable glucose and lipid metabolism profiles (high FBG, high TG, high LDL-C in addition to low HDL-C) than people without the presence of MetS. Individuals having MetS showed increases in all adiposity indicators: specifically BMI, WC, WHtR, LAP, CMI and VAI, in comparison to those not having MetS.

The age-adjusted prevalence of MetS among Thai adults, by different definitions, is reported in Table 2. Overall, 20.0% to 27.0% of adults were diagnosed with MetS; depending on each definition. The prevalence of NCEP/ATP-defined MetS was 22.2% (95% CI: 20.42-23.91) in males and 31.7% (95% CI: 29.89-33.42) in females. A lower MetS prevalence was reported by IDF definition. IDF-defined MetS was given to 13.3% of males (95% CI: 11.71-14.84) and 26.4% of females (95% CI: 24.62-28.21). An age-related increase in the presence of MetS was observed. The corresponding prevalence of MetS defined by NCEP/ATP and IDF among adults aged 18-29 was 9.6% (95% CI: 7.93-11.25) and 8.4% (95% CI: 6.70-10.08),

Table 1 Characteristics of subjects having metabolic syndrome and not having metabolic syndrome, according to the National Cholesterol Education Program/Adult Treatment Panel-III definition

Variables	Not having MetS	Having MetS	p-value
Number of subjects (person)	12,641	6,001	-
Age (years)	43.2 (42.7-43.7)	51.3 (50.8-51.9)	<0.001
Living area			
Rural	70.6 (62.9-77.3)	67.0 (59.0-74.2)	<0.001
Urban	29.4 (22.7-37.1)	33.0 (25.8-41.0)	<0.001
Education background			
Illiterate	3.7 (3.1-4.4)	4.5 (3.9-5.3)	<0.001
Primary school	58.0 (55.3-60.7)	71.3 (69.0-73.5)	<0.001
Secondary and vocational	31.4 (29.6-33.2)	19.8 (18.0-21.7)	<0.001
University and higher	6.9 (5.9-8.1)	4.4 (3.5-5.5)	<0.001
Current regular smoking	23.0 (21.5-24.5)	15.2 (14.2-16.3)	<0.001
Alcohol drinking consumption within 12 months	48.8 (46.6-50.9)	37.4 (35.5-39.5)	<0.001
Alcohol drinking consumption level			
Abstainer	63.8 (62.1-65.4)	74.2 (72.4-76.0)	<0.001
Low risk	27.1 (25.2-29.0)	17.3 (15.7-19.0)	<0.001
Moderate risk	2.9 (2.5-3.4)	2.5 (1.9-3.3)	<0.001
High risk	2.1 (1.8-2.4)	1.9 (1.5-2.6)	<0.001
Severe risk	2.6 (2.2-3.0)	1.8 (1.4-2.4)	<0.001
Drinking N/A amount	1.5 (1.1-2.1)	2.2 (1.5-3.3)	<0.001
Physical activity level			
Low level	17.5 (15.5-19.8)	20.3 (18.2-22.6)	<0.001
Moderate level	24.7 (23.5-26.1)	27.1 (25.8-28.6)	<0.001
High level	57.8 (55.1-60.3)	52.6 (50.1-55.0)	<0.001
Height (cm)	159.3 (159.0-159.5)	158.1 (157.7-158.4)	<0.001
Body Weight (kg)	57.8 (57.3-58.2)	68.4 (67.6-69.2)	<0.001
BMI (kg/m^2)	22.7 (22.6-22.9)	27.3 (27.0-27.5)	<0.001
WC (cm)	76.4 (75.9-76.9)	89.3 (88.7-90.0)	<0.001
HC (cm)	91.0 (90.6-91.3)	98.9 (98.5-99.4)	<0.001
SBP (mmHg)	118.4 (117.8-119.1)	134.2 (133.1-135.3)	<0.001
DBP (mmHg)	73.6 (73.1-74.0)	81.7 (81.2-82.3)	<0.001
FBG (mg/dL)	85.6 (84.2-87.0)	105.3 (102.7-107.8)	<0.001
TG (mg/dL)	125.8 (120.8-130.8)	231.2 (222.6-239.7)	<0.001
HDL-C (mg/dL)	49.2 (48.4-50.1)	40.7 (40.1-41.3)	<0.001
LDL-C (mg/dL)	126.7 (124.5-128.9)	133.6 (130.5-136.7)	<0.001
WHtR	0.48 (0.47-0.48)	0.57 (0.56-0.57)	<0.001
LAP	21.5 (20.7-22.3)	73.4 (70.3-76.6)	<0.001
CMI	1.37 (1.29-1.45)	3.47 (3.30-3.63)	<0.001
VAI	1.76 (1.67-1.85)	4.25 (4.03-4.48)	<0.001

