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Association of pan-immune-inflammatory value with metabolic dysfunction-associated steatotic liver disease: findings from NHANES 2017–2020

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Abstract

Background Metabolic dysfunction-associated steatotic liver disease (MASLD) has become the most common chronic liver disease worldwide. The pan-immune-inflammation value (PIV) has been proposed as a biomarker for assessing immune status and inflammation. There is currently no evidence regarding the effect of PIV on the risk of MASLD. This study aimed to investigate the association between PIV and MASLD.

Methods The cross-sectional study included 6462 adults aged ≥ 20 years from the National Health and Nutrition Examination Survey 2017–2020. PIV was calculated based on blood count data. Weighted multivariable logistic regression was employed to calculate the odds ratio (OR) and 95% confidence interval (CI) to investigate the association of PIV and MASLD. Restricted cubic spline (RCS) analysis was conducted to explore the dose-response relationship between PIV and MASLD. Stratified and sensitivity analyses were performed to confirm the robustness of our findings.

Results Among 6462 participants, 2458 were diagnosed with MASLD. Positive associations between LnPIV and MASLD were observed in all three models (Model 1: OR = 1.46, 95% CI: 1.28–1.66, $P < 0.001$; Model 2: OR = 1.41, 95% CI: 1.24–1.60, $P < 0.001$; Model 3: OR = 1.39, 95% CI: 1.16–1.65, $P = 0.004$). When PIV was classified into quartiles, both Q3 and Q4 exhibited significantly increased risks of MASLD compared with the reference Q1 in full adjusted Model 3 (Q3: OR = 1.63, 95% CI: 1.20–2.22, $P = 0.012$; Q4: OR = 1.76, 95% CI: 1.28–2.41, $P = 0.008$; P for trend = 0.002). RCS analysis did not show a nonlinear relationship between LnPIV and MASLD ($P = 0.093$ for nonlinearity). Stratified analysis showed a consistent positive association between LnPIV and MASLD in all subgroups, and sensitivity analyses supported the reliability of these results.

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Conclusions Higher PIV levels are significantly associated with an increased prevalence of MASLD, indicating that PIV is a potentially effective inflammatory marker for assessing MASLD in participants.

Keywords Pan-immune-inflammatory value, NHANES, MASLD, Cross-sectional study, Inflammation

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), is characterized by excessive fat accumulation in liver cells [1]. It has become the most common chronic liver disease worldwide, with the prevalence in the general population estimated to be 31.3–38.7% in the US, 26% in Japan, and 27.5–47.2% in South Korea [2]. Individuals with MASLD not only face a heightened risk of progressing to severe liver conditions such as metabolic dysfunction-associated steatotic hepatitis, advanced liver fibrosis, cirrhosis, and hepatocellular carcinoma, but also have an increased risk of hypertension, type 2 diabetes, cardiovascular diseases (CVDs), chronic kidney disease, metabolic syndrome, and colorectal cancer [3–8]. These conditions impose a significant economic and healthcare burden. Therefore, it is essential to identify simple, easily accessible, and cost-effective biomarkers for early detection of high-risk MASLD individuals.

Although the pathogenesis of hepatic steatosis is not fully elucidated, substantial evidence suggests that inflammation and immunity play a significant role [9]. Recently, the pan-immune-inflammation value (PIV) has been proposed as a biomarker that reflects local or systemic immune status and inflammatory response [10]. PIV provides a more comprehensive assessment of inflammation than traditional indicators like neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) by incorporating complete blood count (CBC)-derived inflammatory cells, thus offering a more holistic view of the inflammatory state [11]. Initially, PIV was found to be strongly correlated with prognosis in various cancers [12–17]. Subsequent studies have shown that PIV can also be employed to evaluate the onset, monitor progression, and predict outcomes in CVDs, stroke, autoimmune disorders, infections, and other conditions [18–23]. Additionally, one study revealed that PIV is a better inflammatory marker than systemic immunity index for NAFLD assessment [24]. Currently, research on the relationship between PIV and MASLD is limited. Therefore, this study aimed to investigate the association of PIV with MASLD using data from the National Health and Nutrition Examination Survey (NHANES) 2017–2020.

Methods

Study design and population

NHANES, conducted by the National Center for Health Statistics (NCHS), is a research program designed to evaluate the health and nutritional status of US adults and children. It employs a multi-stage cluster probability sampling method and uniquely combines interviews with physical examinations. The interviews cover demographic, dietary, socioeconomic, and health-related topics. The examination section includes medical, dental, and physiological assessments, along with laboratory tests performed by trained healthcare professionals.

