

# Assessing the Prognostic Utility of the New Mayo Adhesive Probability Score in East Asian Populations and its Correlation with Metabolic-Associated Fatty Liver Disease

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Received December 7, 2023

Accepted February 27, 2024

## Summary

We assessed the prognostic utility of the new perinephric fat adherence risk score – Mayo Adhesive Probability (MAP), in patients of East Asian ethnicity undergoing either laparoscopic partial nephrectomy (LPN) or laparoscopic radical nephrectomy (LRN). A retrospective analysis of clinical data was carried out on 169 patients who either underwent LPN or LRN surgery. These patients were categorized into two groups, group A (0-2 points) and group B (3-4 points) using the new MAP score. The overall clinical data between these two groups was compared and potential risk factors were investigated using logistic regression analyses. The new MAP score yielded an area under the curve of 0.761 (95 % CI: 0.691-0.831), indicating its effectiveness. Group B had a significantly higher incidence of adherent perirenal fat (APF) during surgery ( $p < 0.001$ ) and had a greater average age ( $p < 0.001$ ). There was an increased prevalence of hypertension ( $p = 0.009$ ), type 2 diabetes mellitus ( $p < 0.001$ ), and MAFLD ( $p < 0.001$ ) in group B. Additionally, there were significant differences in posterior perinephric fat thickness ( $p < 0.05$ ), lateral perinephric fat thickness ( $p < 0.001$ ), and perinephric stranding ( $p < 0.001$ ) between the two groups. The new MAP score holds significance in predicting APF in people of East Asian ethnicity undergoing LPN or LRN, and there is a strong correlation between elevated MAP scores and risk factors such as MAFLD and advanced age.

## Key words

Adherent perirenal fat • Insulin resistance • Mayo Adhesive Probability (MAP) score • Metabolic syndrome • Metabolic (dysfunction)-associated fatty liver disease

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## Introduction

Currently, most surgeons commonly employ scoring systems such as RENAL, PADUA, or C-index to anticipate surgical complexity and perioperative complications. These scoring systems predominantly emphasize factors linked to the tumor's anatomical characteristics, which impact surgical complexity, without taking into account patient-related factors and the tumor's microenvironment. Notably, adherent perirenal fat (APF) stands out as the primary factor complicating surgery. In the contemporary era, numerous nations, China included, are witnessing the phenomenon of an “aging society”, characterized by a growing proportion of elderly citizens in the population. Factors like urbanization, shifts in population demographics, alterations in dietary habits, and changes in work environments have led to an increased prevalence of conditions such as type 2 diabetes mellitus (T2DM), metabolic (dysfunction)-associated fatty liver disease (MAFLD), and obesity, which are now affecting a younger population [1,2,3].

Obesity often poses challenges during surgical procedures. Among urologists, one of the most common challenges encountered is dealing with APF located

beneath the perirenal fascia. APF refers to the adhesion between the perirenal fat and the renal parenchyma, making it difficult to separate the kidney anatomically. To predict the presence of APF in robot-assisted partial nephrectomy, Davidiuk *et al.* developed an image-based algorithm known as the Mayo Adhesive Probability (MAP) score [4]. In 2019, Borregale *et al.* proposed an enhanced new MAP score, which includes T2DM as an independent predictor, further enhancing the scoring system [5].

Previous research indicates that, when comparing individuals with the same BMI index, Asians tend to exhibit a higher volume of visceral adipose tissue compared to Caucasians, and there is a greater prevalence of T2DM among Asians [6]. The majority of prior studies primarily concentrated on the older MAP score, predominantly involving European and American cohorts. However, the new MAP score and its relevance to people of East Asian ethnicity have received limited attention. Hence, the objective of this study is to assess the prognostic utility of the new MAP score in people of East Asian ethnicity undergoing either laparoscopic partial nephrectomy (LPN) or laparoscopic radical nephrectomy (LRN), while also analyzing associated factors.

## Materials and Methods

### Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Longyan First Hospital Affiliated to Fujian Medical University (No. 2021-005). Since this study was a retrospective study, the Ethics Committee waived the need to obtain informed consent from the patients.

### Data collection

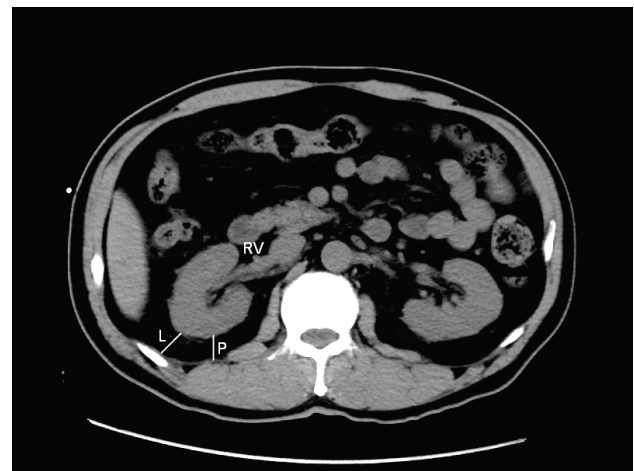
We conducted a retrospective analysis of patient data for individuals who underwent LPN or LRN at our medical facility between January 2020 and December 2022. All imaging and laboratory tests for these patients were conducted within our hospital. LPN or LRN procedures were carried out either through the abdominal cavity or the retroperitoneal space by two highly experienced senior physicians. The baseline characteristics of the patients included age, gender, BMI, smoking and alcohol history, hypertension history, T2DM, coronary heart disease, and MAFLD. Tumor characteristics encompassed aspects such as tumor shape (exophytic, endophytic, or a combination), location within

the kidney, histological type, posterior perinephric fat thickness (PPFT), lateral perinephric fat thickness (LPFT) (as depicted in Fig. 1), perinephric stranding (as shown in Fig. 2), and the occurrence of any complications during the operation. Radiological data of the tumors (*via* CT scans or T1-weighted MRI) were acquired by a skilled radiologist. The final new MAP score was calculated by a proficient attending physician using the algorithm developed by Borregale *et al.*, and it ranged from 0 to 4 (Table 1).

