Diabetes, Metabolic Syndrome and Obesity

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ORIGINAL RESEARCH

Psoas Muscle Index, Systemic Inflammation, and Liver Fibrosis in MAFLD: A Case-Control Study

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Objective: Investigating psoas muscle index (PMI) as a potential biomarker for metabolic dysfunction-associated fatty liver disease (MAFLD) and hepatic fibrosis through a case-control study.

Methods: This case-control study enrolled 80 MAFLD patients and 80 healthy controls from our hospital (2023–2024). Abdominal CT-derived PMI, inflammatory markers, and FIB-4 scores were assessed. ROC and logistic regression analyses evaluated PMI's diagnostic potential for MAFLD and associated fibrosis.

Results: A total of 160 patients met the inclusion criteria. Compared with the non-MAFLD group, the PMI and systemic inflammatory indicators in the MAFLD group were higher. In MAFLD patients, PMI was significantly correlated with systemic inflammation indicators, including the platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII) ($P<0.001$, $P=0.038$, and $P<0.001$, respectively). ROC curve analysis showed that the areas under the ROC curve (AUC) of PMI and other systemic inflammatory indicators (PLR, NLR, LMR, SII) for diagnosing MAFLD were 0.615, 0.526, 0.956, 0.803, and 0.674, respectively. The AUC of PMI combined with LMR, NLR, and LMR plus NLR for diagnosing MAFLD were 0.547, 0.585, and 0.572, respectively. FIB-4 was linearly correlated with PMI and systemic inflammatory indicators (PLR, NLR, SII) ($r=-0.208$, $P=0.008$; $r=-0.211$, $P=0.007$; $r=0.327$, $P<0.001$; $r=0.164$, $P=0.039$). The combination of PMI and systemic inflammatory indicators (PLR, NLR, SII) demonstrated a good diagnostic ability for liver fibrosis in MAFLD (AUC=0.602, $P=0.003$).

Conclusion: PMI significantly correlates with systemic inflammation and hepatic fibrosis in MAFLD patients, serving as a diagnostic biomarker. Combined with inflammatory markers, it improves non-invasive screening efficacy for MAFLD/fibrosis. This study pioneers incorporating muscle metabolism into MAFLD diagnosis, with potential for primary care translation. Dynamic PMI monitoring may assess "muscle-liver axis" targeted therapies.

Keywords: psoas muscle index, systemic inflammation, liver fibrosis, fatty liver, metabolic dysfunction

Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD) is an emerging metabolic disease. Its incidence has been increasing globally in recent years and has become one of the important issues affecting public health.[1,2] MAFLD and its potential complications, such as liver cirrhosis, not only seriously threaten the quality of life and life expectancy of patients, but also impose a significant economic burden on society.[3,4] Therefore, it is crucial to conduct in-depth research on the pathogenesis, diagnostic methods, and treatment strategies of MAFLD.

The core feature of MAFLD is metabolic dysfunction, which is often closely related to nutritional abnormalities.[5] Overnutrition or malnutrition may promote the occurrence and development of MAFLD by affecting mechanisms such as fat metabolism, insulin resistance, and oxidative stress.[6] Therefore, accurately assessing the nutritional status of MAFLD patients and developing personalized nutritional intervention plans have become important aspects of MAFLD management.

Received: 10 February 2025
Accepted: 12 September 2025
Published: 18 September 2025

Novel biomarkers hold significant value in research related to MAFLD. Compared to traditional diagnostic methods, novel biomarkers offer non-invasive, convenient, and economical characteristics, which can significantly enhance diagnostic accuracy and sensitivity. For example, the detection of specific proteins and miRNAs in serum allows for early identification and classification of MAFLD through simple blood samples.[7] MAFLD encompasses various stages, from simple fatty liver to non-alcoholic steatohepatitis (NASH), related cirrhosis, and hepatocellular carcinoma. Different stages of the disease require distinct management and treatment approaches. Novel biomarkers can help doctors distinguish between different stages and severities of the disease, enabling more personalized treatment plans. Studies have shown that the expression levels of certain miRNAs are closely related to the degree of fibrosis in MAFLD patients, which can be used to assess liver fibrosis and guide treatment decisions.[8] MAFLD progression is closely associated with various metabolic diseases, such as obesity, type 2 diabetes, hyperlipidemia, etc. Novel biomarkers can not only reflect the current disease status but also predict future progression and prognosis of the disease. The discovery and research of novel biomarkers not only aid clinical diagnosis and treatment but also advance basic research.

As a convenient and clinically valuable nutritional assessment tool, the psoas muscle index (PMI) has gained widespread attention in the study of MAFLD in recent years.[9,10] PMI indirectly reflects an individual's nutritional status and muscle quality by measuring the amount of psoas muscle, providing an objective basis for assessing the nutritional risk of MAFLD patients.[11] Studies have shown that PMI is closely related to the occurrence, development, and prognosis of MAFLD, with a low PMI potentially indicating a higher risk of disease progression and poor prognosis.[12] Several studies have shown that reduced PMI (reflecting sarcopenia) is significantly associated with worsening liver function, increased risk of infection and decreased survival in patients with cirrhosis.[13] In the field of metabolic diseases, PMI is strongly associated with insulin resistance, visceral fat accumulation and chronic inflammation, and may regulate metabolic homeostasis through the "muscle-liver axis".[14] A study found that reduced skeletal muscle mass in MAFLD patients independently predicted the progression of hepatic fat deposition, suggesting a protective role of muscle metabolism in liver disease.[15] However, the specific association of PMI in MAFLD inflammation and fibrosis is unclear and needs to be explored in depth. PMI has advantages over traditional markers and potential for clinical translation.