Among the initial 15,560 participants in NHANES 2017–2020, we excluded individuals younger than 20 years (n=6328), those lacking complete liver ultrasound vibration-controlled transient elastography (VCTE) measurements (n=1310), those with missing PIV data (n=314), heavy drinkers (defined as >30 g/day for men and >20 g/day for women; n=730), individuals with other liver diseases (n=230), and those with missing covariate data (n=186). Ultimately, 6462 individuals were included in the analyses. The detailed study flowchart is depicted in Fig. 1.

Definition of MASLD

VCTE was performed with the FibroScan® 502 V2 Touch (Echosens) device to measure controlled attenuation parameter (CAP) and liver stiffness measurement values for assessing liver steatosis and fibrosis. The examination required a fasting period of at least 3 h and a minimum of 10 valid stiffness measurements, with the interquartile range/median of liver stiffness being 30% or less, which were considered the criteria for a complete examination. Hepatic steatosis was defined by a median CAP value of at least 285 dB/m [25]. MASLD was defined as having hepatic steatosis and excluding excessive alcohol consumption (≥30 g/day for males and ≥20 g/day for females), and meeting at least one of the following cardiometabolic risk factors: (1) body mass index (BMI) ≥25 kg/m² (≥23 kg/m² for Asians) or waist circumference (WC) ≥94/80 cm (male/female); (2) fasting blood glucose ≥100 mg/dL or glycosylated hemoglobin ≥5.7%, or a history of type 2 diabetes, or currently receiving treatment for type 2 diabetes; (3) blood pressure ≥130/85 mmHg or receiving antihypertensive treatment; (4) plasma triglycerides ≥150 mg/dL or undergoing lipid-lowering treatment; (5) plasma high-density lipoprotein cholesterol (HDL-C) <40 mg/dL for men or <50 mg/dL for women, or receiving lipid-lowering treatment [26].

Calculation of PIV

At the Mobile Examination Center, NHANES professionals utilized the Beckman Coulter DxH 800 device to