Value is expressed as mean (interquartile range) or percentage (95%CI), as appropriate. The p-value denotes significant differences between subjects having MetS and not having MetS. Differences were compared by Mann-Whitney U test, or chi-square test appropriately.

BMI=Body Mass Index, CMI=Cardiometabolic Index, DBP=Diastolic Blood Pressure, FBG=Fasting Blood Glucose, HC=Hip Circumference, HDL-C=High density lipoprotein cholesterol, MetS=Metabolic Syndrome, NCEP/ATP III=National Cholesterol Education Program/Adult Treatment Panel-III, LAP=Lipid Accumulation Product, LDL-C=Low density lipoprotein cholesterol, SBP=Systolic Blood Pressure, TG=Triglyceride, VAI=Visceral Adiposity Index, WC=Waist Circumference, WHtR=Waist-to-Height Ratio

Table 2 Age-adjusted prevalence of metabolic syndrome among Thai adults, by the National Cholesterol Education Program/Adult Treatment Panel-III and International Diabetes Federation definition

Definition	Overall subjects	Age (years)			p for trend
		18-29	30-59	≥60	
Both genders					
NCEP/ATP	27.0 (25.6-28.5)	9.6 (7.9-11.3)	27.6 (26.0-29.1)	41.3 (39.7-42.9)	<0.001
IDF	20.0 (18.6-21.5)	8.4 (6.7-10.1)	21.0 (19.5-22.4)	26.9 (25.1-28.7)	<0.001
Males					
NCEP/ATP	22.2 (20.4-23.9)	9.2 (7.5-11.0)	23.5 (21.5-25.6)	30.3 (28.5-32.2)	<0.001
IDF	13.3 (11.7-14.8)	7.2 (5.3-9.0)	14.2 (12.6-15.9)	15.7 (13.3-18.0)	<0.001
Females					
NCEP/ATP	31.7 (29.9-33.4)	10.0 (7.6-12.5)	31.3 (29.4-33.3)	50.3 (48.5-52.2)	<0.001
IDF	26.4 (24.6-28.2)	9.8 (7.4-12.3)	27.3 (25.4-29.2)	36.1 (34.0-38.2)	<0.001

Values are expressed as prevalence, with a 95% CI indicated in the parentheses. The chi-square test compared the prevalence between males and females corresponding MetS definition and among different age-groups (all p-value<0.001). The overall p for trend of MetS prevalence was analyzed by Mantel-Haenszel chi-square test.
IDF=International Diabetes Federation, NCEP/ATP=The National Cholesterol Education Program/Adult Treatment Panel III

respectively; for those aged 30-59, it was 27.6% (95% CI: 26.04-29.06) and 21.0% (95% CI: 19.53-22.38); and for people ≥60 years, it was 41.3% (95% CI: 39.73-42.93) and 26.9% (95% CI: 25.08-28.73)