In addition, systemic inflammatory indicators play a crucial role in the assessment of MAFLD. Inflammatory indicators such as platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and systemic immune-inflammatory index (SII) reflect the overall level of systemic inflammation, providing important information for evaluating the inflammatory status of MAFLD patients.[16] Inflammation plays a key role in the pathogenesis of MAFLD by modulating immune responses and promoting liver cell damage and fibrosis, thereby affecting the progression and prognosis of the disease by regulating.[17] Recent studies have further revealed that the systemic immune-inflammatory index (SII) is a more sensitive predictor of the risk of progression of MAFLD to cirrhosis than a single index by integrating neutrophil, lymphocyte and platelet counts.[18] However, the combined diagnostic value of inflammatory indicators and muscle metabolic markers (such as PMI) has not been fully explored.

Therefore, this study aims to clarify the potential of PMI as a biomarker for MAFLD and its associated liver cirrhosis through a case-control study. This will provide clinicians with more comprehensive and accurate methods for patient assessment and treatment strategy references. Through in-depth research on MAFLD, we hope to contribute to improving patient prognosis and reducing the social burden.

Methods

Study Design

Patients who underwent abdominal ultrasound examinations at our hospital from January 2023 to January 2024 were selected. Inclusion criteria were patients over the age of 18 (excluding 18 years old). Exclusion criteria were: ① patients with acute infections; ② patients with autoimmune diseases; ③ patients with severe cardiopulmonary, renal, or cerebrovascular diseases; ④ patients with active viral hepatitis or drug-induced liver injury; ⑤ patients with genetic disorders; ⑥ patients with malnutrition; ⑦ patients with mental disorders or malignant tumors; ⑧ patients with chronic schistosomiasis. The study was approved by the Institutional Review Board prior to commencement, and informed

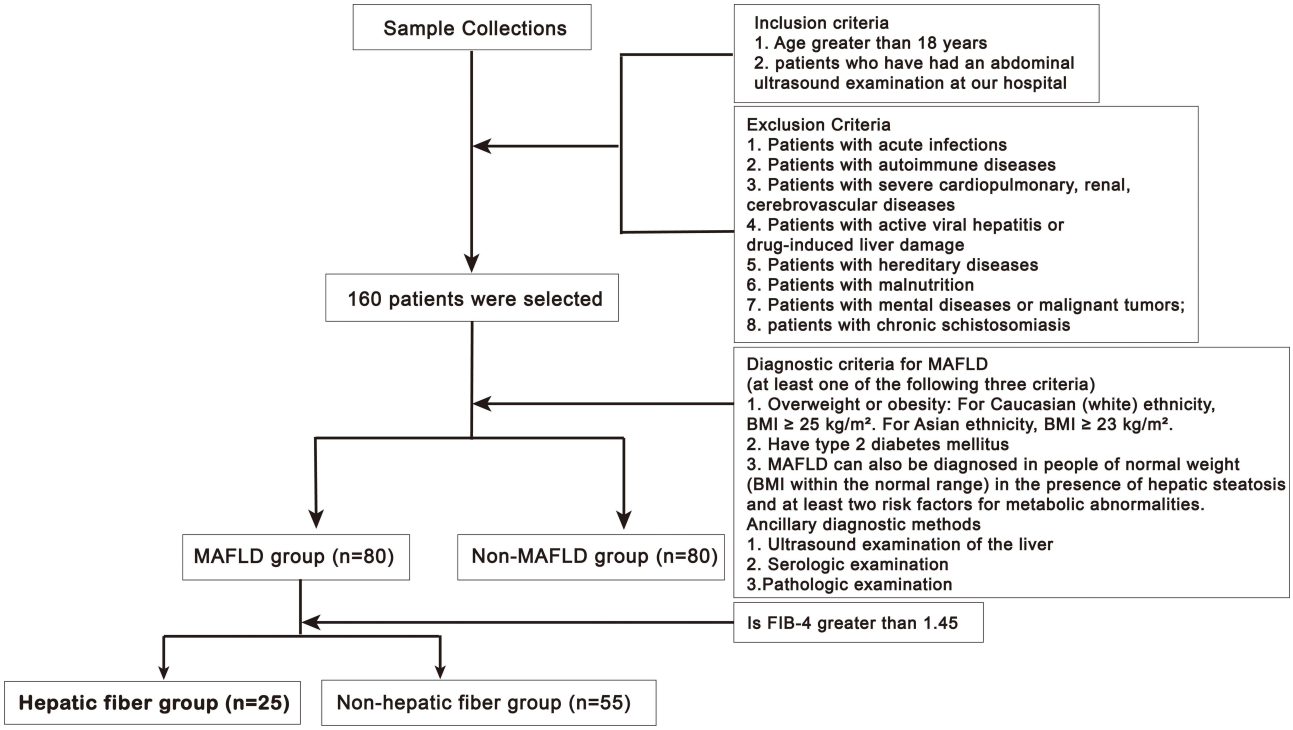

Figure 1 Study design and patient inclusion. According to the inclusion and exclusion criteria and the frailty assessment scale, 160 patients were finally selected, 80 of whom were in the non-MAFLD group and 80 in the MAFLD group. There were 25 cases of liver fibrosis and 55 cases of non-liver fibrosis in the MAFLD group.

consent was obtained from all patients. This study was in line with the Declaration of Helsinki and approved by the Ethics Committee (Ethics Committee, The First Affiliated Hospital of Soochow University).