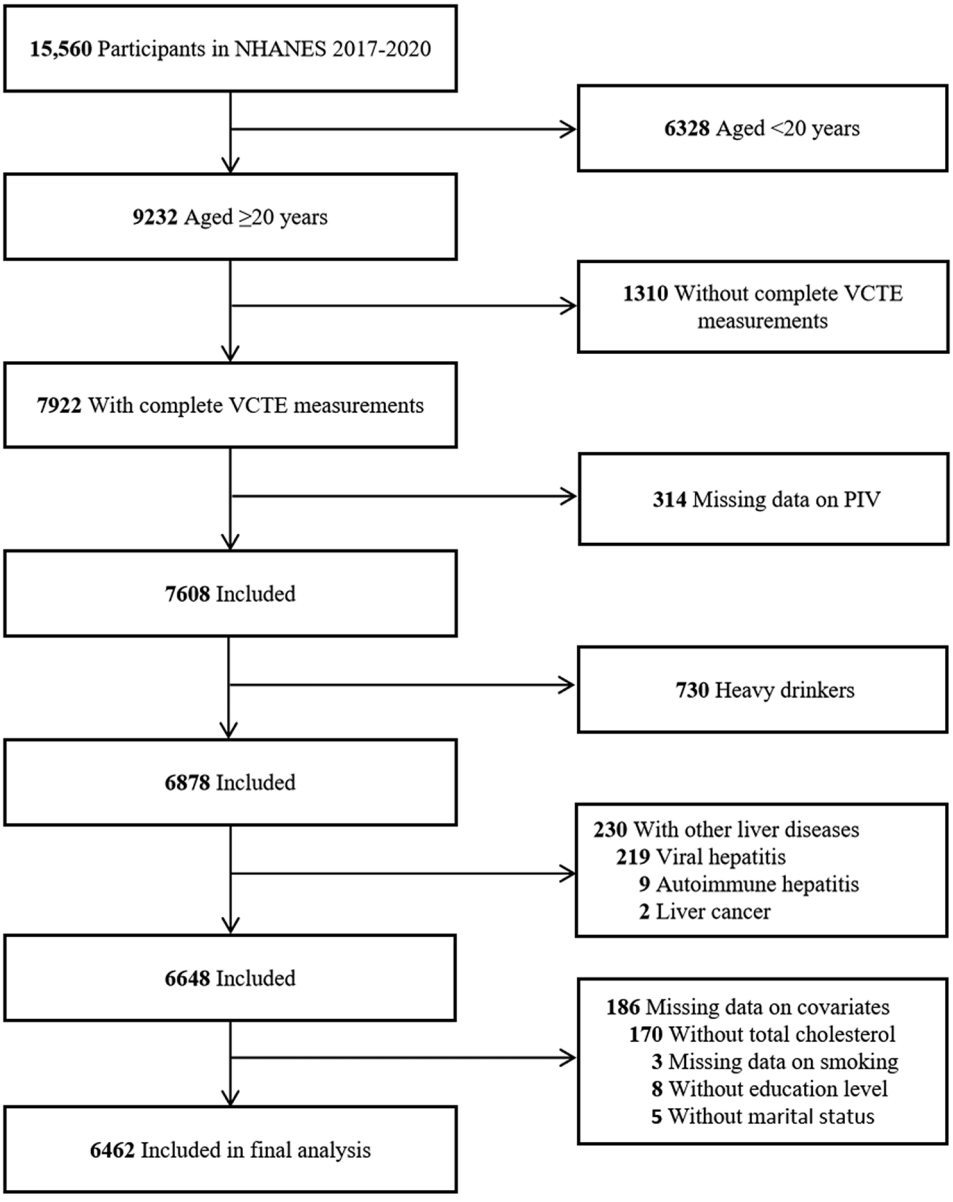

Fig. 1 Flow chart of participant selection. NHANES, National Health and Nutrition Examination Survey; VCTE, vibration controlled transient elastography; PIV, pan-immune-inflammation value

measure complete blood cell counts, expressed as $\times 10^3$ cells/μL. The formula for calculating PIV was: platelet count × neutrophil count × monocyte count / lymphocyte count [27]. Due to the skewed distribution of PIV, a natural logarithmic (Ln) transformation was applied.

Covariates

Confounding factors were chosen based on previous studies [24, 28] and theoretical rationale. This research included several covariates that might be associated with PIV and MASLD, including sex (male/female), age, race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and others), education level (high school or below, some college or associate's degree, college graduate or above), marital status (married/living with a partner, widowed/divorced/separated, never married), poverty income ratio (PIR), smoking, physical activity, Healthy Eating Index 2015 (HEI-2015), total cholesterol, and total energy intake. Smoking status was categorized as never, former, or current based on whether participants had smoked at least 100 cigarettes in their lifetime and their current smoking habits [29]. Physical activity levels were divided into no (<1 MET-h/week), low (1–48 MET-h/week), and high (>48 MET-h/week) [30]. HEI-2015 scores were calculated based on 24-hour dietary recalls, ranging from 0 to 100,

with higher scores representing better diet quality [31]. Detailed scoring criteria are available in Supplementary Table S1.

Statistical analysis

We employed NHANES-recommended weighting method in our statistical analyses to guarantee the sample's national representativeness. R version 4.3.2 software (R Foundation for Statistical Computing, Vienna, Austria) was utilized to analyze and process data. A two-sided P value <0.05 was considered statistically significant. We reported continuous variables as weighted means and standard errors (SEs), while categorical variables were displayed as weighted percentages and the respective 95% confidence intervals (CIs). Weighted multivariable logistic regression models with different levels of adjustment were used to calculate the odds ratios (ORs) and 95% CIs to examine the association between PIV and the risk of MASLD. Model 1 did not adjust for any covariates. Model 2 adjusted for sex, age, and race/ethnicity. Model 3 was a fully adjusted model that accounted for all covariates, including sex, age, race/ethnicity, education level, marital status, PIR, smoking, physical activity, HEI-2015, total cholesterol, and total energy intake.

We conducted restricted cubic spline (RCS) analysis with four knots (at the 5th, 35th, 65th, and 95th percentiles) to explore the nonlinear relationship between LnPIV and MASLD. Likelihood ratio tests were used to evaluate nonlinearity. Furthermore, stratified analyses were performed based on sex, age (20–39 years, 40–59 years, and ≥60 years), race/ethnicity, education level, marital status, PIR (<1.30, 1.30–3.50, and ≥3.50), smoking, and physical activity.

Two sensitivity analyses were also conducted to ensure the robustness of our findings. First, we conducted a repeated analysis defining hepatic steatosis as a median CAP value of 263 dB/m or higher (90% sensitivity) [32, 33]. Second, we applied multivariate multiple imputation with chained equations to address missing values in PIR, HEI-2015, and total energy intake.

Results

Baseline characteristics

Table 1 summarizes the baseline characteristics of the study population. Among the 6462 participants included, 2458 (37.40%) were diagnosed with MASLD. The mean (se) age was 48.43 (0.64) years, with females comprising 51.96% and non-Hispanic whites accounting for 61.80%. The range of PIV across the four quartiles (Q1 to Q4) was as follows: Q1 (<153.00), Q2 (153.00-239.13), Q3 (239.14-375.22), and Q4 (≥375.23). There were significant differences in age, race/ethnicity, education level, PIR, smoke status, and physical activity across the PIV quartiles (all $P<0.05$). Older participants, non-Hispanic whites, moderately education level, and never smoker were associated with higher PIV levels. In contrast, low income, low intensity physical activity, and poor dietary habits were associated with higher PIV levels.