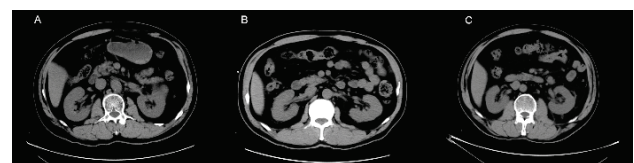
### Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) age of the patient >18 years old; (2) completion of preoperative imaging and laboratory tests within our hospital.

The exclusion criteria were as follows: (1) spontaneous or trauma-induced mass rupture and bleeding; (2) a prior history of retroperitoneal surgery or trauma on the same side; (3) patients suffering from retroperitoneal infections; (4) patients with obstructive infections in the urinary tract; (5) incomplete or non-hospital-conducted preoperative examinations; (6) combined with other tumors.



**Fig. 1.** Measuring perinephric fat thickness at the level of the renal vein. Renal vein: RV; Posterior: P; Lateral: L.



**Fig. 2.** Grading of perinephric stranding. **(A)** None: 0 points. The perirenal fat demonstrates no stranding. The adipose tissue surrounding the kidney is completely black. **(B)** Mild/moderate (type 1): 2 points. The perirenal fat demonstrates some image-dense stranding present but no thick bars. **(C)** Severe stranding (type 2): 3 points. The perirenal fat demonstrates thick image-dense bars of inflammation.

**Table 1.** The new MAP score algorithm.

Variable	Risk score
Posterior perinephric fat thickness (cm)	
0.0-2.0	0
≥2.0	1
Stranding	
None	0
Type1	1
Type2	2
Diabetes mellitus	
No	0
Yes	1

### Assessment of MAFLD

MAFLD is diagnosed based on the guidelines provided by the 2020 international expert consensus statement and the 2021 position statement from the Chinese Society of Hepatology. To establish a positive diagnosis of MAFLD, it is essential to present histological evidence through biopsy, imaging results, or blood biomarker data indicating the accumulation of fat in the liver, known as hepatic steatosis. Additionally, one of the following three criteria should be met: being overweight or obese (with a BMI of  $\geq 25$  kg/m<sup>2</sup> for Caucasians or  $\geq 23$  kg/m<sup>2</sup> for Asians), having T2DM, or presenting of at least two metabolic risk abnormalities. Metabolic risk abnormalities include: (1) A waist circumference of  $\geq 102/88$  cm for Caucasian men and women or  $\geq 90/80$  cm for Asian men and women, respectively; (2) High blood pressure ( $\geq 130/85$  mm Hg) or receiving related drug treatment; (3) Elevated plasma triglycerides ( $\geq 150$  mg/dl) or receiving related drug treatment; (4) Low plasma HDL-cholesterol ( $< 40$  mg/dl for men and  $< 50$  mg/dl for women) or receiving related drug treatment; (5) Prediabetes, characterized by fasting glucose levels between 5.6 to 6.9 mmol/l, 2-hour post-prandial glucose levels ranging from 7.8 to 11.0 mmol, or HbA1c levels of 39-47 mmol/mol; (6) A homeostasis model assessment-insulin resistance score of  $\geq 2.5$ ; (7) Plasma high-sensitivity C-reactive protein levels exceeding 2 mg/l.

### Statistical analysis

Patients were categorized into two groups, group A (0-2 points) and group B (3-4 points), based on the new MAP score. For normally distributed quantitative variables, we presented the data as mean  $\pm$  standard

deviation, while non-normally distributed quantitative variables are presented as median (interquartile range). To compare measurements between the groups, we utilized Student's *t*-test or the Mann-Whitney U test. Categorical variables were assessed through the chi-squared test ( $\chi^2$ ) for larger samples and Fisher's exact test for smaller samples. A  $p < 0.05$  was considered statistically significant.

We conducted both univariate and multivariate logistic regression analyses to examine the association between filtered risk factors of APF and the new MAP score. We generated a receiver operating characteristic (ROC) curve and determined the area under the curve (AUC) for the new MAP score. All statistical analyses were carried out using the R statistical software packages provided by the R Foundation (<http://www.R-project.org>).

## Results

### Patient characteristics

A total of 169 patients (97 males and 72 females) were included for analysis. Group A consisted of 137 patients, 77 males (56.2 %) and 60 females (43.8 %). Group B consisted of 32 patients, 20 males (62.5 %) and 12 females (37.5 %). There was no statistical significance in gender between the two groups ( $p > 0.05$ ). The mean age of all patients was (56.8 $\pm$ 12.22) years old. Patients in group B (63.0 $\pm$ 9.93 years old) were older than in group A (55.35 $\pm$ 12.28 years old) ( $p < 0.001$ ).

