Interrelation between the lipid accumulation product index and diabetic kidney disease in patients with type 2 diabetes mellitus

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Research Article

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Abstract

Aims: The purpose of this study was to determine the relation between the lipid accumulation product index (LAPI) and diabetic kidney disease (DKD) in patients with type 2 diabetes mellitus (T2DM).

Methods: Herein, 931 patients were enrolled and their data were collected. Then the interrelation between LAPI and DKD was assessed using multivariate logistic regression analyses (LRAs) and by a restricted cubic spline (RCS). Receiver operating characteristic (ROC) curves were plotted to compare the performance of discrepant indicators of abdominal obesity (AO) in predicting DKD.

Results: After adjusting for several confounders, the odds ratio for DKD was increased evidently in the third LAPI tertile compared with that in the first LAPI tertile. In addition, the RCS revealed a positive interrelation between LAPI and DKD. As illustrated by ROC curves, LAPI showed better performance in predicting DKD than the other indicators.

Conclusions: LAPI is positively linked with DKD, so LAPI may be a suitable indicator for clinically screening patients at risk of DKD.

Introduction

In 2021, about 10.5% of the global population aged 20–79 years suffered from diabetes. This percentage is expected to rise to approximately 12.2% in 2045[1]. The proportion of diabetes patients with type 2 diabetes mellitus (T2DM) is estimated to be 90%[2]. Diabetes can lead to disability and mortality, which largely result from diabetic kidney disease (DKD)[3]. DKD has become a major cause of end-stage renal disease (ESRD), and the incidence of DKD increases as the global prevalence of diabetes rises[1]. Of all ESRD cases worldwide, 30–50% are estimated to be caused by DKD[4]. Moreover, DKD increases the risk of cardiovascular and cerebrovascular diseases[4]. Early surveillance and treatment of DKD are critical for reducing the burden on the healthcare system. Therefore, an effective tool for screening patients at a high risk of DKD is necessary.

Accumulating evidence has revealed that abdominal obesity (AO) is related to diabetes and its complications[5, 6]. Moreover, it has been unveiled that relative to the total amount of adipose tissue, the distribution of adipose tissue is more important in the progression of vascular complications[7, 8]. Some examinations, such as computed tomography and magnetic resonance imaging, can precisely detect abdominal adiposity. However, these examinations cannot be widely used because of their high cost and inconvenience. Therefore, indicators for AO, such as the body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR)[9], waist-to-height ratio (WHR)[10], the lipid accumulation product index (LAPI)[11], the visceral adiposity index (VAI)[12], and the Chinese visceral adiposity index (CVAI)[13], have been employed to assess abdominal adiposity. LAPI is a new marker of central lipid accumulation, indicative of the risk of metabolic syndrome and T2DM[14, 15]. However, little is known about the interrelation between LAPI and DKD.
Therefore, we conducted a cross-sectional study to decipher the relation between LAPI and DKD and the efficacy of LAPI in predicting DKD.

**Methods**

**Study design**

In total, 931 individuals who presented at the National Metabolic Management Center (MMC) of Shanghai General Hospital (Songjiang District) were enrolled in this cross-sectional study. This study was approved by the Ethics Committee of the hospital. Informed consent was provided by all subjects before participating.

**Study subjects**

The data of 931 participants between April 2017 and September 2021 were obtained from the electronic medical database of the MMC, which was established to conveniently and precisely diagnose and treat metabolic diseases[16]. The inclusion criteria were as follows: patients met the World Health Organization's 1999 criteria for diagnosis of T2DM[17] and patients were aged > 18 years. The exclusion criteria were as follows: pregnancy, malignant tumor, chronic nephritis, and missing data.

**Patient data collection**

Data including name, sex, age, educational level, coexisting diseases, and medical therapy were collected. A variety of anthropometric measurements were taken, including WC, hip circumference (HC), height, weight, blood pressure (BP), and heart rate. WC and HC were evaluated by trained staff in accordance with standard protocols. Biochemical data were collected from the MMC, including leukocyte counts, hemoglobin levels, and high-sensitivity C-reactive protein (hs-CRP) levels.