Figure 1 showed the patient screening process. First, patients who had undergone abdominal ultrasound examinations in our hospital were screened based on inclusion and exclusion criteria, resulting in 160 patients being enrolled. Then, based on the diagnostic criteria of MAFLD, the patients were divided into the MAFLD group (n=80) and the non-MAFLD group (n=80). In the MAFLD group, patients were further classified into the liver fibrosis group (FIB-4 ≥ 1.45) and the non-liver fibrosis group (FIB-4 < 1.45). Finally, there were 25 cases of liver fibrosis (31.25%) and 55 cases of non-liver fibrosis (68.75%) in the MAFLD group (Figure 1).

General Condition and Laboratory Tests

All patients underwent relevant examinations, including basic laboratory blood tests, electrocardiograms, and abdominal ultrasounds. The age, gender, BMI, complete blood count, and blood biochemical indicators of the patients were recorded. Venous blood was drawn from the arm for the complete blood count and blood cell morphology examination. Biochemical indicators (liver function, blood sugar, blood lipids, renal function, electrolytes, etc) were tested using a biochemical analyzer and other equipment.

Evaluation of the PMI

We measured the psoas muscle area and calculated the PMI using preoperative CT scans. A Siemens SOMATOM Definition AS+ 64-row CT machine was used, with a scanning layer thickness of 5 mm, a window width of 400 HU, and a window position of 40 HU. The cross-sectional area of the bilateral psoas muscles was measured using preoperative plain film CT images at the lower border of the third lumbar vertebra (L3) with manual tracing. PMI (mm^2/m^2) was calculated using the following formula: PMI = cross-sectional area of bilateral psoas muscles (lower border of L3)/ $height^2$ (mm^2/m^2).

https://doi.org/10.2147/DMSO.S521829

Evaluation of the FIB-4 Index

The FIB-4 index is a non-invasive method used to assess liver fibrosis in patients with chronic liver disease. It is based on the patient's age, serum aspartate aminotransferase (AST) level, platelet count (PLT), and serum alanine aminotransferase (ALT) level. The calculation formula is as follows: FIB-4 = age×AST (U/L) / PLT count (10^9/L) × ALT (U/L).

Diagnostic Criteria for MAFLD

According to an existing study,[19] meeting any one of the following three criteria qualifies a patient as having MAFLD:

① Overweight or obesity: BMI ≥ 23 kg/m^2. ② People with type 2 diabetes ③ People with normal weight (BMI within the normal range) can also be diagnosed with MAFLD if they have liver steatosis and at least two metabolic risk factors.

Auxiliary diagnostic methods: ① liver ultrasound examination; ② serological tests; ③ pathological examination.

Statistical Analysis

SPSS 26.0 was used for statistical analysis. If normality (P>0.05) was satisfied, between-group comparisons were made using the independent samples *t*-test; otherwise, the nonparametric Mann–Whitney *U*-test was used. Dichotomous data such as gender and smoking history were tested using chi-square test or Fisher's exact test. Associations between PMI and continuous variables were selected according to data distribution: Pearson's correlation coefficient (r) was used for normal variables, and Spearman's rank correlation coefficient (ρ) was used for non-normal variables. α = 0.05 (two-tailed) was set and 95% CIs were calculated to assess the strength of association precision. The receiver operating characteristic (ROC) curve was used to evaluate the diagnosis of PMI and systemic inflammatory factors for MAFLD and the diagnosis of liver fibrosis in the MAFLD group. Independent predictors were identified using multivariate logistic regression, starting with univariate logistic regression of potential covariates to screen for variables significantly associated with MAFLD and liver fibrosis. Then forward stepwise regression was used to control the covariance problem and finally determine the independent predictors. A standardised between-group effect size of 0.65 (medium effect) was assumed for PMI. A two-sample *t*-test analysis was performed using G*Power 3.1 software, and the total sample size was calculated to require ≥128 cases (64 cases per group). The actual inclusion of 160 cases (80 cases per group) in this study provides 84% statistical power to meet the need to detect a medium effect. P<0.05 was considered statistically significant.