Group B had a higher percentage of patients with a history of hypertension (50.0 % vs. 24.82 %,  $p = 0.009$ ), T2DM (59.38 % vs. 2.92 %,  $p < 0.001$ ), and MAFLD (31.25 % vs. 10.22 %,  $p < 0.001$ ) compared to Group A. However, there were no statistically significant differences between the two groups regarding BMI, history of coronary heart disease, alcoholism, and smoking ( $p > 0.05$ ) (Table 2). The AUC calculation (0.761, 95 % CI: 0.691-0.831) confirmed the diagnostic accuracy of the new MAP score (Fig. 3).

### APF and tumor imaging characteristics

The occurrence of intraoperative APF was notably higher in group B compared to group A (93.75 % vs. 48.91 %,  $p < 0.001$ ). Group B exhibited a significantly greater median thickness of LPFT (14.46 cm, interquartile range [IQR]: 10.15-18.47 cm) in contrast to the thinner LPFT in group A (8.63 cm, IQR: 4.83-14.49 cm) ( $p < 0.001$ ). The median thickness of PPFT also displayed

a significant difference ( $p < 0.05$ ) between the two groups. Furthermore, there was a significant difference between the two groups regarding perinephric stranding ( $p < 0.001$ ). However, there were no statistically significant differences in tumor morphology and histological type between the groups ( $p > 0.05$ ) (Table 2).

#### *Comparison of operative time, bleeding volume, and hospitalization time*

The mean length of hospitalization time in group B (17.5 days, IQR: 13-24 days) was longer than in group A (14.0 days, IQR: 11-19 days) ( $p < 0.05$ ). Nevertheless, there was no significant difference between group A and B in terms of operative time and bleeding volume (Table 2).

Furthermore, we conducted an analysis on patients who underwent the same type of surgery. Among those who received LPN, there were no significant differences in terms of operative time, bleeding volume, and hospitalization time between the low-score group (0-2 points) and the high-score group (3-4 points) ( $p > 0.05$ ). A similar situation was observed among patients who underwent LRN, with the exception of hospitalization time (Table 3).

#### *Univariate and multivariate analysis of age, hypertension, and MAFLD*

The new MAP score did not identify age, hypertension, or MAFLD as predictive factors of APF. To delve deeper into potential risk factors for experiencing APF, age, hypertension and MAFLD were assessed through both univariate and multivariate logistic regression analyses.

In the univariate analysis, a high new MAP score exhibited a significant correlation with age ( $p < 0.01$ ), hypertension ( $p < 0.01$ ), and MAFLD ( $p < 0.01$ ). However, in the multivariate analysis, a high new MAP score was notably correlated with age (odds ratio [OR]=1.054 [1.015-1.098],  $p < 0.01$ ) and MAFLD (OR=3.614 [1.324-9.756],  $p < 0.05$ ), with the exception of hypertension (OR=2.019 [0.855-4.730],  $p > 0.05$ ) (Table 4).

## **Discussion**

As widely recognized, obesity often presents substantial challenges in surgical procedures. Urologists commonly face a recurring challenge during renal tumor surgeries, referred to as APF, denoting the adhesion between perinephric fat and the kidney. This adhesion

complicates the dissection of the kidney, adding complexity to the procedure. This phenomenon has even been described as “toxic fat”. Numerous studies emphasize that APF is significantly associated with operative time, blood loss, length of hospitalization, and complications, but some studies have shown the opposite [7,8,9,10].

Hence, accurately predicting APF could enhance preoperative risk assessment and help prevent postoperative complications. The MAP score and its newer version have been validated in Western populations. However, there has been limited research in Asian cohorts who have undergone LPN or LRN on the relationship between APF and the new MAP score, and the predictive capabilities of the new MAP score have yet to be explored in this context.

Different studies have drawn varying conclusions regarding the incidence of APF. A 2017 review by Lee *et al.* noted that most studies reported APF rates ranging from 10.6 % to 55.2 %, whereas their current study found a slightly higher incidence of 57.4 % [11]. This difference could be attributed to variations in the prevalence of metabolic disorders like T2DM, MAFLD, and obesity rates between people of East Asian ethnicity and Caucasians [1,6,12,13].

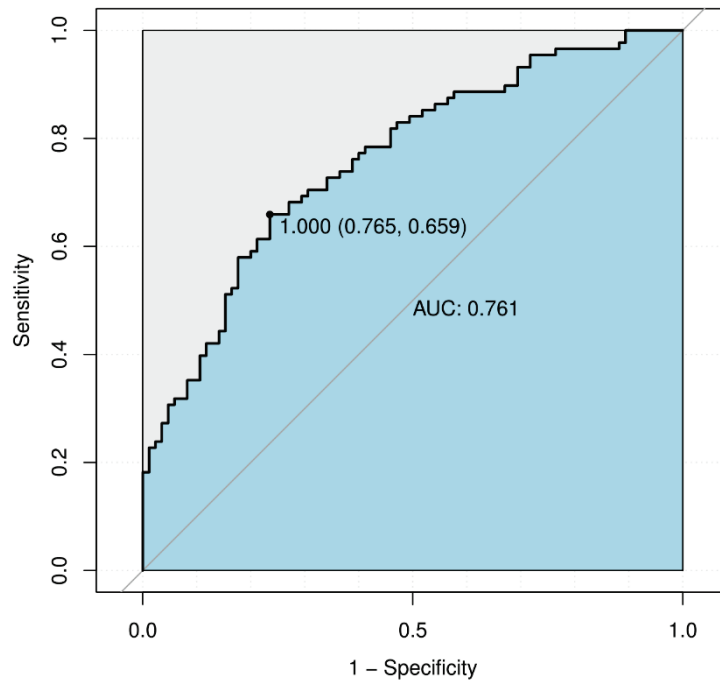
Our study shows that group B, which has higher scores, has more APF patients. Additionally, compared to group A, the patients in group B are older and have more patients with underlying diseases such as hypertension, diabetes, and MAFLD. Previous studies have shown that advanced age and underlying diseases can negatively impact patients' postoperative recovery and increase their hospitalization time [14,15]. Our doctors tend to adopt a more conservative attitude towards these patients, which may prolong their hospitalization. Patients who underwent LRN had longer hospital stays if they had higher scores, while this was not observed in patients who underwent LPN. This may be due to the limited number of cases, which requires more time and cases. Multi-center studies can provide more accurate conclusions. As all surgeons performing LRN and LPN in this study were experienced, there may be no difference in the operative time and bleeding volume, as has been observed in previous studies [9,10]. We think these two items are also related to the surgeon's surgical proficiency and experience.