**Definition of variables**

A diagnosis of hypertension was made when systolic BP (SBP) ≥ 140 mmHg and/or diastolic BP (DBP) ≥ 90 mmHg during repeated examinations[18], patients used antihypertensive drugs, or patients had a history of hypertension. A diagnosis of hyperlipidemia was made when total cholesterol (TC) ≥ 5.2 mM, triglycerides (TG) ≥ 1.7 mM, patients used lipid-lowering medications, or patients had a prior history of hyperlipidemia. BMI, WHtR, and WHR were calculated as per the following formulas: BMI = weight [kg] / height [m$^2$], WHtR = WC [cm] / height [cm], and WHR = WC [cm] / HC [cm]. The formulas to calculate LAPI, VAI, and CVAI were previously published[12, 19]. Estimated glomerular filtration rate (eGFR) scores were computed with reference to a previous study[20]. We calculated the albumin (ALB)-to-creatinine ratio (ACR) based on the following formula: ACR = ALB / creatinine. The diagnosis of DKD was made in accord with a previous study [21].

**Statistical analyses**
Numbers or medians (interquartile range) are used to present data. Continuous variables with skewed distributions were parsed by use of the Mann–Whitney U test, and an analysis of categorical variables was conducted for pairwise comparison using the $\chi^2$ test. $P<0.05$ was indicative of statistical significance. SPSS 13.0 and R-4.1.3 were employed for statistical processing.

LAPI was divided into tertiles; the first tertile of LAPI was the lowest tertile, and the third tertile was the highest tertile. How LAPI is linked with DKD was parsed via multivariate logistic regression analyses (LRAs). Model 1 was adjusted for gender and age, Model 2 was further adjusted for DBP, SBP, educational level, and current drinking status, Model 3 was further adjusted for the duration of diabetes and hypertension, and Model 4 was further adjusted for fasting plasma glucose (FPG), leukocyte, ALB, hs-CRP, and glycated hemoglobin (HbA1c) levels. The interrelation between LAPI and DKD was examined by use of a restricted cubic spline (RCS).

Additionally, by multivariate LRAs, we examined the association of LAPI with DKD based on age, sex, hyperlipidemia, hypertension, and HbA1c in different subgroups and computed the odds ratio (OR) and 95% confidence interval (CI). Moreover, we evaluated how the aforementioned subgroup variables interact with LAPI.

The receiver operating characteristic (ROC) curves were plotted and utilized the area under the ROC curve (AUC) and the Youden index to analyze the ability of the BMI, WC, WHtR, WHR, LAPI, VAI, and CVAI to predict DKD.

**Results**

**Baseline characteristics of the study subjects**

In total, 931 participants (352 females and 579 males) aged 55 years on average were enrolled. Of these participants, 327 had DKD and 604 did not. The two groups displayed significant differences in clinical data such as age, sex, educational level, hypertension, current drinking, SBP, DBP, height, BMI, WC, duration of diabetes, FPG, HbA1c, hemoglobin, leukocytes, gamma-glutamyl transferase, ALB, TG, TC, hs-CRP, ACR, and eGFR. Clinical data are illustrated in Table 1.
<table>
<thead>
<tr>
<th>Variables</th>
<th>No DKD (n = 604; 64.88%)</th>
<th>DKD (n = 327; 35.12%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55 (42–63)</td>
<td>55 (47–65)</td>
<td>0.011</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>75 (67–80)</td>
<td>78 (69–84)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>120 (113–130)</td>
<td>128 (120–140)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart rate (beats per minute)</td>
<td>78 (76–86)</td>
<td>78 (75–88)</td>
<td>0.155</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167 (160–173)</td>
<td>164 (158–172)</td>
<td>0.022</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.2 (61.0–78.0)</td>
<td>69.8 (63.4–80.0)</td>
<td>0.177</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.9 (23.0–27.3)</td>
<td>25.8 (23.6–28.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>92 (86–96)</td>
<td>93 (88–100)</td>
<td>0.004</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>96 (93–100)</td>
<td>96 (93–101)</td>
<td>0.116</td>
</tr>
<tr>
<td>WHtR</td>
<td>0.55 (0.52–0.59)</td>
<td>0.57 (0.53–0.60)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.95 (0.91–0.98)</td>
<td>0.96 (0.93–0.99)</td>
<td>0.002</td>
</tr>
<tr>
<td>LAPI</td>
<td>45.92 (29.25–72.94)</td>
<td>60.52 (39.90–90.65)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>VAI</td>
<td>2.81 (1.71–4.10)</td>
<td>3.35 (2.30–5.43)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CVAI</td>
<td>122.97 (99.58–144.06)</td>
<td>132.24 (109.00–154.73)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Duration of diabetes (months)</td>
<td>61 (1–144)</td>
<td>97 (12–171)</td>
<td>0.001</td>
</tr>
<tr>
<td>FPG (mmol/L)</td>
<td>6.9 (5.6–8.5)</td>
<td>7.7 (6.0–9.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>8.6 (7.2–10.6)</td>
<td>9.3 (7.5–11.0)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Data are presented N or median (interquartile range). Continuous variables with skewed distribution used Mann-Whitney U test and categorical variables used chi-squared test for comparing the baseline characteristics of patients with diabetic kidney disease and without diabetic kidney disease.

