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Linking Traditional Chinese Medicine Constitution with Metabolically Dysfunctional Fatty Liver Disease in the Elderly: A Cross-Sectional Analysis

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ABSTRACT

Research examining the connection between traditional Chinese medicine constitution (TCMC) and metabolic dysfunction-associated fatty liver disease (MAFLD) in older adults remains limited. This study aimed to characterize the distribution of TCMC types and MAFLD prevalence among the elderly, providing insights for constitution-based prevention and management strategies. A cross-sectional survey was performed in Zhongshan, China, involving participants aged 65 years and older. Data were collected on demographics, health history, anthropometrics, and TCMC classification. Associations between TCMC types and MAFLD were assessed using chi-square tests, multivariate logistic regression, subgroup analyses, and propensity score-based inverse probability weighting. Of 7,085 participants, 1,408 (19.9%) were identified with MAFLD. The predominant TCMC types among those with MAFLD were phlegm-dampness, gentleness, and yin-deficiency. After adjusting for potential confounders including age, sex, smoking, alcohol use, BMI, waist-to-hip ratio, hypertension, diabetes, and dyslipidemia, PDC was significantly associated with MAFLD (adjusted OR = 1.776, 95% CI: 1.496–2.108, P < 0.001), whereas qi-depression constitution showed a negative association (adjusted OR = 0.643, 95% CI: 0.481–0.860, P = 0.003). The link between PDC and MAFLD was more pronounced in men compared with women (adjusted OR = 2.04 vs. 1.70, Pinteraction = 0.003) and in smokers versus non-smokers (2.11 vs. 1.75, Pinteraction = 0.006).In the elderly population of Zhongshan, PDC is positively correlated with MAFLD, with stronger effects observed in men and individuals who smoke. Targeted early detection and management of PDC may help prevent the development and progression of MAFLD.

Keywords: Older, Phlegm-dampness constitution (PDC), Traditional Chinese medicine constitution (TCMC), Metabolic dysfunction-associated fatty liver disease (MAFLD)

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Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD) has emerged as the most prevalent chronic liver condition worldwide, affecting an estimated 37% of the population [1]. Evidence from observational studies on non-alcoholic fatty liver disease (NAFLD) indicates a higher likelihood of MAFLD diagnosis in these patients [2]. This updated disease classification not only reshapes current understanding but also poses significant health risks and considerable economic burdens on society [3]. Currently, there are no approved pharmacological treatments for MAFLD in the USA or European Union. The clinical heterogeneity of MAFLD—encompassing its manifestations and progression—can be influenced by factors such as age, sex, ethnicity, dietary habits, smoking, alcohol intake, genetics, gut microbiota, and metabolic health [4, 5].

The concept of "traditional Chinese medicine constitution" (TCMC; or Ti Zhi in Chinese) is used in TCM to characterize individual differences in physiological and psychological traits. TCMC represents an integrated state of health, combining structural, functional, and mental aspects of the human body [6]. In 2009, the Chinese Academy of Traditional Chinese Medicine established the Classification and Determination of TCM Constitution through extensive nationwide epidemiological surveys, standardizing the identification of TCMC types [6].

Variability in an individual's TCMC, shaped by both innate and acquired factors, can influence susceptibility to specific diseases, forming a predisposition for certain health conditions [7, 8]. This feature highlights the value of TCMC in the prevention and management of chronic illnesses.

TCMC types vary widely across individuals and populations [9]. In older adults, declining metabolic function, multiple comorbidities, polypharmacy, and prolonged disease history contribute to dysregulation of glucose and lipid metabolism. Furthermore, aging often coincides with shifts in TCMC patterns, which are linked to frailty and vulnerability to illness [10, 11]. Previous studies have documented associations between TCMC and metabolic disorders [12–14], and research has examined TCMC distribution in NAFLD [15, 16]. However, large-scale, rigorous studies on MAFLD that account for updated diagnostic criteria and physical characteristics are limited. Unlike NAFLD, which emphasizes hepatic steatosis, MAFLD explicitly requires the presence of metabolic dysfunction and captures additional patients not identified under NAFLD criteria, with a higher burden of comorbidities and poorer outcomes [17]. Geographic and regional factors further contribute to heterogeneity in both disease prevalence and TCMC distribution, influenced by climate, environment, and lifestyle [18]. Existing studies are therefore restricted by regional or population-specific factors, and there is a shortage of large, multicenter clinical epidemiological investigations on MAFLD in the context of TCMC.

In this study, we aimed to examine the association between MAFLD and TCMC among individuals aged 65 years and older in Zhongshan, a city in southern China's Lingnan region. Our objectives were to delineate the distribution of TCMC types in older adults with MAFLD, identify constitution types predisposed to the disease, and provide evidence for constitution-based preventive strategies. Ultimately, this research seeks to support the development of individualized approaches for MAFLD prevention and management in the elderly population grounded in TCM theory.

