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RESEARCH LETTER

Prospective Association of Novel Metabolic Indices with Metabolic Syndrome in Middle-Aged and Elderly Chinese

Jiao-Yang Li[1,2]
Jing Yang[1,2]
Xiao-Yan Qi[1]
Yan-Hua Luo[1]
Ya-Di Wang[1,2]
Zhe-Zhen Liao[1,2]
Li Ran[1]
Xin-Hua Xiao[1,2]
Jiang-Hua Liu[1,2]

[1]Department of Metabolism and Endocrinology, The First Affiliated Hospital of University of South China, Hengyang, 421001, Hunan Province, People's Republic of China; [2]Institute of Endocrine and Metabolic Diseases, The First Affiliated Hospital of University of South China, Hengyang, 421001, Hunan Province, People's Republic of China

Correspondence: Jiang-Hua Liu; Xin-Hua Xiao
Email jianghua990@hotmail.com; xinhua0102@163.com

Metabolic syndrome (MS) refers to the metabolic disorders of proteins, fat and carbohydrates that represent risk factors for cardiovascular disease, diabetes and cancer. The prevalence of MS is increasing worldwide due to deteriorating lifestyles, current statistic estimates suggest that one-quarter of the global population, more than 1 billion people, has MS.[1] Prevention of MS is an important public health objective as it will reduce of the future societal burden of diabetes and cardiovascular disease. Recently, novel metabolic indices combining both anthropometric and lipid measures were coming out as estimators of visceral adiposity dysfunction and lipid overaccumulation. These new indices, including visceral adiposity index (VAI), lipid accumulation product (LAP) and the product of triacylglycerol and glucose (TyG), have been suggested as early markers of insulin resistance.[2] Researchers have highlighted that these new indices are more sensitive indicator of diabetes compared to the traditional adiposity markers (such as BMI and WC), although it remains disputed due to the difference between diverse regions.[3,4] Additional, TyG is a novel candidate to predict chronic kidney diseases,[5] while LAP index reported to show the highest ability to predict insulin resistance and subclinical vascular damage.[6] Accumulating evidence also has suggested that the three parameters have been regarded as simple and novel clinical markers of MS, but they are all cross-sectional.[7–9] Hence, a comprehensive consensus has not been reached about the best indices for evaluating the status and risk of MS. It is important to find simple and reliable indicators for easy prediction of patients with MS in clinical settings. We therefore studied the associations of different novel metabolic indices with incident MS among women and men from the population-based study.

The study was a retrospective cohort study carried out in Hengyang, a district of Hunan, China, which was part of the China National Stroke Screening and Prevention Project (CNSSPP). A total of 4008 subjects, aged over 40 years, were enrolled by cluster sampling at baseline 2013, and follow-up examinations 2019. On both occasions, all participants were assessed using a structured interview (including demographic characteristics, behavioral risk factors, medical history), clinical and anthropometric measurements, and biochemical and serological test. Notably, for persons who failed to participate punctually, we took measures by telephone counseling and home visits to reduce the loss of participants in the follow-up survey. In addition, the death outcome

data was supplemented with the death registration system. Among 4008 community residents, 1406 subjects were excluded, including who had already been diagnosed with MS (n = 995), or a history of cardiovascular disease (n = 39), viral hepatitis, liver cirrhosis, autoimmune liver disease, renal disease (n = 57) or bariatric surgery (n = 2) at baseline, or a missing baseline data of physical examination or laboratory assessments (n = 31), or lost to follow-up or unwilling to participate (n = 235), death (16), and missing data to diagnose MS at follow-up (n = 23). Finally, 2602 individuals (1382 women and 1220 men) were included in our study to identify the baseline novel metabolic indices to predict the presence of MS at follow-up. Baseline data of the study subjects are shown in supplementary information (Table S1).