<table>
<thead>
<tr>
<th>Variables</th>
<th>No DKD (n = 604; 64.88%)</th>
<th>DKD (n = 327; 35.12%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/L)</td>
<td>145 (132–154)</td>
<td>137 (124–148)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Leukocyte (×10^9/L)</td>
<td>5.99 (5.10–7.11)</td>
<td>6.50 (5.45–7.69)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>20 (14–34)</td>
<td>20 (14–30)</td>
<td>0.184</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>18 (15–24)</td>
<td>18 (15–25)</td>
<td>0.500</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>24 (16–39)</td>
<td>27 (18–41)</td>
<td>0.004</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>43.2 (40.8–45.5)</td>
<td>42.3 (39.2–45.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Blood urea nitrogen (mmol/L)</td>
<td>5.20 (4.12–6.84)</td>
<td>5.74 (4.47–7.76)</td>
<td>0.001</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>58.35 (47.70-67.63)</td>
<td>58.70 (45.00-79.80)</td>
<td>0.204</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>1.58 (1.14–2.25)</td>
<td>1.87 (1.40–2.76)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.56 (3.73–5.23)</td>
<td>4.71 (3.87–5.50)</td>
<td>0.019</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>0.91 (0.79–1.08)</td>
<td>0.90 (0.78–1.05)</td>
<td>0.622</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>2.61 (1.91–3.17)</td>
<td>2.60 (1.96–3.34)</td>
<td>0.450</td>
</tr>
<tr>
<td>Hs-CRP (mg/L)</td>
<td>1.2 (0.5–2.6)</td>
<td>1.9 (0.9–4.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ACR (µg/mg)</td>
<td>13.16 (8.71–19.18)</td>
<td>71.83 (41.90-244.71)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>eGFR (mL/min per 1.73 m^2)</td>
<td>110.90 (100.81-123.03)</td>
<td>105.62 (88.15-119.26)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Sex(male/female)</td>
<td>400/204</td>
<td>179/148</td>
<td>0.001</td>
</tr>
<tr>
<td>Educational level (under high school/ high school or above)</td>
<td>300/304</td>
<td>140/187</td>
<td>0.045</td>
</tr>
</tbody>
</table>

### Association between LAPI and DKD

As demonstrated by multivariate LRAs, after adjusting for several confounding factors, elevated LAPI was associated with a higher likelihood of DKD (Table 2). Subsequent to the adjustment of the multivariate regression model for age, sex, DBP, SBP, educational level, current drinking, duration of diabetes, hypertension, FPG, HbA1c, leukocytes, ALB, and hs-CRP, higher OR values for DKD were found in the third LAPI tertile than in the first LAPI tertile ($P < 0.001$), and the OR (95% CI) for DKD was 2.135 (1.438–3.171) in the third tertile of LAPI compared to that in the first tertile. Additionally, RCS was performed to identify the relationship of LAPI with DKD. Consistently, the RCS curve demonstrated a positive relationship between LAPI and DKD in the study participants (Fig. 1).
Table 2

Relations of lipid accumulation product index with diabetic kidney disease in patients with type 2 diabetes mellitus.