The study also identified certain risk factors associated with APF, including male gender, advanced

**Table 2.** Association with patient background grouped by new MAP Score.

<i>Variables</i>	<b>Total (n=169)</b>	<b>Group A (n=137)</b>	<b>Group B (n=32)</b>	<i>p</i>
<i>Age, Mean ± SD</i>	56.8±12.22	55.35±12.28	63±9.93	<0.001
<i>Sex, n (%)</i>				0.653
<i>Female</i>	72 (42.6)	60 (43.8)	12 (37.5)	
<i>Male</i>	97 (57.4)	77 (56.2)	20 (62.5)	
<i>BMI (kg/m<sup>2</sup>), Median (Q1, Q3)</i>	23.63 (21.63, 25.71)	23.48 (21.61, 25.71)	24.22 (22.4, 25.86)	0.345
<i>Alcoholism, n (%)</i>				1
<i>No</i>	128 (75.74)	104 (75.91)	24 (75)	
<i>Yes</i>	41 (24.26)	33 (24.09)	8 (25)	
<i>Smoking, n (%)</i>				0.603
<i>No</i>	130 (76.92)	107 (78.1)	23 (71.88)	
<i>Yes</i>	39 (23.08)	30 (21.9)	9 (28.12)	
<i>Hypertension, n (%)</i>				0.009
<i>No</i>	119 (70.41)	103 (75.18)	16 (50)	
<i>Yes</i>	50 (29.59)	34 (24.82)	16 (50)	
<i>T2DM, n (%)</i>				<0.001
<i>No</i>	146 (86.39)	133 (97.08)	13 (40.62)	
<i>Yes</i>	23 (13.61)	4 (2.92)	19 (59.38)	
<i>CHD, n (%)</i>				0.19
<i>No</i>	153 (90.53)	126 (91.97)	27 (84.38)	
<i>Yes</i>	16 (9.47)	11 (8.03)	5 (15.62)	
<i>MAFLD, n (%)</i>				0.005
<i>No</i>	145 (85.8)	123 (89.78)	22 (68.75)	
<i>Yes</i>	24 (14.2)	14 (10.22)	10 (31.25)	
<i>Pathology, n (%)</i>				0.38
<i>Benign</i>	56 (33.14)	48 (35.04)	8 (25)	
<i>Malignant</i>	113 (66.86)	89 (64.96)	24 (75)	
<i>Morphology, n (%)</i>				0.225
<i>Exophytic</i>	48 (34.53)	40 (35.09)	8 (32)	
<i>Endophytic</i>	59 (42.45)	45 (39.47)	14 (56)	
<i>Mixing</i>	32 (23.02)	29 (25.44)	3 (12)	
<i>LPFT (cm), Median (Q1, Q3)</i>	10.06 (5.17, 15.18)	8.63 (4.83, 14.49)	14.46 (10.15, 18.47)	<0.001
<i>PPFT (cm), Median (Q1, Q3)</i>	13.31 (8.87, 19.43)	11.99 (7.95, 18.66)	16 (13.44, 20.61)	0.005
<i>Stranding, n (%)</i>				<0.001
<i>0</i>	72 (42.6)	72 (52.55)	0 (0)	
<i>1</i>	76 (44.97)	64 (46.72)	12 (37.5)	
<i>2</i>	21 (12.43)	1 (0.73)	20 (62.5)	
<i>APF, n (%)</i>				<0.001
<i>No</i>	72 (42.6)	70 (51.09)	2 (6.25)	
<i>Yes</i>	97 (57.4)	67 (48.91)	30 (93.75)	
<i>OT (min), Median (Q1, Q3)</i>	165 (130, 238)	165 (130, 240)	172.5 (138.75, 214.25)	0.669
<i>BV (ml), Median (Q1, Q3)</i>	50 (30, 100)	50 (30, 100)	50 (30, 200)	0.545
<i>HT, Median (Q1, Q3)</i>	14 (11, 20)	14 (11, 19)	17.5 (13, 24)	0.035

Note: SD: Standard Deviation; BMI: Body mass index; CHD: Coronary heart disease; MAFLD: metabolic (dysfunction)-associated fatty liver disease; LPFT: Lateral perinephric fat thickness; PPFT: Posterior perinephric fat thickness; APF: Adherent perirenal fat; OT: Operative time; BV: Bleed volume; HT: Hospitalization time.