Results

Basic Demographics, Complete Blood Count, and Biochemical Indicators

The comparison of general data showed that among the 160 valid cases included in the study, there were 84 males and 76 females. There was no significant difference in the sex ratio between the MAFLD group and the non-MAFLD group (Male 43: Female 37 vs Male 41: Female 39, P=0.159). The average age was 55.55±1.39 years in the non-MAFLD group and 54.23±1.19 years in the MAFLD group, with no significant difference between the two groups (P=0.468). There were 13 smokers in the MAFLD group and 11 in the non-MAFLD group, showing no significant difference statistically (P=0.159). The MAFLD group had a higher BMI (26.14±0.38 vs.22.06±0.36 kg/m^2, P<0.001) and a greater proportion of hypertensive patients (16.25% vs.6.25%, P=0.004). In the complete blood count analysis, there were no significant differences in hemoglobin (Hb) and red blood cells (RBC) between the two groups, but there were significant differences in neutrophils, lymphocytes, monocytes, and platelets (P<0.001, P<0.001, P<0.001, and P=0.005, respectively). For biochemical indicators, there was no significant difference in total bilirubin (TBIL) between the two groups (P>0.05), while the MAFLD group had significantly higher aspartate aminotransferase (AST) (19.15±0.49 vs.17.60±0.50 U/L, P=0.032) and alanine aminotransferase (ALT) levels (18.32±0.43 vs.14.00 ±0.38 U/L, P<0.001) (Table 1).

Table 1 Basic Information on MAFLD and Non-MAFLD Patients

Parameter		Non-MAFLD	MAFLD	P
Age (years)		55.55 ± 1.39	54.23 ± 1.19	0.468
Gender (male/female)		41/39	43/37	0.159
BMI		22.06 ± 0.36	26.14 ± 0.38	<0.001
Smokers (%)		11 (13.75%)	13 (16.25%)	0.159
Hypertension (%)		5 (6.25%)	13 (16.25%)	0.004
Complete Blood Count	Hb (g/dL)	12.16 ± 0.22	11.64 ± 0.21	0.086
	RBC	22.56 ± 0.45	21.67 ± 0.40	0.175
	Neutrophils (10^9/L)	8.26 ± 0.07	10.671 ±0.13	<0.001
	Lymphocytes (10^9/L)	0.82 ± 0.01	0.68 ± 0.01	<0.001
	Monocytes	0.71 ± 0.01	0.47 ± 0.02	<0.001
	Platelets (10^9/L)	273.27±12.31	230.06± 9.02	0.005
Biochemical Indicators	TBIL (μmol/L)	36.59 ± 0.87	37.20 ± 0.80	0.626
	ALT (U/L)	14.00 ± 0.38	18.32± 0.43	<0.001
	AST (U/L)	17.60 ± 0.50	19.15 ± 0.49	0.032

Table 2 PMI and Systemic Inflammatory Indicators in MAFLD and Non-MAFLD Patients

Parameter		Non-MAFLD	MAFLD	P
PMI		12.89 ± 1.04	12.85 ± 0.97	0.007
Systemic Inflammation Indicators	PLR	340.96 ± 16.98	345.43 ± 15.35	0.843
	NLR	10.28 ± 0.22	15.92 ± 0.30	<0.001
	LMR	1.19 ± 0.03	1.84± 0.09	<0.001
	SII	2835.06 ± 147.39	3653.27 ± 161.37	<0.001

PMI and Systemic Inflammation Indicators in Both Patient Groups

In the comparison of PMI and systemic inflammation indicators between the two groups, the PMI of the MAFLD group was 12.85, which was significantly lower than that of the non-MAFLD group (12.89) (P=0.007). Among the systemic inflammatory indicators, the MAFLD group showed significantly higher levels of NLR, LMR, and SII, with all P-values less than 0.001. There was no significant difference in PLR between the two groups (P=0.843, Table 2).

Significant Correlation Between PMI and Systemic Inflammation Indicators in the MAFLD Group

In the MAFLD group, PMI showed a significant correlation with the systemic inflammation indicators PLR, NLR, and SII (r=−0.987, P<0.001; r=−0.232, P=0.038; r=−0.934, P<0.001). However, its correlation with LMR was not significant (r=0.049, P=0.662, Table 3).

PMI and Other Systemic Inflammation Indicators for the Diagnosis of MAFLD

The results of the ROC curve analysis showed that PMI and systemic inflammatory indicators (PLR, NLR, LMR, and SII) can be used independently for the diagnosis of MAFLD, with the areas under the ROC curve (AUC) being 0.585, 0.526, 0.572, 0.547 and 0.674 respectively. The combined diagnosis of MAFLD using PMI and LMR had an AUC of 0.803; PMI and NLR had an AUC of 0.615; and the combined use of PMI, NLR, and LMR for the diagnosis of MAFLD had an AUC of 0.956 (Figure 2).

https://doi.org/10.2147/DMSO.S521829

Table 3 Correlation Analysis Between PMI and Other Indicators in MAFLD Patients: Showed a Significant Correlation with Systemic Inflammation

Parameter	r	P
PLR	−0.987	<0.001
NLR	−0.232	0.038*
LMR	0.049	0.662
SII	−0.934	<0.001
TBIL	0.031	0.784
ALT	0.075	0.507
AST	0.058	0.611

Note: *P<0.05.