<table>
<thead>
<tr>
<th>LAPI</th>
<th>T1 (N = 311)</th>
<th>T2 (N = 310)</th>
<th>T3 (N = 310)</th>
<th>P value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref.</td>
<td>1.667 (1.174–2.368)</td>
<td>2.587 (1.819–3.679)</td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>Model 1</td>
<td>1.558 (1.084–2.241)</td>
<td>2.407 (1.667–3.476)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>Model 2</td>
<td>1.431 (0.988–2.074)</td>
<td>2.168 (1.490–3.156)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>Model 3</td>
<td>1.391 (0.944–2.051)</td>
<td>2.135 (1.438–3.171)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>Model 4</td>
<td>1.667 (1.174–2.368)</td>
<td>2.587 (1.819–3.679)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Model 1 was adjusted for sex, age. Model 2 was further adjusted for diastolic blood pressure, systolic blood pressure, educational level, current drinker. Model 3 was further adjusted for duration of diabetes, hypertension. Model 4 was further adjusted for fasting plasma glucose, glycated hemoglobin, leukocyte, albumin, high-sensitivity C-reactive protein. The quartile ranges of T1, T2 and T3 of LAP were < 38.08, 38.08–67.65, 67.65, respectively. T1 is the reference group. Multivariate logistic regression analyses were performed to estimate the ORs and corresponding 95% CIs for diabetic kidney disease. Abbreviations: T: tertile, OR: odds ratio, CI: confidence interval, LAPI: lipid accumulation product index.

Subgroup analyses

To further investigate the association of LAPI with DKD in different populations, the participants were grouped by age (< 65 or ≥ 65 years), hyperlipidemia (N or Y), sex (female or male), HbA1c (< 7% or ≥ 7%), and hypertension (N or Y). In most categories, LAPI was positively correlated with DKD according to the subgroup analyses. Age, sex, hyperlipidemia, hypertension, and HbA1c did not significantly interact with LAPI (Fig. 2).

ROC analysis

The ROC curve showed the ability of BMI, WC, WHtR, WHR, LAPI, VAI, and CVAI to predict DKD in all participants (Fig. 3). LAPI had the best prediction ability among these indicators in all participants (Table S1). The AUC of LAPI was the largest among these indicators, and the cut-off of LAPI calculated according to the largest Youden index was 51.03 (sensitivity, 63.3%; specificity, 58.1%).

Discussion

In conclusion, LAPI was higher in the DKD group than in the no-DKD group, and a positive relationship between LAPI and DKD was found. According to the ROC curves, LAPI had a greater ability to predict DKD than BMI, WC, WHtR, WHR, VAI, and CVAI. Therefore, LAPI may be a reliable screening tool for DKD in clinical practice.
AO has been shown to be associated with a high risk of DKD in T2DM[22–24]. A population-based cohort study has reported longitudinal associations of VAI and CVAI with DKD and suggested that VAI is independently related to the incidence of DKD[25]. LAPI was calculated using TG and WC, which are novel indicators of central lipid accumulation[11]. Accumulating evidence indicates that patients with diabetes display a higher LAPI level[14, 26]. One study reported that the ability of LAPI to predict CKD was better than that of VAI. Similar results were obtained in the present study, even though we only included T2DM patients. Another study unveiled that several indicators pertaining to obesity, including BMI, WHR, WHtR, LAPI, and VAI, show relevance to kidney disease in late-stage T2DM patients[27]. These results are in agreement with ours. Moreover, we found that LAPI performed better than BMI, WC, WHtR, WHR, VAI, and CVAI in predicting DKD after comparing different indicators for AO, providing new scientific evidence for further study.

A previous study indicated that plasma TG levels are correlated with reduced eGFR in new-onset cases of T2DM[28], and a high TG level contributes to DKD progression[29]. These results are consistent with our conclusion that LAPI is positively associated with DKD. It is well acknowledged that oxidative stress and inflammation are common causes of DKD[30]. Lipids accumulated in the kidney may induce oxidative stress or promote the release of proinflammatory cytokines, resulting in glomerular damage, glomerulosclerosis, and interstitial fibrosis[31, 32]. Dysfunction of lipid metabolism in DKD could lead to podocyte damage, thus promoting DKD progression, which results in the disruption of mitochondrial function and lipid metabolism[33].

LAPI is recognized as a new indicator of accumulated visceral adipose tissue[34]. Several studies reported that LAPI can be used to evaluate the risk of metabolic syndrome, diabetes, and cardiovascular disease[11, 14, 35]. A higher LAPI in patients with T2DM was correlated with increased oxidative stress, insulin resistance, and inflammation[36]. The use of LAPI to assess visceral adipose tissue is characterized by higher lipolytic and proinflammatory activity[37]. LAPI can be calculated easily, quickly and cheaply, which makes it suitable for use in clinical practice and in a large population[38]. Our study revealed that LAPI was correlated with DKD and had superior performance in predicting DKD compared with BMI, WC, WHR, WHtR, VAI, and CVAI, so LAPI may be a simple and reliable marker of DKD in T2DM patients.