Table 3 illustrates the discriminating ability of different adiposity indicators for MetS, by different definitions. The top four excellent abilities to discriminate MetS-NCEP/ATP in Thai adults aged ≥18 years old and older was for LAP (AUC: 0.889; 95% CI: 0.884-0.894), followed by CMI (AUC: 0.871; 95% CI: 0.866-0.876). The third best performance was VAI (AUC: 0.868; 95% CI: 0.863-0.873), followed by WHtR (AUC: 0.823; 95% CI: 0.817-0.830). By applying IDF, WHtR appeared to be the most reliable indicators in discriminating MetS (AUC: 0.926; 95% CI: 0.922-0.929), the second-best discriminating ability was for LAP (AUC: 0.915; 95% CI: 0.911-0.919). Notably, the AUC value of CMI and VAI was decreased, which was significantly inferior to BMI (p-value<0.001). The influence of age on the discriminating ability was explored in stratified analyses (ages 18-29, 30-59, and ≥60 years), and the results exhibited that the overall trend did not vary substantially by age (data was omitted). Regarding the optimal cut-off point, the best value for LAP cut-off point in this study population to discriminate MetS according to NCEP/ATP and IDF criteria was 34.38 cm.mmol/L and 37.96 cm.mmol/L, respectively.

As shown in Table 3, the indicators with highest AUC value were LAP, CMI, VAI, and WHtR. These indices were selected for further exploration. However, VAI was not chosen due to its complication (with five components), expensiveness, and being statistically inferior to LAP in discriminating MetS among Thai adults. Therefore, WHtR, LAP and CMI were further analyzed. Cohen's Kappa coefficients between WHtR, LAP and CMI, and two references (NCEP/ATP and IDF) in the discrimination of MetS in Thai adults aged ≥18 years old and older were performed (Table 4). Overall, LAP performed with moderate agreements in both references (κ-values were 0.577 and 0.598, with IDF and NCEP/ATP, respectively); whereas, CMI and WHtR showed good agreement with only one definition. Specifically, the highest agreement values for MetS-NCEP/ATP were reported in LAP (κ=0.598, p-value <0.001), followed by CMI (κ=0.567, p-value<0.001), and

Table 3 Discriminating ability of different adiposity indices, with metabolic syndrome, based on the National Cholesterol Education Program/Adult Treatment Panel-III and the International Diabetes Federation definition

Indices	AUC	Cutoff	J	Sensitivity	Specificity	Likelihood ratio	PPV	NPV
NCEP/ATP criterion								
Body mass index	0.765 (0.758–0.772)	24.24	0.418	70.1 (68.9–71.2)	71.7 (70.9–72.5)	2.47 (2.39–2.55)	54.0 (52.9–55.1)	83.4 (82.7–84.1)
Waist circumference	0.804[a] (0.797–0.810)	80.47	0.488	80.1 (79.0–81.1)	68.7 (67.9–69.5)	2.56 (2.49–2.63)	54.9 (53.8–55.9)	87.9 (87.2–88.5)
Waist-to-height ratio	0.823[a,b] (0.817–0.830)	0.52	0.513	76.7 (75.6–77.8)	74.5 (73.8–75.3)	3.01 (2.91–3.11)	58.8 (57.7–59.9)	87.1 (86.4–87.7)
Lipid accumulation product	0.889[a–d] (0.884–0.894)	34.38	0.624	80.0 (78.9–81.0)	82.4 (81.8–83.1)	4.56 (4.38–4.74)	68.4 (67.3–69.5)	89.7 (89.1–90.2)
Cardiometabolic index	0.871[a–c] (0.866–0.876)	1.70	0.603	80.4 (79.4–81.4)	79.7 (79.0–80.4)	3.96 (3.82–4.11)	65.3 (64.2–66.4)	89.5 (88.9–90.1)
Visceral adiposity index	0.868[a–d] (0.863–0.873)	2.13	0.590	80.9 (79.9–81.9)	78.0 (77.3–78.8)	3.69 (3.56–3.82)	63.6 (62.5–64.7)	89.6 (89.0–90.2)
IDF criterion								
Body mass index	0.867 (0.861–0.872)	24.61	0.596	84.8 (83.6–85.8)	74.8 (74.0–75.5)	3.36 (3.26–3.46)	49.4 (48.3–50.6)	94.4 (94.0–94.8)
Waist circumference	0.907[a] (0.903–0.911)	80.03	0.672	100.0 (99.9–100.0)	67.2 (66.4–68.0)	3.05 (2.98–3.12)	47.0 (46.0–48.1)	100.0 (99.9–100.0)
Waist-to-height ratio	0.926[a,b] (0.922–0.929)	0.53	0.728	93.1 (92.2–93.8)	79.6 (78.9–80.2)	4.55 (4.41–4.71)	57.0 (55.8–58.2)	97.5 (97.2–97.8)
Lipid accumulation product	0.915[a,b] (0.911–0.919)	37.96	0.677	86.0 (84.9–87.0)	81.7 (81.1–82.3)	4.70 (4.53–4.88)	57.8 (56.5–59.0)	95.2 (94.9–95.6)
Cardiometabolic index	0.814[a–d] (0.807–0.820)	1.60	0.499	81.5 (80.3–82.6)	68.3 (67.6–69.1)	2.57 (2.50–2.65)	42.8 (41.7–43.9)	92.7 (92.2–93.2)
Visceral adiposity index	0.808[a–e] (0.801–0.814)	2.06	0.485	80.3 (79.0–81.5)	68.2 (67.5–69.0)	2.53 (2.46–2.60)	42.4 (41.3–43.5)	92.2 (91.7–92.7)