**Fig. 3.** ROC curve of the new MAP score in the cohort.

**Table 3.** Association with patient surgery method grouped by new MAP Score.

Variables	Low score (n=137)	High score (n=32)	<i>p</i>
LRN	n=77	n=23	
OT (min), Median (Q1, Q3)	210 (155, 280)	180 (145, 257.5)	0.359
BV (ml), Median (Q1, Q3)	50 (30, 200)	60 (50, 200)	0.29
HT, Median (Q1, Q3)	14 (11, 19)	19 (13, 24)	0.022
LPN	n=60	n=9	
OT (min), (Mean (SD))	142.73 (43.73)	152.56 (22.36)	0.513
BV (ml), (Median (IQR))	50 (20, 100)	30 (20, 50)	0.302
HT, (Mean (SD))	16.32 (9.59)	16.22 (7.05)	0.977

Note: SD: Standard Deviation; IQR: Interquartile range; OT: Operative time; BV: Bleed volume; HT: Hospitalization time; LRN: Laparoscopic radical nephrectomy (LRN); LPN: Laparoscopic partial nephrectomy.

**Table 4.** Variables association with the new MAP Score.

Variables	Univariate			Multivariate		
	<i>p</i>	OR	95 % CI	<i>p</i>	OR	95 % CI
Age	<0.01	1.06	1.02-1.10	<0.01	1.05	1.01-1.10
Hypertension	<0.01	3.03	1.37-6.75	0.11	2.02	0.85-4.73
MAFLD	<0.01	3.99	1.55-10.12	0.01	3.61	1.32-9.76

Note: OR: Odds ratio; CI: Confidence interval; MAFLD: metabolic (dysfunction)-associated fatty liver disease.

age, high BMI, larger waist circumference, and increased perinephric fat thickness. The exact cause of APF is multifactorial and not entirely clear, but the prevailing view suggests a link with long-term systemic chronic inflammation and metabolic dysfunction, commonly

referred to as metabolic syndrome (MetS). Some researchers also suggest connections to metaflammation and inflammaging, although these are essentially similar to the concept of metabolic syndrome [16].

Adipose tissue serves not only as a storage depot

for energy but also plays a crucial role in metabolic inflammation. The concept of metabolic inflammation initially emerged in adipose tissue, where it exhibits the greatest complexity. Previous research has revealed disparities between people of East Asian ethnicity and Caucasians in terms of visceral fat accumulation, the prevalence of T2DM, MAFLD, BMI indices, and more. These variations suggest potential differences in risk factors for abdominal obesity-related health issues between these two populations.

The original three independent factors (diabetes, PPFT, and stranding) in the new MAP score also demonstrated significant statistical differences between the two groups, aligning with earlier findings. Our investigation identified a strong correlation between MAFLD and advanced age as significant risk factors for a high MAP score in people of East Asian ethnicity. To the best of our knowledge, our study is the first to report a significant correlation between MAFLD and a high MAP score (OR=3.614,  $p<0.05$ ). As indicated in a study by Borregale *et al.*, a higher MAP score is associated with an increased likelihood of abdominal obesity.

The worldwide occurrence of MAFLD stands at approximately 25.24 %, with significant regional variations. The Middle East exhibits the highest occurrence at 31.79 %, followed by South America (30.45 %), Asia (27.37 %), North America (24.13 %), Europe (23.71 %), and Africa (13.48 %) [17]. In overweight and obese individuals, the prevalence of MAFLD is around 50.7 %, with people of East Asian ethnicity (52.1 %) having notably higher rates than North Americans (34.0 %) [18]. A study also indicated that 3.72 % of the general population without obesity has non-obese MAFLD [13].

Even within the same country, there are disparities in MAFLD prevalence. For instance, in China, the occurrence of MAFLD is 46.7 % in Shanghai, 32.4 % in Beijing, 46.46 % in Zhejiang, 31.38 % in Henan, 26.1 % in Chongqing, 27.3 % in Hong Kong, and 11.5 % in Taiwan [13,19]. The overarching global trend demonstrates that, irrespective of a country's or region's development and economic status, the prevalence of MAFLD is rising across diverse populations.

In recent years, there has been a growing international consensus favoring the replacement of NAFLD with MAFLD as the preferred term. The diagnosis of MAFLD in this study was established based on the consensus statements provided by both Chinese and international experts [20,21]. Numerous studies have

demonstrated that the prevalence of MAFLD in the population surpasses that of NAFLD, and MAFLD is associated with a higher incidence of complications and a worse prognosis [22]. These complications encompass conditions such as T2DM, hypertension, and MetS. This association is evident in the shared underlying pathological mechanisms between MetS and MAFLD, with both conditions exhibiting a nearly identical global prevalence range. Moreover, a significant proportion of patients with MAFLD, ranging from 18 % to 33 %, are afflicted with T2DM, while 66 % to 83 % of them experience insulin resistance. Notably, T2DM is one of the risk factors considered in the new MAP score [23,24]. Recent research has indicated that the prevalence of T2DM in the Middle East is the highest worldwide, at 9.3 %, while it ranges from 10 % to 14 % in East Asia and 4 % to 6 % in Europe, mirroring the global prevalence of MAFLD [13,25].