Association between PIV and MASLD

As presented in Table 2, positive associations between LnPIV and MASLD were observed in all three models (Model 1: OR=1.46, 95% CI: 1.28–1.66, $P<0.001$; Model 2: OR=1.41, 95% CI: 1.24–1.60, $P<0.001$; Model 3: OR=1.39, 95% CI: 1.16–1.65, $P=0.004$). When PIV was classified into quartiles, both Q3 and Q4 exhibited significantly increased risks of MASLD compared with the reference Q1 in full adjusted Model 3 (Q3: OR=1.63, 95% CI: 1.20–2.22, $P=0.012$; Q4: OR=1.76, 95% CI: 1.28–2.41, $P=0.008$; P for trend=0.002). RCS analysis did not show a nonlinear relationship between LnPIV and MASLD after adjusting for multiple covariates ($P=0.093$ for nonlinearity, Fig. 2).

Stratified and sensitivity analyses

As shown in Fig. 3, a consistent positive association between LnPIV and MASLD was observed in all subgroups stratified by sex, age, race/ethnicity, education level, marital status, PIR, smoking, and physical activity (P for interaction <0.05).

We also performed two sensitivity analyses in this study (Table 3). First, we used the median CAP value of 263 dB/m as the cutoff for defining hepatic steatosis. A positive association between LnPIV and MASLD were observed in Model 3 (OR=1.32, 95% CI: 1.08–1.61, $P=0.014$). When PIV was divided into quartiles, both Q3 and Q4 showed significantly increased risks of MASLD compared to Q1 in Model 3 (Q3: OR=1.67, 95% CI: 1.42–2.45, $P=0.020$; Q4: OR=1.55, 95% CI: 1.10–2.16, $P=0.023$; P for trend=0.010). Additionally, the results remained robust after employing multiple imputation to address missing covariates in the repeated analysis.

Discussion

In this study, we found a positive association between PIV and the risk of MASLD. Higher PIV quartiles were associated with a higher incidence of MASLD. Specifically, for each one unit increase in LnPIV, the likelihood of MASLD increased by 39% (OR=1.39, $P=0.004$). RCS analysis did not show a nonlinear relationship between LnPIV and MASLD. Stratified analysis suggested that the association between PIV and MASLD prevalence remained consistent across all subgroups (P for interaction >0.05). Sensitivity analysis also confirmed the robustness of our findings.

Over the past few decades, PIV has been extensively studied in the field of oncology [10, 34–36]. A meta-analysis involving 30 studies and 8799 patients with

Table 1 Baseline characteristics of participants in NHANES 2017-2020[a]