Values in parentheses are 95% confidence intervals (CI)

AUC=Area under curve, IDF=International Diabetes Federation, J=Youden index, NCEP/ATP=The National Cholesterol Education Program/Adult Treatment Panel III, NPV=negative predictive value, PPV=positive predictive value

[a]Indicates a significant difference as compared to BMI, [b]Indicates a significant difference as compared to WC, [c]Indicates a significant difference as compared to WHtR, [d]Indicates a significant difference as compared to LAP, [e]Indicates a significant difference as compared to CMI

the lowest of WHtR (κ=0.474, p-value<0.001). Whereas, the coefficient values for MetS-IDF were WHtR (κ=0.593, p-value<0.001), followed by LAP (κ=0.577, p-value <0.001), and poor-to-fair agreement was observed in CMI (κ=0.378, p-value<0.001).

Table 4 Cohen's kappa coefficient (κ) between standard definitions (NCEP/ATP or IDF) and adiposity indices (WHtR, LAP, and CMI)

Variables	Cohen's kappa coefficient (κ)	SE	p-value
NCEP/ATP definition			
WHtR (Cut-off point >0.52)	0.474	0.006	<0.001
LAP (Cut-off point >34.38)	0.598	0.006	<0.001
CMI (Cut-off point >1.70)	0.567	0.006	<0.001
IDF definition			
WHtR (Cut-off point >0.53)	0.593	0.006	<0.001
LAP (Cut-off point >37.96)	0.577	0.006	<0.001
CMI (Cut-off point >1.60)	0.378	0.006	<0.001

Values are expressed as Cohen's Kappa coefficient value (κ). CMI=Cardiometabolic Index, IDF=International Diabetes Federation (IDF), NCEP/ATP=The National Cholesterol Education Program/Adult Treatment Panel III (NCEP/ATP), LAP=Lipid Accumulation Product, SE=Standard error, WHtR=Waist-to-Height Ratio

Table 5 exhibits the multiple adjusted association between WHtR, LAP and CMI, and the prevalence of MetS. The result revealed that LAP consistently remained as having a robust association with MetS in all models. For each, additional 1 S.D. increment of the adiposity index score in the simplest model (model 1), the OR of MetS-NCEP/ATP were raised from 4.84 to 21.10; as highest from LAP, OR: 21.10 (95% CI: 17.90-24.87), followed by CMI, OR: 6.17 (95% CI: 5.57-6.83); and WHtR, OR: 4.84 (95% CI: 4.41-5.32). By applying the IDF definition, LAP continuously exhibited the highest association with MetS, by OR of 32.00 (95% CI: 28.00-36.56) value, followed by WHtR (OR: 11.24) and CMI (OR: 3.68). After adjusting for age, demographic, lifestyle and biochemical confounding factors, we observed the increment of OR is associated with MetS in LAP and CMI; whereas, reduction in WHtR [LAP, OR: 22.09 (95% CI: 18.18-26.85); CMI, OR: 8.56 (95% CI: 7.76-9.45) and WHtR, OR: 4.70 (95% CI: 4.23-5.23); all p-values<0.001]. Similar trending was observed in the IDF definition.