Comparison of PMI and Systemic Inflammation Indicators in Liver Fibrosis and Non-Fibrosis in MAFLD

This study compared PMI, systemic inflammatory indicators, and FIB-4 indexes in patients with liver fibrosis and non-fibrosis in the MAFLD group and found that PMI, systemic inflammatory indicators (PLR and SII), and FIB-4 indexes in patients with liver fibrosis were significantly different from those in patients without liver fibrosis (P values were all less than 0.001). There was no significant difference in systemic inflammatory indicators (NLR and LMR) between patients with liver fibrosis and non-fibrosis (P=0.274, 0.431, Table 4).

Significant Correlation Between FIB-4, PMI, and Systemic Inflammation Indicators

Pearson correlation analysis showed that FIB-4 was significantly negatively correlated with PMI and PLR (r=−0.208, P=0.008; r=−0.211, P=0.007). FIB-4 was significantly positively correlated with NLR and SII among systemic inflammatory indicators (r=0.327, P<0.001; r=0.164, P=0.039). There was no significant correlation between FIB-4 and the systemic inflammation indicator LMR (P=0.192) (Figure 3).

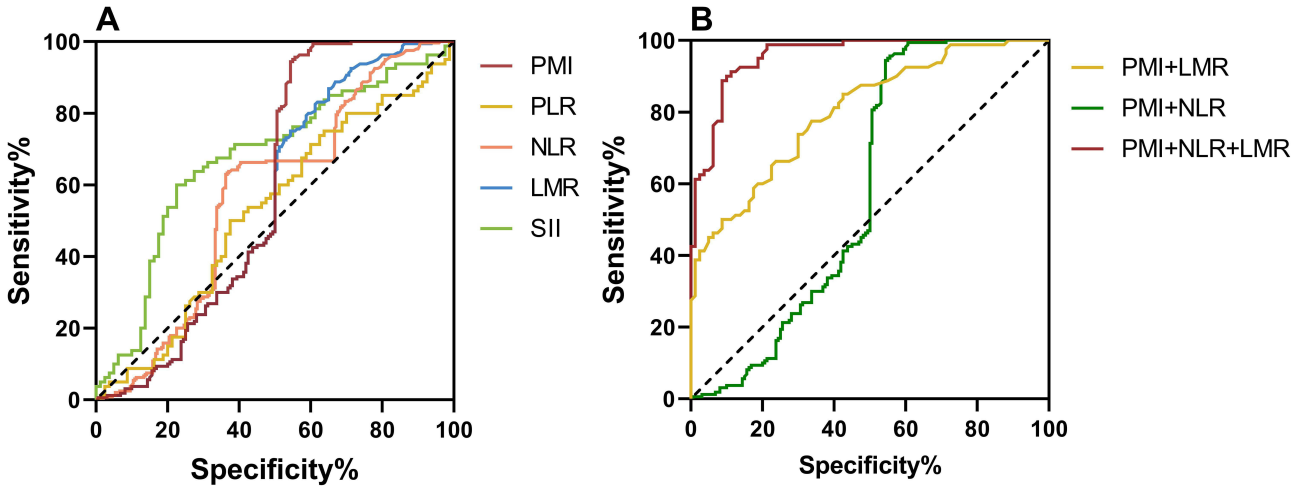

Figure 2 ROC curves of PMI and systemic inflammatory indicators for the diagnosis of MAFLD. (**A**) is the ROC curve of PMI and systemic inflammatory indicators used independently for the diagnosis of MAFLD; (**B**) is the ROC curve of PMI and systemic inflammatory indicators used in combination for the diagnosis of MAFLD.

Table 4 Indicators of PMI, Systemic Inflammation, and FIB-4 in Liver Fibrosis and Non-Liver Fibrosis in MAFLD

Parameter	Liver Fibrosis	Non-Liver Fibrosis	P
PLR	417.11 ± 27.52	198.04 ± 15.61	<0.001
NLR	16.05 ± 0.65	15.11 ± 0.53	0.274
LMR	2.10 ± 0.21	1.88± 0.15	0.431
SII	4375.51 ± 296.10	2101.52± 166.51	<0.001
FIB-4	2.29 ± 0.29	0.80 ± 0.04	<0.001
PMI	484.29± 25.14	686.91± 17.06	<0.001

PLR, SII, FIB-4, and PMI Could Serve as Independent Risk Factors for Liver Fibrosis in MAFLD

Multivariate logistic regression analysis was used to analyze the relationship between each factor and the occurrence of liver fibrosis in MAFLD. In the univariate model, each factor (PLR, SII, FIB-4, PMI) could be used as an independent risk factor for liver fibrosis in MAFLD (P<0.001, P<0.001, P=0.019, P<0.001). Similarly, in the multivariate model, each factor (PLR, SII, FIB-4, PMI) could also be used as an independent risk factor for liver fibrosis in MAFLD (P=0.011, P=0.024, P=0.043, P=0.010, Table 5).

PMI, PLR, SII, and FIB-4 Could Be Used for Liver Fibrosis Diagnosis in MAFLD

The results of ROC curve analysis showed that PMI, PLR, and SII could independently be used for the diagnosis of liver fibrosis in MAFLD, with the areas under the ROC curve (AUC) of 0.663, 0.553, and 0.642, respectively. The combined use of PMI, PLR, and SII for diagnosing hepatic fibrosis in MAFLD resulted in an AUC of 0.602 (Figure 4).