The criteria of MS were based on the Joint Interim Statement (JIS) in 2009.[10] LAP, VAI, and TyG index were computed based on the sex-specific mathematical model formula.[2] LAP = (WC - 58) × TG for women, and (WC - 65) × TG for men. VAI = (WC/[36.58 + (1.89 × BMI)]) × (TG/0.81) × (1.52/HDL) for women, and (WC/[39.68 + (1.88 × BMI)]) × (TG/1.03) × (1.31/HDL) for men. TyG index was calculated by using the equation Ln (TG [mg/dL] × FPG (mg/dL)/2). Considering sex differences in fat distribution and the formulae of metabolic indices differ in sex, all analyses were performed among women and men separately. The independent effect of each novel metabolic indices on the risk of MS was estimated using logistic regression models. Two models with different sets of covariates were fitted. Model 1 included age at baseline. Model 2 additionally adjusted for education, profession, family income, alcohol intake, smoking status, physical activity, dietary habits, medication history. We additionally assessed a receiver operating characteristic (ROC) curve to examine the potential of the above indices to identify the risk of MS. The DeLong test was used to compare the areas under the ROC curves. Multiple imputation procedure was performed (five imputations) to impute missing data for covariates. SPSS version 24.0 (Chicago, IL, USA) statistical software was applied to analyze the data.

Variables		Odds Ratio (95% CI)	*P* - value
Women (1382 cases)			
VAI	Model 1	1.394(1.168-1.676)	< 0.001
	Model 2	1.353(1.107-1.687)	< 0.001
LAP	Model 1	1.624(1.282-2.067)	< 0.001
	Model 2	1.541(1.251-1.837)	< 0.001
TyG	Model 1	1.287(1.085-1.724)	< 0.001
	Model 2	1.253(1.074-1.706)	< 0.001
Men (1220 cases)			
VAI	Model 1	1.431(1.134-1.877)	< 0.001
	Model 2	1.312(1.080-1.854)	< 0.001
LAP	Model 1	1.478(1.183-1.948)	< 0.001
	Model 2	1.395(1.120-1.796)	< 0.001
TyG	Model 1	1.238(1.063-1.575)	0.002
	Model 2	1.187(0.963-1.494)	0.084

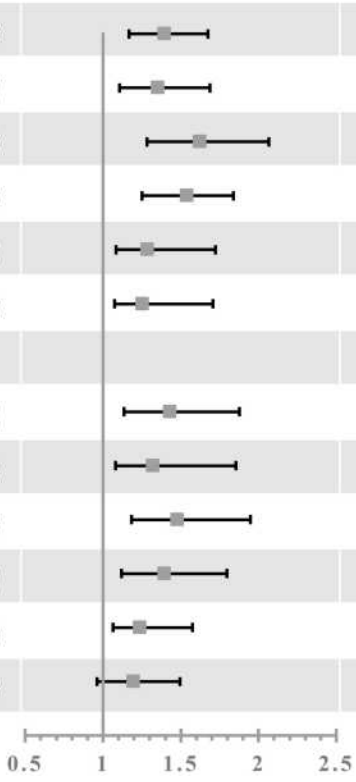

Figure 1 Associations between different metabolic indices and incident MS. ORs are presented per 1 SD increase in the marker. Model 1, adjusted for age; model 2, additionally adjusted for education, profession, family income, alcohol intake, smoking status, physical activity, dietary habits, medication history.
Abbreviations: MS, metabolic syndrome; CI, confidence interval; VAI, visceral adiposity index; LAP, lipid accumulation product; TyG, product of triacylglycerol and glucose.

Here, we showed that during a median follow-up of 5.3 years, 327 (12.6%) cases of participants were identified as MS (183 women and 144 men). All indices VAI, LAP, and TyG were significantly associated with the risk of MS in age-adjusted models both in men and women (Figure 1). In the fully adjusted model, elevated LAP was the most highly associated with increased MS risk both in women (odds ratio [OR]; 95% confidence interval [*CI*]) (1.541; 1.251, 1.837) and in men (1.395; 1.120, 1.796) (Table 1). VAI remained significantly associated with the risk of MS in both sexes (1.353; 1.107, 1.687 for women and 1.312; 1.080, 1.854 for men) (Table 1). However, TyG remained strongly associated with the risk of MS only in women (1.253; 1.073, 1.706) (Figure 1).