There are multiple potential biological pathways connecting MAFLD and abdominal obesity with MetS. Prolonged MetS results in a persistent, mild inflammation in the body, which plays a central role in the development of insulin resistance associated with obesity. This, in turn, contributes to the onset and progression of MAFLD [26]. Consequently, MAFLD can be seen as a liver-specific manifestation of systemic insulin resistance [27]. Elevated levels of TNF- $\alpha$  in the bloodstream due to lipopolysaccharide (LPS) can initiate and worsen insulin resistance by activating the NF- $\kappa$ B pathway. Hepatic insulin resistance is a significant factor in the development of MAFLD [28,29]. Thus, the chronic, low-grade inflammation linked to MetS and the exacerbation of insulin resistance create a potential mechanistic connection between MAFLD and abdominal obesity-related insulin resistance (APF).

Another plausible factor in this association is an imbalance in the gut microbiota. The composition of the gut microbiota is frequently disrupted in patients with MetS and MAFLD, leading to damage to the intestinal barrier. Lipopolysaccharide (LPS), also known as endotoxin, enters the bloodstream when this barrier is compromised, binding to LPS-binding protein (LBP). Toll-like receptor 4 (TLR4), a pattern recognition receptor, acts as an LPS sensor and plays a crucial role in regulating the body's innate immune responses and the development of insulin resistance. Gut-derived endotoxemia induces insulin resistance through its impact on LPS-TLR4 interactions, which activate the Jun N-terminal kinase (JNK) and NF- $\kappa$ B pathways [27,28,29,30].

A further potential mechanism involves lower levels of adiponectin in patients with MAFLD, which have an inverse relationship with insulin resistance. Adiponectin is a highly secreted peptide from adipocytes and plays a significant role in the intricate interplay between insulin resistance and inflammation [31,32]. Furthermore, Yang *et al.* discovered that individuals with MAFLD exhibited notably greater paranephric fat thickness (PnFT) and perirenal fat thickness (PrFT) in comparison to those without MAFLD. Both PnFT and PrFT were independently correlated with the occurrence of MAFLD. It is worth noting that posterior perinephric fat thickness serves as an independent predictor of APF. Excessive visceral fat is susceptible to fat breakdown, resulting in the death and malfunction of fat cells. This, in turn, leads to an increase in free fatty acids and the accumulation of triglycerides in the liver, along with the production of inflammatory adipokines and cytokines like interleukin 6 and tumor necrosis factor- $\alpha$ . These processes activate the NF- $\kappa$ B pathways and boost diacylglycerol levels in the liver, ultimately triggering chronic inflammation and hepatic insulin resistance [33]. In conclusion, the presence of APF is intricately linked to chronic inflammation, T2DM, and MAFLD.

Prior studies have established that advanced age is considered a potential risk factor for APF based on multivariate analysis [11], although certain research has indicated no connection between advanced age and APF [9]. Our investigation corroborates the notion that advanced age indeed poses a risk for APF. Furthermore, as previously noted, advanced age is correlated with inflammaging, a gradual, inflammatory condition [34]. Aging encourages the shift of fat storage from under the skin to the inner abdominal area [35]. This increase in visceral fat can result in subsequent alterations in how insulin signaling and lipid regulation function. Visceral fat cells release an excessive amount of cytokines, which triggers the infiltration of macrophages and the activation of chronic inflammation pathways [14,36].

Malignant growth leads to the creation of a persistent environment of inflammation, in which the process of cancer formation collaborates with the body's cellular network. While it is commonly recognized that chronic inflammatory conditions increase the risk of developing cancer, the presence of inflammatory infiltrates associated with tumors remains a significant aspect of malignancies, whether or not pre-existing inflammatory disorders are present. Oncogenes actively affect pathways involved in promoting inflammation,

both directly and indirectly. For example, the Ras gene initiates the transcription of the pro-inflammatory cytokine interleukin-8 (IL-8) [37]. These factors contribute to the elevated incidence of age-related cancer in older patients.

Caucasians and people of East Asian ethnicity exhibit varying MAFLD prevalence rates, influenced by their distinct dietary customs, lifestyles, and genetic factors. Consequently, investigations into the connection between MAFLD and APF may yield diverse outcomes. Both MAFLD and age are intricately linked to MetS, T2DM, metabolic inflammation, and inflammaging in terms of underlying biological mechanisms. The new MAP score serves as a promising algorithm for predicting the occurrence of APF in people of East Asian ethnicity, although there is room for potential enhancements.

This study has certain constraints to consider. Since it is a retrospective investigation, it solely relies on data from a single medical center, and the available case count is quite restricted. Consequently, to enhance its accuracy and validity, it is essential to collect additional data from multiple centers and increase the number of cases. Furthermore, acquiring more clinical data is crucial for examining the connection between patients with MAFLD with a lean/normal weight and APF.

## Conclusions

In summary, the high new MAP score is highly correlated with MAFLD. Patients with high score may have a longer hospital stay, but the length of surgery and bleeding do not increase. Hence, there is room for enhancing the new MAP score specifically for East Asian populations.

## Conflict of Interest

There is no conflict of interest.

## Acknowledgements

Startup Fund for scientific research, Fujian Medical University (grant number: 2020QH1332). We thank Dr. Yongfei Liu for proofreading draft version of the manuscript.