These results revealed that LAP was strongly associated with the odds of the presence of MetS by both definitions. The association between abnormal adiposity indices (defined by excess of the optimal cut-off value) and MetS was also analyzed. In the most complex model (model 3), Thai adults having abnormal adiposity indicators were approximately 10-23 times and 11-42 times more likely to have MetS (defined by NCEP/ATP and IDF, respectively) than those at the normal cut-off point. Specifically, the highest OR indicating the strongest association with MetS-NCEP/ATP were for CMI and LAP [OR: 23.39 (95% CI: 20.81-26.30) and OR: 23.37 (95% CI: 20.61-26.49), respectively]; whereas, WHtR had a lower association (OR: 10.38 95% CI: 9.23-11.67). Inversely, the cut-off point of WHtR performed as having the strongest association with MetS-IDF (OR: 42.51), followed by LAP (OR: 27.22) and CMI (OR: 4.40).

Discussion

Our findings revealed that LAP has outstanding discriminating ability to MetS, with an AUC of 0.889 and 0.915, by NCEP/ATP and IDF definitions. Compared to other advanced adiposity indicators (for instance. VAI, and CMI), LAP appeared to be a simpler indicator, requiring only two components of TG and WC. This present study indicated the nationwide age-adjusted prevalence of MetS-NCEP/ATP and MetS-IDF among Thai adults as 27.0% and 20%, respectively. These prevalence are lower than previous studies in Thailand as well as in other Asian

Table 5 Multivariate logistic regression of WHtR, LAP and CMI for the presence of metabolic syndrome, defined by the National Cholesterol Education Program/Adult Treatment Panel-III and International Diabetes Federation definition in Thai adults aged ≥18 years old and older

Variable	Model 1 Odds ratio (95% CI)	p-value	Model 2 Odds ratio (95% CI)	p-value	Model 3 Odds ratio (95% CI)	p-value
NCEP/ATP definition						
WHtR						
Cut-off point >0.52	11.10 (10.00-12.31)	<0.001	11.28 (10.19-12.49)	<0.001	10.38 (9.23-11.67)	<0.001
Per 1 S.D. increment	4.84 (4.41-5.32)	<0.001	5.04 (4.59-5.52)	<0.001	4.70 (4.23-5.23)	<0.001
LAP						
Cut-off point >34.38	23.03 (20.53-25.84)	<0.001	23.21 (20.66-26.07)	<0.001	23.37 (20.61-26.49)*	<0.001
Per 1 S.D. increment[a]	21.10 (17.90-24.87)	<0.001	22.28 (18.78-26.44)	<0.001	22.09 (18.18-26.85)*	<0.001
CMI						
Cut-off point >1.70	16.21 (14.60-18.00)	<0.001	18.62 (16.50-21.03)	<0.001	23.39 (20.81-26.30)	<0.001
Per 1 S.D. increment[a]	6.17 (5.57-6.83)	<0.001	7.23 (6.55-7.97)	<0.001	8.56 (7.76-9.45)	<0.001
IDF definition						
WHtR						
Cut-off point >0.53	48.01 (40.78-56.53)	<0.001	46.38 (39.47-54.49)	<0.001	42.51 (35.83-50.43)	<0.001
Per 1 S.D. increment	11.24 (9.48-11.33)	<0.001	11.34 (9.51-13.52)	<0.001	10.87 (9.02-13.09)	<0.001
LAP						
Cut-off point >37.96	30.09 (26.53-34.14)	<0.001	31.82 (28.15-35.97)	<0.001	27.22 (24.07-30.77)	<0.001
Per 1 S.D. increment[a]	32.00 (28.00-36.56)	<0.001	41.39 (35.37-48.44)	<0.001	39.44 (33.36-46.63)	<0.001
CMI						
Cut-off point >1.60	10.27 (9.12-11.57)	<0.001	12.04 (10.52-13.77)	<0.001	11.20 (9.89-12.67)	<0.001
Per 1 S.D. increment[a]	3.68 (3.42-3.97)	<0.001	4.35 (4.02-4.70)	<0.001	4.40 (4.09-4.74)	<0.001

Model 1: adjusted for age

Model 2: further adjusted for living area, education background, current-regular smoking, current alcohol consumption, alcohol consumption level and physical activity.