Characteristic	Total	Q1	Q2	Q3	Q4	*P* value
N[b]	6462	1615	1616	1615	1616	
Sex						
Male	48.04 (46.05–50.03)	46.36 (42.53–50.24)	50.91 (47.49–54.32)	48.30 (44.13–52.50)	46.49 (42.55–50.48)	0.289
Female	51.96 (49.97–53.95)	53.64 (49.76–57.47)	49.09 (45.68–52.51)	51.70 (47.50-55.87)	53.51 (49.52–57.45)	
Age, y	48.43 (0.64)	46.98 (0.77)	47.11 (0.83)	48.80 (0.85)	50.34 (0.71)	< 0.001
Age strata, y						
20–39	35.92 (33.14–38.80)	39.65 (35.36–44.11)	37.84 (33.54–42.34)	34.56 (30.87–38.45)	32.66 (28.71–36.87)	0.009
40–59	34.16 (32.11–36.27)	33.19 (29.58–36.99)	35.42 (30.52–40.65)	35.44 (32.70-38.28)	32.55 (28.36–37.04)	
≥ 60	29.92 (26.67–33.39)	27.16 (23.12–31.61)	26.74 (22.46–31.51)	30.00 (25.34–35.11)	34.79 (30.89–38.92)	
Race and ethnicity						
Mexican American	9.08 (6.73–12.15)	9.49 (6.23–14.19)	10.11 (7.28–13.89)	9.21 (7.22–11.68)	7.74 (5.49–10.80)	< 0.001
Other Hispanic	7.92 (6.39–9.78)	8.31 (6.50-10.57)	8.28 (6.58–10.37)	7.28 (5.58–9.46)	7.92 (5.66–10.98)	
Non-Hispanic White	61.80 (56.13–67.17)	48.26 (39.50-57.13)	60.35 (55.99–64.55)	66.03 (59.86–71.71)	69.34 (62.52–75.41)	
Non-Hispanic Black	11.07 (8.40-14.46)	20.91 (15.65–27.36)	10.86 (8.25–14.17)	7.72 (5.64–10.47)	6.98 (5.05–9.57)	
Others	10.12 (7.95–12.81)	13.03 (9.87–17.02)	10.40 (7.79–13.74)	9.75 (7.49–12.60)	8.03 (5.74–11.11)	
Education level						
High school or less	3.95 (3.12–4.99)	4.17 (3.05–5.67)	4.12 (2.87–5.89)	4.16 (3.38–5.12)	3.42 (2.53–4.60)	0.003
Some college or associates degree	34.44 (30.86–38.21)	28.91 (24.47–33.79)	33.16 (28.60-38.06)	36.79 (32.26–41.58)	37.53 (32.30-43.07)	
College graduate or above	61.61 (57.67–65.41)	66.93 (61.72–71.74)	62.72 (57.83–67.36)	59.04 (54.13–63.78)	59.05 (53.60-64.29)	
Marital status						
Married/Living with Partner	61.77 (58.49–64.94)	63.01 (59.17–66.69)	60.63 (54.64–66.32)	62.26 (58.41–65.96)	61.37 (56.99–65.57)	0.865
Widowed/Divorced/Separated	18.54 (16.86–20.34)	16.93 (15.22–18.79)	18.91 (16.09–22.11)	19.18 (16.13–22.65)	18.81 (16.38–21.51)	
Never married	19.69 (17.28–22.35)	20.06 (16.93–23.61)	20.45 (16.02–25.74)	18.56 (15.89–21.56)	19.82 (16.52–23.59)	
Poverty income ratio	3.12 (0.06)	3.15 (0.1)	3.12 (0.08)	3.20 (0.09)	3.01 (0.06)	0.041
Poverty income ratio categories						
< 1.3	18.71 (17.50-19.98)	20.03 (17.22–23.17)	18.61 (16.25–21.22)	18.48 (16.04–21.20)	18.02 (16.02–20.21)	0.012
1.3–3.5	35.89 (34.06–37.76)	32.75 (28.65–37.14)	36.05 (31.38-41.00)	33.06 (28.40-38.07)	40.91 (37.10-44.84)	
≥ 3.5	45.40 (43.34–47.48)	47.22 (41.37–53.14)	45.34 (40.08–50.71)	48.46 (42.54–54.42)	41.06 (37.08–45.17)	
Smoking						
Never	14.78 (12.30-17.65)	11.74 (9.41–14.55)	12.09 (10.15–14.34)	15.85 (12.44–19.98)	18.47 (15.01–22.51)	< 0.001
Former	25.06 (22.83–27.43)	21.20 (17.45–25.50)	26.77 (23.49–30.32)	25.67 (22.13–29.56)	25.90 (22.97–29.06)	
Current	60.16 (57.45–62.80)	67.07 (62.58–71.27)	61.14 (57.14-65.00)	58.48 (55.35–61.55)	55.63 (51.64–59.55)	
Physical activity						
No	20.60 (19.20-22.08)	18.08 (15.74–20.68)	18.86 (16.15–21.91)	20.97 (17.51–24.92)	23.73 (21.23–26.43)	0.004
Low intensity	42.02 (40.04–44.04)	42.55 (38.80-46.38)	39.72 (36.25–43.29)	41.93 (39.05–44.86)	43.78 (39.76–47.89)	
High intensity	37.37 (35.46–39.33)	39.38 (36.06–42.80)	41.43 (37.61–45.34)	37.10 (34.07–40.23)	32.49 (28.44–36.81)	
MASLD						
No	62.60 (60.31–64.84)	71.55 (69.07–73.92)	66.41 (61.65–70.85)	58.47 (53.78–63.01)	56.34 (51.85–60.72)	< 0.001
Yes	37.40 (35.16–39.69)	28.45 (26.08–30.93)	33.59 (29.15–38.35)	41.53 (36.99–46.22)	43.66 (39.28–48.15)	

Table 1 (continued)

Characteristic	Total	Q1	Q2	Q3	Q4	*P* value
HEI-2015 score	49.86 (0.47)	52.01 (0.78)	50.74 (0.57)	48.46 (0.44)	48.74 (0.64)	< 0.001
Total cholesterol, mg/dL	186.64 (1.41)	187.00 (2.21)	186.39 (1.9)	188.05 (2.21)	185.23 (1.78)	0.738
Total energy intake, kcal/d	2102.39 (15.52)	2093.38 (35.06)	2128.21 (29.77)	2154.69 (40.08)	2035.40 (29.45)	0.055
PIV	321.29 (8.05)	108.30 (1.27)	195.77 (1.21)	300.16 (1.5)	615.35 (12.39)	< 0.001
LnPIV	5.54 (0.02)	4.63 (0.01)	5.27 (0.01)	5.70 (0)	6.34 (0.01)	< 0.001