**Comparisons with other studies and what the current work adds to existing knowledge**

LAPI as an novel index for AO, was linked with oxidative stress, insulin resistance, and inflammation in T2DM patients. However, oxidative stress and inflammation are common causes of DKD. Moreover, an earlier study indicated that plasma TG levels are correlated with reduced eGFR in new-onset cases of T2DM, and a high TG level contributes to DKD progression. However, little study investigated the dose-response relationship between LAPI and DKD. This study verified the dose-response relationship between LAPI and DKD, and LAPI may be a simple index to diagnose the DKD.
Study strengths and limitations

The strengths of the current study deserved to be mentioned. The study found the dose-response relationship between LAPI and DKD, and LAPI was evidently linked with DKD. Moreover, LAPI had a better performance in diagnosing DKD, which may be a simple and reliable index to screen DKD in clinical practice. There were a number of limitations to this study. First, it was cross-sectional study; longitudinal correlations between LAPI and DKD need to be examined in future studies. Second, this study had a small sample size. In order to verify these results, further studies with larger samples are needed. Third, the insulin resistance index and the effects of lipid-lowering drugs were not analyzed in our study. Finally, further investigations of different ethnic groups are essential to examine the correlation between LAPI and DKD.

Conclusion

LAPI was significantly and positively correlated with DKD and had a better performance in diagnosing DKD. Therefore, LAPI may be an applicable and reliable indicator for screening patients with T2DM at risk of DKD in clinical practice.

Abbreviations

LAPI
lipid accumulation product index
DKD
diabetic kidney disease
T2DM
type 2 diabetes mellitus
LRAs
logistic regression analyses
RCS
restricted cubic spline
ROC
Receiver operating characteristic
AO
abdominal obesity
BMI
body mass index
WC
waist circumference
WHR
waist-to-hip ratio
WHR
waist-to-height ratio
VAI
visceral adiposity index
CVAI
Chinese visceral adiposity index
MMC
Metabolic Management Center
HC
hip circumference
BP
blood pressure
hs-CRP
high-sensitivity C-reactive protein
SBP
systolic blood pressure
DBP
diastolic blood pressure
TC
total cholesterol
TG
triglycerides
eGFR
Estimated glomerular filtration rate
ALB
albumin
ACR
albumin-to-creatinine ratio
FPG
fasting plasma glucose
HbA1c
glycated hemoglobin
OR
odds ratio
CI
confidence interval
AUC
area under the receiver operating characteristic curves.

Declarations
Acknowledgements

Not applicable.

Author Contributions

NGF and YDP designed this study. MT and SSY collected and analyzed the study data. All authors wrote and reviewed the manuscript of the study. All authors approved the final manuscript.

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Availability of data and materials

The corresponding authors can provide the data.

Ethics approval and consent to participate

Shanghai General Hospital Ethics Committee approved the study. All participants signed an informed consent form before participating.

Consent for publication

Not applicable.

Competing interests

The authors declare that there are no competing interests.

References


**Figures**
Figure 1

Association of lipid accumulation product index on a continuous scale with diabetic kidney disease in study participants. The solid line represents the odds ratio and the shad area represents the 95% confidence interval. Model was adjusted for age, diastolic blood pressure, systolic blood pressure, educational level, current drinker, duration of diabetes, hypertension, fasting plasma glucose, glycated hemoglobin, leukocyte, albumin and high-sensitivity C-reactive protein. Abbreviations: OR: odds ratio, CI: confidence interval, RCS: restricted cubic spline, LAPI: lipid accumulation product index.
### Figure 2

Subgroup analyses of associations between lipid accumulation product index and diabetic kidney disease. Model was adjusted for age, sex, diastolic blood pressure, systolic blood pressure, educational level, current drinker, duration of diabetes, hypertension, fasting plasma glucose, glycated hemoglobin, leukocyte, albumin and high-sensitivity C-reactive protein. Subgroup variable was excluded from the model. Abbreviations: OR: odds ratio, CI: confidence interval, HbA1c: glycated hemoglobin.
Figure 3


Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarymaterials.docx