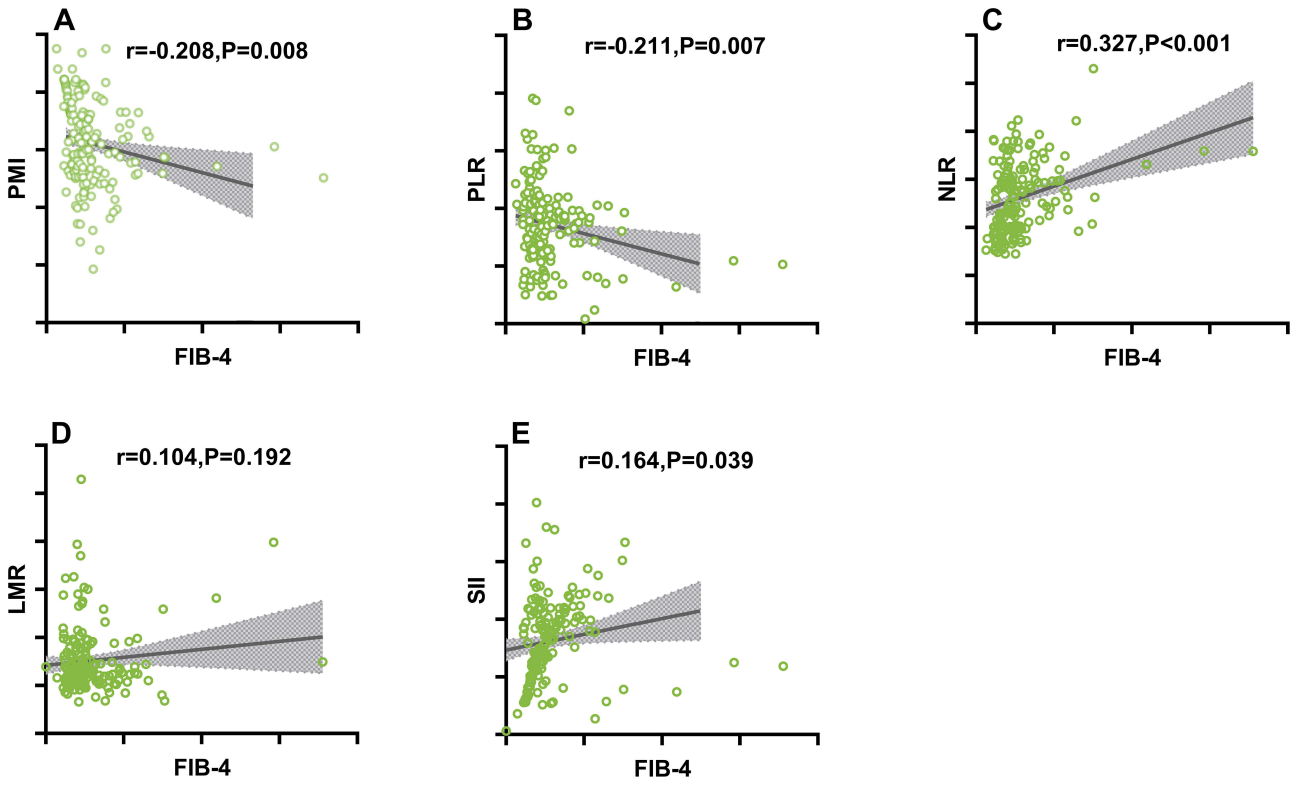

Figure 3 Correlation diagram of FIB-4 with PMI and systemic inflammatory indicators. (**A**–**E**) are the correlation diagrams of FIB-4 with PMI, and systemic inflammatory indicators PLR, NLR, and SII.

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Table 5 Multivariate Logistic Regression Analysis of Factors Associated with Liver Fibrosis in MAFLD

Parameter	Univariate Regression Model		Multivariate Regression Model	
	OR (95% CI Lower–Upper)	p value	OR (95% CI Lower–Upper)	p value
PLR	0.008 (0.005 ~ 0.013)	<0.001	0.363 (0.172 ~0.795)	0.011
SII	0.001 (0.000 5~ 0.0012)	<0.001	2.707 (2.692~ 2.713)	0.024
PMI	2.712 (2.707 ~ 2.716)	<0.001	0.266 (0.124 ~ 0.568)	0.010

Discussion

In this study, we investigated the correlation between PMI and systemic inflammation and liver fibrosis in MAFLD. The results showed that, compared to the non-MAFLD group, the MAFLD group had higher PMI and systemic inflammatory indicators. In MAFLD patients, PMI was significantly correlated with PLR, NLR, and SII in systemic inflammatory indicators. ROC curve analysis indicated that PMI, along with other systemic inflammation indicators, could be used both individually and in combination for the diagnosis of MAFLD. FIB-4 was linearly correlated with PMI and systemic inflammatory indicators (PLR, NLR, SII); and the combination of PMI and systemic inflammatory indicators had a good diagnostic ability for liver fibrosis in MAFLD.