NHANES, National Health and Nutrition Examination Survey; PIV, pan-immune-inflammation; MASLD, metabolic dysfunction-associated steatotic liver disease; HEI, healthy eating index

[a] Continuous variables are reported as weighted mean (standard error), while categorical variables are reported as weighted percentage with 95% confidence interval

[b] Numbers of each stratum may not add up to the total population due to missing data

[c] Others include Non-Hispanic Asian, other non-Hispanic, and multi-race individuals

malignant tumors indicated that pre-treatment PIV can serve as an effective and non-invasive prognostic biomarker for overall survival in cancer patients [37]. Another meta-analysis focused on breast cancer also yielded similar results [38]. In recent years, the prognostic value of PIV has been recognized in non-cancer diseases such as frailty [39], hypertension [40], myocardial infarction [41], heart failure [42], and kidney disease [43]. Currently, there is limited research on PIV in the context of steatotic liver disease. A retrospective study involving only 133 obese children and adolescents aged 6 to 18 confirmed that elevated PIV levels were linked to the presence and severity of hepatic steatosis [44]. Another study indicated that higher PIV levels were associated with an increased risk of NAFLD and liver fibrosis, especially in individuals under 60 years old [24]. However, both studies utilized the definition of NAFLD rather than MASLD, and one study had a notably limited sample size. Our research not only adopted the latest recognized definition of steatotic liver disease but also leveraged the large sample size of the NHANES database, enhancing the credibility of the results.

A recent study has revealed that fat accumulation plays a critical role in the development of NAFLD and metabolic-associated fatty liver disease in young adult males, even among non-obese individuals [45]. This accumulation can trigger inflammation and immune responses within the body. Increasing evidence underscores the significance of the host immune response in the pathogenesis of MASLD [46]. Neutrophils, monocytes, lymphocytes, and platelets all contribute to the development of this disease. Neutrophils contribute to liver cell damage and inflammation by forming neutrophil extracellular traps, releasing pro-inflammatory factors (such as tumor necrosis factor-α, interleukin-1β, and interleukin-6) and reactive oxygen species, and promoting ferroptosis [47]. Monocytes, after differentiating into macrophages, enhance liver inflammation and fibrosis by releasing pro-inflammatory factors, activating the CCR2 signaling pathway, and promoting lipid accumulation [48]. Lymphocytes influence liver inflammation and fibrosis through immune regulation, activation of intestinal innate lymphoid cells and $CD8^+$ T cells, and the function of regulatory T cells [49, 50]. Platelets exacerbate liver inflammation and damage by producing soluble factors (such as platelet factor 4, platelet-derived growth factor, and transforming growth factor-β), interacting with immune cells, promoting fibrosis, and forming microthrombi [51]. The interaction of these cells, along with systemic inflammation and immune dysfunction, collectively contributes to the pathogenesis of MASLD. Higher PIV values indicate greater potential inflammation and poorer immune response capability, which is associated

Table 2 Association of PIV with MASLD

Model	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
LnPIV	1.46 (1.28–1.66)	< 0.001	1.41 (1.24–1.60)	< 0.001	1.39 (1.16–1.65)	0.004
PIV quartile						
Q1	Reference		Reference		Reference	
Q2	1.27 (1.02–1.59)	0.036	1.22 (0.97–1.54)	0.081	1.20 (0.86–1.67)	0.204
Q3	1.79 (1.43–2.23)	< 0.001	1.72 (1.39–2.13)	< 0.001	1.63 (1.20–2.22)	0.012
Q4	1.95 (1.57–2.42)	< 0.001	1.87 (1.52–2.31)	< 0.001	1.76 (1.28–2.41)	0.008
P for trend		< 0.001		< 0.001		0.002

PIV, pan-immune-inflammation; MASLD, metabolic dysfunction-associated steatotic liver disease; OR, odds ratio; CI, confidence interval

[a] Crude model

[b] Adjusted for sex, age, and race/ethnicity

[c] Additionally adjusted for education level, marital status, poverty income ratio, smoking, physical activity, HEI-2015, total cholesterol, and total energy intake