## Abbreviations

APF, Adherent perirenal fat; AUC, area under the curve; BMI, body mass index; HDL, high-density lipoprotein; IL-8, interleukin-8; IR, insulin resistance; JNK, Jun N-terminal kinase; LPB, LPS-binding protein; LPFT,



lateral perinephric fat thickness; LPN, laparoscopic partial nephrectomy; LPS, lipopolysaccharide; LRN, laparoscopic radical nephrectomy; MAFLD, Metabolic(dysfunction)-associated fatty liver disease; MAP, Mayo adhesive probability; MetS, metabolic syndrome; NF- $\kappa$ B, nuclear factor kappa-light-chain-

enhancer of activated B cells; PnFT, paranephric fat thickness; PPFT, posterior perinephric fat thickness; PrFT, perirenal fat thickness; ROC, receiver operating characteristic; T2DM, Type 2 diabetes mellitus; TLR4, Toll-like receptor 4; TNF- $\alpha$ , tumor necrosis factor- $\alpha$

## References

1. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* 2023;402:203-234. [https://doi.org/10.1016/S0140-6736\(23\)01301-6](https://doi.org/10.1016/S0140-6736(23)01301-6)
2. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, Zelber-Sagi S, ET AL. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. *J Hepatol* 2020;73:202-209. <https://doi.org/10.1016/j.jhep.2020.03.039>
3. Nan Y, An J, Bao J, Chen H, Chen Y, Ding H, Dou X, ET AL. The Chinese Society of Hepatology position statement on the redefinition of fatty liver disease. *J Hepatol* 2021;75:454-461. <https://doi.org/10.1016/j.jhep.2021.05.003>
4. Davidiuk AJ, Parker AS, Thomas CS, Leibovich BC, Castle EP, Heckman MG, Custer K, Thiel DD. Mayo adhesive probability score: an accurate image-based scoring system to predict adherent perinephric fat in partial nephrectomy. *Eur Urol* 2014;66:1165-1171. <https://doi.org/10.1016/j.eururo.2014.08.054>
5. Borregales LD, Adibi M, Thomas AZ, Reis RB, Chery LJ, Devine CE, Wang X, ET AL. Predicting Adherent Perinephric Fat Using Preoperative Clinical and Radiological Factors in Patients Undergoing Partial Nephrectomy. *Eur Urol Focus* 2021;7:397-403. <https://doi.org/10.1016/j.euf.2019.10.007>
6. Kadowaki T, Sekikawa A, Murata K, Maegawa H, Takamiya T, Okamura T, El-Saed A, ET AL. Japanese men have larger areas of visceral adipose tissue than Caucasian men in the same levels of waist circumference in a population-based study. *Int J Obes (Lond)* 2006;30:1163-1165. <https://doi.org/10.1038/sj.ijo.0803248>
7. Yanishi M, Kinoshita H, Koito Y, Taniguchi H, Mishima T, Sugi M, Matsuda T. Adherent Perinephric Fat Is a Surgical Risk Factor in Laparoscopic Single-Site Donor Nephrectomy: Analysis Using Mayo Adhesive Probability Score. *Transplant Proc* 2020;52:84-88. <https://doi.org/10.1016/j.transproceed.2019.11.027>
8. Dariane C, Le Guilchet T, Hurel S, Audenet F, Beaugerie A, Badoual C, Tordjman J, ET AL. Prospective assessment and histological analysis of adherent perinephric fat in partial nephrectomies. *Urol Oncol* 2017;35:39.e9-39.e17. <https://doi.org/10.1016/j.urolonc.2016.09.008>
9. Kawamura N, Saito K, Inoue M, Ito M, Kijima T, Yoshida S, Yokoyama M, ET AL. Adherent Perinephric Fat in Asian Patients: Predictors and Impact on Perioperative Outcomes of Partial Nephrectomy. *Urol Int* 2018;101:437-442. <https://doi.org/10.1159/000494068>
10. Davidiuk AJ, Parker AS, Thomas CS, Heckman MG, Custer K, Thiel DD. Prospective evaluation of the association of adherent perinephric fat with perioperative outcomes of robotic-assisted partial nephrectomy. *Urology* 2015;85:836-842. <https://doi.org/10.1016/j.urology.2014.12.017>
11. Lee SM, Robertson I, Stonier T, Simson N, Amer T, Aboumarzouk OM. Contemporary outcomes and prediction of adherent perinephric fat at partial nephrectomy: a systematic review. *Scand J Urol* 2017;51:429-434. <https://doi.org/10.1080/21681805.2017.1357656>
12. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies [published correction appears in *Lancet* 2004;363:902]. *Lancet* 2004;363:157-163. [https://doi.org/10.1016/S0140-6736\(03\)15268-3](https://doi.org/10.1016/S0140-6736(03)15268-3)
13. Yuan Q, Wang H, Gao P, Chen W, Lv M, Bai S, Wu J. Prevalence and Risk Factors of Metabolic-Associated Fatty Liver Disease among 73,566 Individuals in Beijing, China. *Int J Environ Res Public Health* 2022;19:2096. <https://doi.org/10.3390/ijerph19042096>