MAFLD is widely prevalent worldwide, with a prevalence rate of about 30% and a steady upward trend in recent years.[20] The disease is closely related to obesity, diabetes, hyperlipidemia, and hypertension, which complicates treatment.[21] Non-invasive diagnostic methods such as magnetic resonance imaging proton density fat fraction (MRI-PDFF) have been widely used in the diagnosis of MAFLD and can accurately assess liver fat content.[22] Studies on THR-β agonists such as HSK31679, have shown in studies of MAFLD patients in China to significantly reduce liver fat

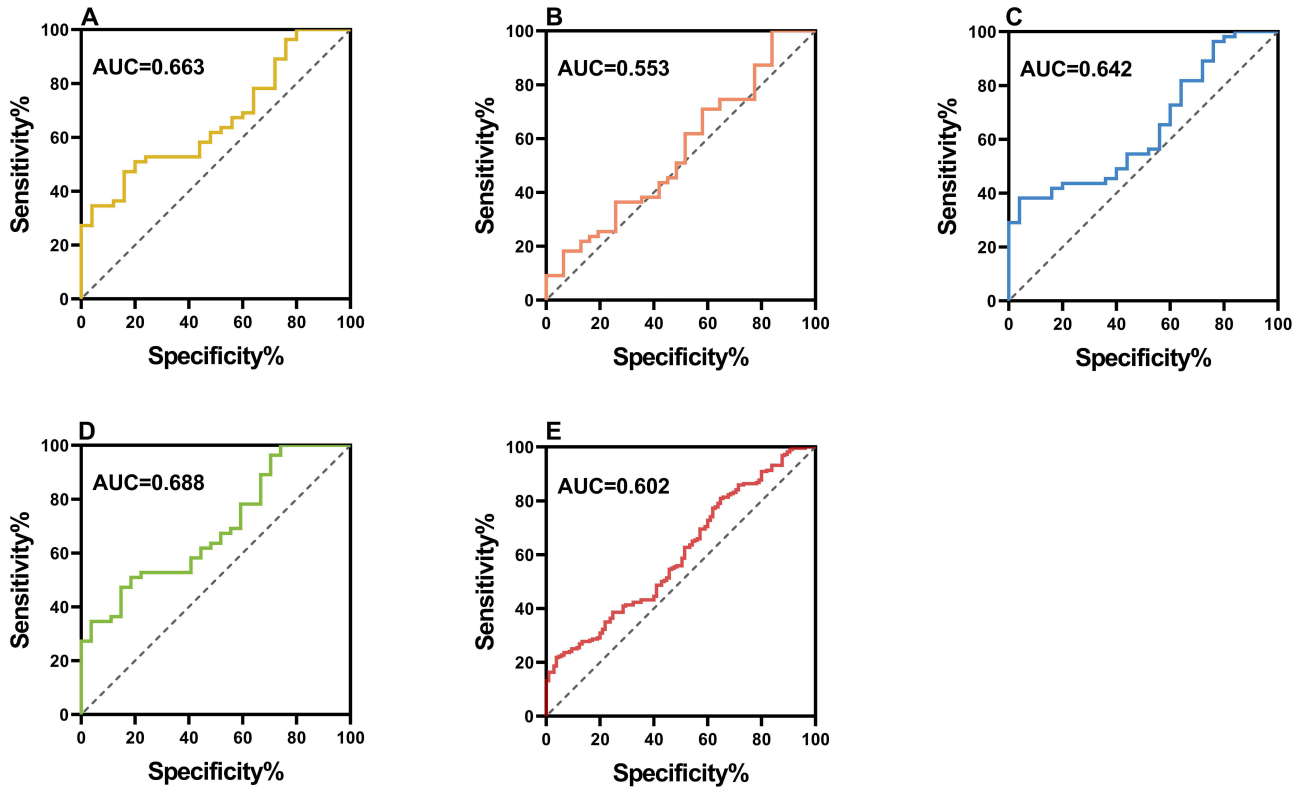

Figure 4 ROC curves of PMI and other factors for the diagnosis of liver fibrosis in the MAFLD group. (**A**–**D**) are the ROC curves of PLR, NLR, SII, and PMI used independently for the diagnosis of liver fibrosis in the MAFLD group; (**E**) is the ROC curve of PLR, NLR, SII, and PMI used in combination for the diagnosis of liver fibrosis in the MAFLD group.

content and have good safety profiles, providing a new option for the treatment of MAFLD.[23] Liver-protecting drugs such as polyene phosphatidylcholine capsules can significantly improve liver enzyme levels and fibrosis indicators when used in combination with conventional treatment.[24] Medications that regulate glucose and lipid metabolism such as pioglitazone, semaglutide, and dapagliflozin improve liver steatosis and inflammation by regulating glucose and lipid metabolism pathways.[25] Although significant progress has been made in diagnostic technology and treatment strategies for MAFLD, the complexity and multi-system impact of the disease necessitate further exploration of the role of biomarkers in the diagnosis and prognosis of MAFLD.