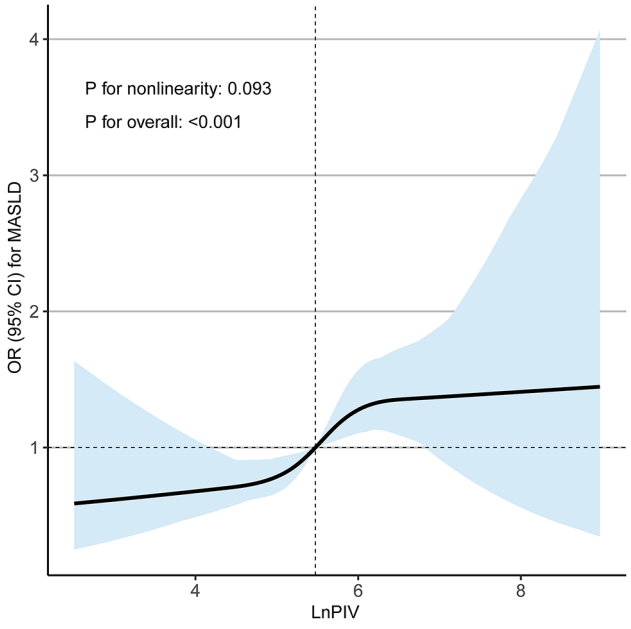

Fig. 2 Dose-response relationship between PIV and MASLD. Adjusted for sex, age, race/ethnicity, education level, marital status, poverty income ratio, smoking, physical activity, HEI-2015, total cholesterol, and total energy intake. The black solid line and shaded area represent estimates and their corresponding 95% CIs, respectively. Vertical dotted lines indicate the minimal threshold for the beneficial association with estimated OR = 1. OR was calculated for each unit increase in the natural logarithm of PIV (LnPIV). PIV, pan-immune-inflammation value; MASLD, metabolic dysfunction-associated steatotic liver disease; OR, odds ratio; CI, confidence interval

with an increased risk of MASLD, making our study finding unsurprising.

There are several strengths in this study. Our research is the first to investigate the association between PIV and MASLD. Additionally, all data we utilized were collected from NHANES, which has a standardized process for data collection to ensure accuracy. Furthermore, we explored the dose-response relationship between PIV and MASLD. However, this study has several limitations that warrant consideration. First, its cross-sectional design limited our ability to establish a causal relationship between PIV and MASLD. Second, NHANES data, while comprehensive, has inherent limitations, such as reliance on self-reported information and selection biases. Third, our analysis was based on participants from a single country, which may affect the generalizability of the findings to other populations. Fourth, although we effectively controlled for various cardiometabolic factors (e.g. smoking, physical activity, and HEI-2015) that could influence the relationship between PIV and MASLD through multiple mechanisms, such as directly affecting the inflammatory state and fat metabolism, other covariates like genetic factors and environmental exposures were not adequately explored in this study. Fifth, we used VCTE instead of liver biopsy to diagnose steatotic liver. While liver biopsy is considered the gold standard, it is neither feasible nor practical for large-scale population studies. VCTE is regarded as a suitable tool due to its significant