Model 3: further adjusted for SBP, DBP, fasting blood glucose[a], LDL-C[a].

[a]variables were log-transformed before analysis

Per S.D. increment: per 1 S.D. increment of log lipid accumulation product

Cut-off: The OR for presence of MetS in the comparison between above and below the cut-off value

CMI=Cardiometabolic Index, IDF=International Diabetes Federation, NCEP/ATP=The National Cholesterol Education Program/Adult Treatment Panel III, LAP=Lipid Accumulation Product, SE Standard error, WHtR=Waist-to-Height Ratio, SBP=Systolic blood pressure, DBP=diastolic blood pressure, LDL-C=low-density lipoprotein cholesterol

and Western countries. The InterASIA study reported that 32.6% and 24.0% of Thai's ≥35 years old were diagnosed with MetS, defined by NCEP/ATP and IDF, respectively.[4] Besides the prevalence of MetS, according to NCEP/ATP definition in 97,098 Chinese adults ≥18 years was published at 33.9%[20], whereas, 31.3% of Korean[21], and 46.1% of Srilankan adults had been diagnosed with MetS.[22] On the other hand, a review analyzed among 34,821 subjects, from 10 European countries revealed that the prevalence of MetS in this continent was 24.3%, by adopting the similar criteria of NCEP/ATP.[23] Ethnicity, race and age considerably affects abdominal adiposity; especially large, central and visceral fat accumulation in Asians could account for the high prevalence of MetS among these populations.[13,24]

Our AUC results for LAP were consistent with previous findings, indicating the usefulness of LAP in discriminating MetS among different populations and ethnics. A study conducted among 552, healthy Argentinian men, reported the AUC for LAP in MetS-NCEP/ATP was 0.91[11], LAP also exhibits the highest diagnostic accuracy for MetS-NCEP/ATP and MetS-IDF among Spanish and Iranian individuals.[9,10] In Asian populations, LAP was revealed as an accurate predictor of MetS-NCEP/ATP in Taiwanese people ≥50 years, with an AUC of 0.91.[12] The comparison of LAP with VAI and TyG also affirmed that LAP was a reliable indicator for MetS in Chinese people ≥40 years, with an AUC of 0.855 and 0.865; defined by NCEP/ATP and IDF criteria, respectively.[25] However, the AUC found in this study was slightly lower than those previously reported. The possible explanation for this might be the disparities in the ethnicity, race, surveyed population and sample size.

Notably, the ROC analysis in this study disclosed that WHtR was a potential index for discriminating MetS among Thai adults. WHtR showed a higher AUC value than LAP in discriminating MetS-IDF; however, it was inferior in discriminating MetS-NCEP/ATP. Analyses on Cohen's kappa coefficient agreement showed that WHtR might be applied to discriminate MetS-IDF only (κ=0.593), but not for MetS-CEP/ATP (κ=0.474); whereas, LAP performed with moderate agreement in both definitions (κ=0.577 and 0.598 in IDF and NCEP/ATP, respectively. Multiple regression analysis indicated a similar observation. The OR between the cut-off point of WHtR and MetS presence fluctuated (OR of 10.38 and 42.51 in MetS-NCEP/ATP and IDF, respectively, while in LAP these ratios were 23.37 and 27.22).