14. Eskandari M, Alizadeh Bahmani AH, Mardani-Fard HA, Karimzadeh I, Omidifar N, Peymani P. Evaluation of factors that influenced the length of hospital stay using data mining techniques. *BMC Med Inform Decis Mak* 2022;22:280. <https://doi.org/10.1186/s12911-022-02027-w>
15. Khosravizadeh O, Vatankhah S, Bastani P, Kalhor R, Alirezai S, Doosty F. Factors affecting length of stay in teaching hospitals of a middle-income country. *Electron Physician* 2016;8:3042-3047. <https://doi.org/10.19082/3042>
16. Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. *Nature* 2017;542:177-185. <https://doi.org/10.1038/nature21363>
17. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016;64:73-84. <https://doi.org/10.1002/hep.28431>
18. Liu J, Ayada I, Zhang X, Wang L, Li Y, Wen T, Ma Z, ET AL. Estimating Global Prevalence of Metabolic Dysfunction-Associated Fatty Liver Disease in Overweight or Obese Adults. *Clin Gastroenterol Hepatol* 2022;20:e573-e582. <https://doi.org/10.1016/j.cgh.2021.02.030>
19. Liang Y, Chen H, Liu Y, Hou X, Wei L, Bao Y, Yang C, ET AL. Association of MAFLD With Diabetes, Chronic Kidney Disease, and Cardiovascular Disease: A 4.6-Year Cohort Study in China. *J Clin Endocrinol Metab* 2022;107:88-97. <https://doi.org/10.1210/clinem/dgab641>
20. Nan Y, An J, Bao J, Chen H, Chen Y, Ding H, Dou X, ET AL. The Chinese Society of Hepatology position statement on the redefinition of fatty liver disease. *J Hepatol* 2021;75:454-461. <https://doi.org/10.1016/j.jhep.2021.05.003>
21. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, Zelber-Sagi S, ET AL. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. *J Hepatol* 2020;73:202-209. <https://doi.org/10.1016/j.jhep.2020.03.039>
22. Nguyen VH, Le MH, Cheung RC, Nguyen MH. Differential Clinical Characteristics and Mortality Outcomes in Persons With NAFLD and/or MAFLD. *Clin Gastroenterol Hepatol* 2021;19:2172-2181.e6. <https://doi.org/10.1016/j.cgh.2021.05.029>
23. Noubiap JJ, Nansseu JR, Lontchi-Yimagou E, Nkeck JR, Nyaga UF, Ngouo AT, Tounouga DN, ET AL. Geographic distribution of metabolic syndrome and its components in the general adult population: A meta-analysis of global data from 28 million individuals. *Diabetes Res Clin Pract* 2022;188:109924. <https://doi.org/10.1016/j.diabres.2022.109924>
24. Chi ZC. Research status and progress of metabolic associated fatty liver disease. (Article in Chinese) *Shijie Huaren Xiaohua Zazhi* 2022;30:1-16. <https://doi.org/10.11569/wcj.v30.i1.1>
25. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* 2023;402:203-234. [https://doi.org/10.1016/S0140-6736\(23\)01301-6](https://doi.org/10.1016/S0140-6736(23)01301-6)
26. Hotamisligil GS. Inflammation and metabolic disorders. *Nature* 2006;444:860-867. <https://doi.org/10.1038/nature05485>
27. Sakurai Y, Kubota N, Yamauchi T, Kadowaki T. Role of Insulin Resistance in MAFLD. *Int J Mol Sci* 2021;22:4156. <https://doi.org/10.3390/ijms22084156>
28. Spranger J, Kroke A, Möhlig M, Hoffmann K, Bergmann MM, Ristow M, Boeing H, Pfeiffer AF. Inflammatory cytokines and the risk to develop type 2 diabetes: results of the prospective population-based European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study. *Diabetes* 2003;52:812-817. <https://doi.org/10.2337/diabetes.52.3.812>
29. Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. *Diabetes Care* 2004;27:813-823. <https://doi.org/10.2337/diacare.27.3.813>
30. Han R, Ma J, Li H. Mechanistic and therapeutic advances in non-alcoholic fatty liver disease by targeting the gut microbiota. *Front Med* 2018;12:645-657. <https://doi.org/10.1007/s11684-018-0645-9>
31. Fisman EZ, Tenenbaum A. Adiponectin: a manifold therapeutic target for metabolic syndrome, diabetes, and coronary disease? *Cardiovasc Diabetol* 2014;13:103. <https://doi.org/10.1186/1475-2840-13-103>
32. Zhang H, Niu Y, Gu H, Lu S, Zhang W, Li X, Yang Z, Qin L, Su Q. Low serum adiponectin is a predictor of progressing to nonalcoholic fatty liver disease. *J Clin Lab Anal* 2019;33:e22709. <https://doi.org/10.1002/jcla.22709>

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33. Yang Y, Li S, Xu Y, Ke J, Zhao D. The Perirenal Fat Thickness Was Associated with Nonalcoholic Fatty Liver Disease in Patients with Type 2 Diabetes Mellitus. *Diabetes Metab Syndr Obes* 2022;15:1505-1515. <https://doi.org/10.2147/DMSO.S350579>
  34. Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. *J Gerontol A Biol Sci Med Sci* 2014;69(Suppl 1):S4-S9. <https://doi.org/10.1093/gerona/glu057>
  35. Kuk JL, Saunders TJ, Davidson LE, Ross R. Age-related changes in total and regional fat distribution. *Ageing Res Rev* 2009;8:339-348. <https://doi.org/10.1016/j.arr.2009.06.001>
  36. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr* 2004;92:347-355. <https://doi.org/10.1079/BJN20041213>
  37. Demaria S, Pikarsky E, Karin M, Coussens LM, Chen YC, El-Omar EM, Trinchieri G, ET AL. Cancer and inflammation: promise for biologic therapy. *J Immunother* 2010;33:335-351. <https://doi.org/10.1097/CJI.0b013e3181d32e74>
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