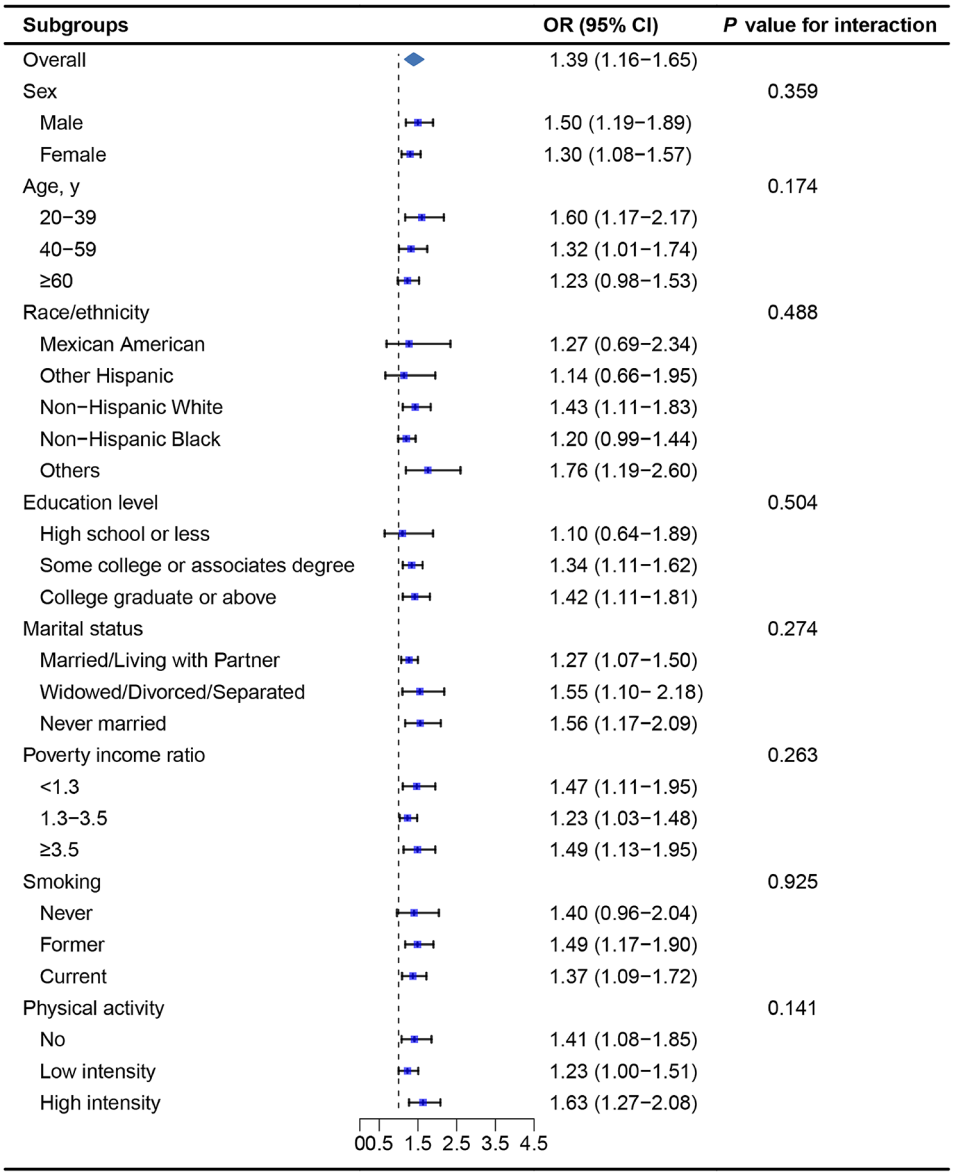

Fig. 3 Stratified analysis of the association between PIV and MASLD. ORs were calculated for each unit increase in the natural logarithm of PIV (LnPIV). Each stratification was adjusted for sex, age, race/ethnicity, education level, marital status, poverty income ratio, smoking, physical activity, HEI-2015, total cholesterol, and total energy intake except the stratification factor itself. PIV, pan-immune-inflammation value; MASLD, metabolic dysfunction-associated steatotic liver disease; OR, odds ratio; CI, confidence interval

sensitivity and specificity [52]. Finally, current guidelines recommend non-invasive serological scoring followed by imaging techniques for MASLD patients [53]. Although our findings have potential clinical applications, we did not construct a risk prediction model that incorporates PIV. Future research should address this issue and conduct prospective studies to assess the role of PIV in the progression and treatment response of MASLD.

Table 3 Sensitivity analysis of the association of PIV with MASLD[a]

	CAP ≥ 263 dB/m		Multiple imputation[b]	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
LnPIV	1.32 (1.08–1.61)	0.014	1.36 (1.15–1.59)	0.004
PIV quartile				
Q1	Reference		Reference	
Q2	1.16 (0.86–1.55)	0.241	1.20 (0.90–1.59)	0.151
Q3	1.67 (1.42–2.45)	0.020	1.62 (1.22–2.15)	0.010
Q4	1.55 (1.10–2.16)	0.023	1.78 (1.31–2.42)	0.006
P for trend		0.010		0.001

PIV, pan-immune-inflammation; MASLD, metabolic dysfunction-associated steatotic liver disease; CAP, controlled attenuation parameter; OR, odds ratio; CI, confidence interval

[a] Adjusted for sex, age, race/ethnicity, education level, marital status, poverty income ratio, smoking, physical activity, HEI-2015, total cholesterol, and total energy intake

[b] Missing data for HEI-2015, poverty income ratio, and total energy intake were imputed

Conclusions

Our research identified high PIV levels as an independent risk factor for MASLD, with elevated PIV levels being associated with an increased prevalence of MASLD. Further prospective studies are warranted to investigate the causal relationship underlying this observation.

Abbreviations

NHANES	National Health and Nutrition Examination Survey
VCTE	Vibration controlled transient elastography
PIV	Pan-immune-inflammation value
MASLD	Metabolic dysfunction-associated steatotic liver disease
OR	Odds ratio
CI	Confidence interval
HEI	Healthy eating index
CAP	Controlled attenuation parameter

Supplementary Information

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Supplementary Material 1

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Author contributions

L.H., Y.W., and J.Z. contributed to conception and design of the study. J.Z. provided administrative support. L.H., Z.N., and Q.Y. collected and analyzed the data. W.H. and J.L. prepared the tables and figures. L.H. and Z.N. drafted the manuscript. Q.Y., W.H., J.L., and Y.W. critically revised the manuscript. All authors read and approved the final manuscript.

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Data availability

Publicly available datasets were analyzed in this study. The data underlying this article are available in NHANES (https://www.cdc.gov/nchs/nhanes/index.htm).

Declarations

Ethics approval and consent to participate

The ethics review board of the National Center for Health Statistics (NCHS) approved all NHANES protocols, and written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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