In this study, we explored the relationship between PMI and systemic inflammation and liver fibrosis in patients with MAFLD. Our findings revealed that PMI and multiple systemic inflammatory indicators (such as PLR, NLR, and SII) were significantly higher in patients with MAFLD than those in the non-MAFLD group, indicating a close relationship between MAFLD and systemic inflammation. This finding is consistent with previous research results. For example, some studies have pointed out that the diagnosis of severe intestinal disease is an independent predictor of MAFLD and an independent risk factor for late-stage liver fibrosis.[26] Other studies also highlighted that MAFLD patients experience persistent inflammatory response that extends beyond the liver and potentially affects multiple systems throughout the body.[27]

This study found that PMI has a significant correlation with systemic inflammatory indicators in patients with MAFLD, and can be used both individually and in combination for MAFLD diagnosis. This finding provides strong support for the application of PMI as a potential biomarker for MAFLD. Previous studies have also shown that obesity-related indicators such as waist circumference and BMI are closely related to the risk of MAFLD. However, PMI, which reflects both abdominal muscle mass and nutritional status, may offer a more comprehensive view of the patient's metabolic status.[28–30]

The results of this study reveal a linear correlation between the FIB-4 index and both PMI and systemic inflammatory indicators in MAFLD patients, suggesting a close connection between metabolism, inflammation, and fibrosis. This finding is consistent with previous research results,[31,32] which indicates that MAFLD patients are prone to liver fibrosis, and the progression of liver fibrosis is closely related to systemic inflammation levels. In recent years, there have been significant breakthroughs in MAFLD treatment strategies, but existing therapies still face challenges in individualised stratification and efficacy monitoring, and PMI may provide a new dimension to optimise treatment. PMI may serve as a predictive marker for efficacy, as muscle mass is closely related to mitochondrial function, and patients with a low PMI (<12.5 mm^2/m^2) may have a reduced response to drugs due to impaired muscle energy metabolism.[33] PMI in combination with inflammatory markers (eg, SII) may enrich the responding population, as reduced PMI (muscle atrophy) is strongly associated with high CCR2/5 expression.[34]

PMI has complementary advantages in the management of MAFLD compared to traditional indicators. BMI only reflects overall obesity and cannot distinguish between fat and muscle distribution. PMI is independently associated with fibrosis, suggesting that reduced muscle mass is a risk factor for MAFLD independent of obesity, providing a new dimension for metabolic health assessment. Although systemic inflammatory indexes can reflect the systemic inflammatory load, they cannot be traced back to the pathological mechanism, and the strong negative correlation between PMI and SII suggests that PMI may regulate inflammation through the "muscle-liver axis", and the combination of PMI+SII may improve the diagnostic efficacy of fibrosis.

Although this study primarily focuses on the relationship between PMI and MAFLD, it is worth noting that the treatment of MAFLD still faces many challenges. In recent years, some studies have revealed potential therapeutic targets for MAFLD. For example, a research team found that CHRNA4, a subunit of nicotinic acetylcholine receptors (nAChRs), plays a significant role in the progression of MAFLD. They pointed out that CHRNA4 is specifically expressed in hepatocytes, and its elevated level is positively correlated with the severity of MAFLD.[35,36] In addition, acetylcholine released by immune cells or nicotine produced by smoking can activate CHRNA4, thereby promoting the occurrence of liver inflammation and fibrosis.[37] This finding provides a new perspective for MAFLD treatment, suggesting that targeting CHRNA4 might be a promising therapeutic strategy.

The global prevalence of MAFLD is as high as 25.2% and continues to rise with the increasing prevalence of metabolic diseases such as obesity and diabetes.[38] This high prevalence not only adds to the burden on the medical

system but also has a serious impact on the quality of life and life expectancy of patients.[39] Although machine learning technology was not directly used in this study, the existing literature suggests that ML has significant advantages in accurate typing, dynamic monitoring and mechanism resolution of MAFLD. One study combined clinical indicators (BMI, ALT, platelets) and serum metabolomics data to construct a random forest model to predict the risk of liver fibrosis in patients with MAFLD.[40] Some scholars used SVM combined with Angptl8 protein and ultrasound features to classify subtypes of MAFLD (simple fatty liver vs NASH).[41] Some scholars developed LightGBM-based models to predict hepatic steatosis improvement by skeletal muscle mass and inflammatory indicators (NLR, CRP).[42] Therefore, a deep understanding of the pathogenesis of MAFLD and the development of effective treatments are of great public health significance.

While this study has made significant progress, it still has several limitations. During the data collection process, there may have been information bias or omissions, affecting the accuracy of the assessment of relevant indicators. Some studies may also have design flaws, such as insufficient sample size, which could compromise the reliability and validity of the research results. In future studies, we will strive to overcome these limitations and improve the accuracy and reliability of our findings by expanding the sample size, conducting multicentre studies, comprehensively considering potential confounding variables, and strengthening the quality control of data collection.

Conclusion

In summary, this study systematically investigated the association of PMI with systemic inflammation and hepatic fibrosis in patients with MAFLD through a case-control design. For the first time, PMI was introduced into the study of MAFLD, revealing its potential as a dual marker of inflammation and fibrosis, breaking through the neglect of muscle metabolism in the traditional assessment of liver disease. PMI measurement is based on conventional abdominal CT, which is low-cost and highly accessible, and is suitable for large-scale screening in primary healthcare. The diagnostic efficacy of PMI combined with LMR is significantly higher than that of conventional indicators, reducing the risk of missed diagnosis.

Funding

This work was supported by Suzhou Municipal Health Science and Technology Project (LCZX202305).

Disclosure

The authors report no conflicts of interest in this work.

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