Although, WHtR required only two, unmixed anthropometric components of WC and height, the use of LAP as a discriminating tool for MetS appeared more advantageous. First, by assessing total body fat, WHtR is unable to classify between subcutaneous adipose tissue (SAT) and intra-abdominal fat or visceral adipose tissue (VAT).[26] Comparing with SAT, VAT is more strongly associated, has more detrimental influences with cardio-metabolic risks and is firmly corroborated for MetS prediction.[27,28] The accumulation of excessive VAT adipocytes may result in possessing higher rates of lipolysis, producing extra adipocytokines; for instance, tumor necrosis factor-alpha (TNF-a), interleukin-6 (IL-6), IL-1, and plasminogen activator inhibitor-1 (PAI-1) and so forth[29], which are more prone to develop insulin resistance, as well as to escalate inflammation, than SAT adipocytes.[30] Second, the measurement of WHtR brings confrontations in both height and WC components. In adult populations, height is a constant variable; thus, the assessment of WHtR was considerably affected by the WC measurement. Any potential under- or over-evaluation of WC may make a sizable miscalculation. Indeed, the measurement of WC and its calibration still faces challenges (examples; assistance requirements, time-consumption, measuring in obese or bed-ridden patients);[31] whereas, the height variable revealed its limitation in assessing people with anatomy and physical disabilities (examples; frail individuals, subjects with amputation, wheelchair users and so on).[26] Furthermore, several criticisms dismiss WHtR in its application for monitoring, such as its vague biological interpretation, its greater variability across age; especially in elderly people, gender, race and ethnic groups, additionally its fluctuation waist values depend on weight change.[26]

LAP, comprised of WC and TG, showed more potential in assessment; markedly in the role of TG.[8] Inflammation and insulin resistance played a crucial role in the pathogenic mechanisms of MetS.[6] TG, accurate measurement by biochemical testing, has been reported to be a robust, positive determinant associated with VAT in both healthy and obese adults: even after controlling for SAT.[32,33] Distinctly, previous studies indicated that the turnover of TG in VAT is a reliable indicator of metabolic

risk, that was not related to the adipokine release, or to be taken into consideration as to the size of SAT, as well as the pathogenic characteristics of this tissue.[30] Moreover, the relationship between TG and insulin is well-characterized.[34] Insulin facilitates the stimulation of glucose and fatty acid uptake, which intensifies the TG synthesis and esterification processes.[34] Therefore, LAP proposed to estimate visceral fat accumulation, and therefore the significantly higher levels of LAP may mediate less favorable IR, cardiovascular risks and metabolic profiles.[8] Furthermore, the combination of TG with WC; termed: triglyceridemic-waist, has been applied to discriminating individuals with the excess of VAT[35], and is associated with an increased risk of MetS.[36] However, visceral accumulation may not be described adequately by a dichotomous index, as obesity itself is a continuous process.[8] Indeed, it has been suggested that accurate detection of discrete metabolic conditions requires models, composed by continuous rather than dichotomous risk factors. LAP appeared to be more advantageous by formulating to be a remarkable, continuous index, to reflect the combined anatomic and physiological changes associated with visceral fat deposition.[8]

There are some limitations in this study. First, we were unable to assign causality to our findings, due to the nature of the cross-sectional study. Second, given that our study was principally conducted among Thai adults, it is uncertain to extrapolating these findings to other racial or ethnic populations. Nevertheless, several strengths in the study should be acknowledged. Firstly, the study is a national survey, with a large, representative sample. Secondly, we used standardized protocols and data collection procedures, the data collectors were all trained and there was quality control assurance. Additionally, all blood samples were analyzed in a central laboratory in Bangkok, according to clinic laboratory standards. Hence, all of the abovementioned factors largely avoided measurement bias.

Conclusion

This is the first study to investigate the discriminating performance of adiposity indices to MetS in Thai adults. LAP was strongly associated and found to be an accurate index for discriminating MetS. Our findings suggest that this simple marker may help, in a primary care setting, to identify subjects who require further biochemical evaluation in MetS examinations.

Acknowledgement

The NHES IV was conducted by the NHES Office, Health Systems Research Institute, Thailand. NHES IV was supported by the Health System Research Institute; the Bureau of Policy and Strategy, Ministry of Public Health; the Thai Health Promotion Foundation; and the National Health Security Office, Thailand.

Funding sources

This present study received no funding.

Conflict of interest

All authors have no conflicts of interest to declare for this study.

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