In addition, Table 1 presents the areas under ROC curves (AUCs) (95% Cl) for novel metabolic (VAI, LAP, TyG), the anthropometric (BMI, WC, waist-to-height ratio [WHtR]) and laboratory components (inverse HDL-cholesterol, TG) in relation to MS. The results showed that the LAP had the largest AUCs in both genders (0.678 [0.623–0.726] in women and 0.653 [0.592–0.711] in men). The discriminatory ability of the anthropometric indices and laboratory components in predicting MS was not high, excepted WHtR. The DeLong test further revealed that the AUC of LAP was significantly larger than all the other parameters in women (all $p < 0.05$). However, LAP has approximately the same AUC as WHtR ($p > 0.05$) in men.

Table 1 AUCs of Different Metabolic Indices in Predicting of MS at Baseline

Index	AUC	95% CI	*p*
Women			
AVI	0.629*	0.577–0.682	<0.001
LAP	0.678	0.623–0.726	<0.001
TyG	0.616**	0.567–0.665	<0.001
WC	0.623*	0.589–0.675	<0.001
BMI	0.614**	0.564–0.664	<0.001
WHtR	0.646*	0.602–0.689	<0.001
1/HDL-C	0.551**	0.512–0.601	0.021
TG	0.593**	0.547–0.646	0.003
Men			
AVI	0.612#	0.554–0.674	<0.001
LAP	0.653	0.592–0.711	<0.001
TyG	0.594##	0.533–0.651	0.007
WC	0.571##	0.514–0.630	0.014
BMI	0.533##	0.486–0.589	0.106
WHtR	0.642	0.587–0.698	<0.001
1/HDL-C	0.525##	0.482–0.579	0.134
TG	0.550##	0.509–0.603	0.033

Notes: The DeLong's test was used to compare the AUCs of indices. *Compared with the AUC of LAP in women, $p < 0.05$; **Compared with the AUC of LAP in women, $p < 0.01$; #Compared with the AUC of LAP in men, $p < 0.05$; ##Compared with the AUC of LAP in men, $p < 0.01$.

Abbreviations: AUC, areas under the curve; MS, metabolic syndrome; Cl, confidence interval; VAI, visceral adiposity index; LAP, lipid accumulation product; TyG, product of triacylglycerol and glucose; WC, waist circumference; BMI, body mass index; WHtR, waist-to-height ratio; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.

In those subjects followed for a median of 5.3 years, elevated VAI, LAP, and TyG were each directly associated with increased risk of MS, independent of other known MS risk factors. We also observed that LAP serves as the stronger predictive marker for incident MS compared with traditional anthropometric among women. It is noteworthy that LAP and WHtR provide similar predictive values of MS risk, both being stronger compared to other indices among men. These data indicate the LAP could be more appropriately choice in predicting MS incidence regardless of man or woman. Additional advantage is that LAP as a convenient indicator only requiring the determination of circulating triglycerides and measurement of waist circumference. Therefore, LAP could be a simple and useful tool for MS risk screening in all middle-aged and elderly people.

In addition, the limitations of our study also warrant attention. Our population comprised individuals aged 40 years and older of Asian ancestry. One might speculate that the impact of visceral adipose tissue on MS incidence would have been even stronger in a younger population. Thus, generalization of the results to younger age groups and other ethnicities should be made with caution. Moreover, as with other cohort studies, the possibility of selection bias could not be entirely ruled out. Although a variety of relevant confounding factors were controlled, residual confounders could not be eliminated. Due to the unavailability of computed tomography or magnetic resonance imaging in our population, visceral adiposity was not directly assessed. Thus, comparison of our results against the gold standard measures for visceral fat is not possible. This study defined MS using 2009 "JIS". Therefore, further studies are needed to determine whether the results are consistent under different criteria.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding authors (Jiang-Hua Liu and Xin-Hua Xiao) upon reasonable request.

Ethical Conduct

This study was approved by the Ethics Committee of the First Affiliated Hospital of University of South China, following the principles of the Declaration of Helsinki. All participants provided written informed consent. The privacy of the participants was kept through using unique code.

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Disclosure

The authors report no conflicts of interest in this work.

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