Materials and Methods

Study participants

This study was approved by the Ethics Committee of Guangdong Pharmaceutical University (Medical Ethics [2019] No. 109), and written informed consent was obtained from all participants. A cross-sectional investigation was conducted from August to October 2020 among older adults (≥65 years) attending routine medical check-ups at Torch Development Zone Hospital and Minzhong Hospital in Zhongshan City, as part of China's National Basic Public Health Service Program. High participation and compliance at these hospitals ensured reliable on-site data collection. Information was gathered by trained personnel using structured questionnaires, anthropometric assessments, Traditional Chinese Medicine Constitution (TCMC) evaluations, laboratory blood tests, electrocardiography, B-ultrasound imaging, and other clinical assessments.

Participants were included if they were aged 65 or older, could communicate effectively, completed the TCMC questionnaire, were able to provide fasting venous blood samples, and had available imaging data. Individuals were excluded if they were younger than 65, had major chronic illnesses (e.g., cancer, stroke, psychiatric disorders), could not independently complete the questionnaire, submitted incomplete questionnaires, or lacked clinical examination data. After applying these inclusion and exclusion criteria, 7,085 individuals were enrolled in the study (**Figure 1**).

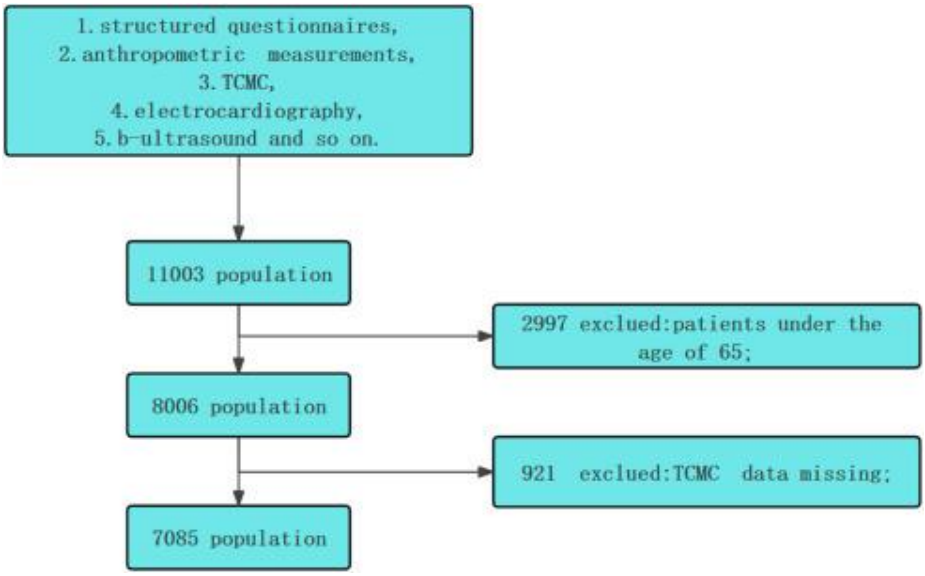

Figure 1. Flowchart of the study population.

The required sample size for this cross-sectional survey was calculated using the following formula (Eq. 1):

$$N = \frac{Z_{2\,(1-\alpha)/2}{}^{P}(1-p)}{\delta^{2}} \quad (1)$$

In this study, N denotes the sample size, (Z(1−α)/2) represents the percentile corresponding to an area of 1 − α in a standard normal distribution, p indicates the expected prevalence, and δ is the permissible margin of error for p. The reported prevalence of MAFLD in Asia is 29.62% [19]. Based on this, the sample size was determined using α = 0.05, (Z(1−α)/2) = 1.96, p = 0.2962, δ = 0.1, and p = 0.03, yielding a calculated sample size of 890 participants. After accounting for a potential 20% dropout rate, a minimum of 1,113 participants was required, and the study ultimately included 7,085 respondents.

Measurement of main variables

Diagnosis of MAFLD

The diagnosis of metabolic dysfunction-associated fatty liver disease (MAFLD) was determined following a recent international expert consensus [19, 20]. According to this definition, MAFLD is confirmed by evidence of hepatic steatosis on ultrasound along with at least one of the following conditions: overweight or obesity (BMI ≥23 kg/m² for Asian populations), type 2 diabetes mellitus (T2DM), or metabolic dysfunction. Metabolic dysfunction was defined as the presence of at least two of these abnormalities: (1) waist circumference (WC) ≥90 cm for men or ≥80 cm for women; (2) blood pressure ≥130/85 mmHg or current use of antihypertensive medication; (3) plasma triglycerides (TG) ≥1.70 mmol/L or relevant drug therapy; (4) plasma HDL-C <1.0 mmol/L for men or <1.3 mmol/L for women, or use of specific medications; (5) prediabetes, defined as fasting glucose 5.6–6.9 mmol/L, 2-hour post-load glucose 7.8–11.0 mmol/L, or HbA1c 5.7–6.4%; (6) HOMA-IR ≥2.5; and (7) high-sensitivity C-reactive protein (HS-CRP) >2 mg/L. The present study did not include 2-hour post-load glucose, insulin, or HS-CRP measurements, so these three indicators were not evaluated.

Determination of TCMC

Participants' Traditional Chinese Medicine Constitution (TCMC) was assessed using the "TCM Constitution in the Elderly" scale for classification and determination [21]. This scale, issued by the Chinese Association of Traditional Chinese Medicine, categorizes individuals into nine constitution types: gentleness, qi-deficiency, yang-deficiency, yin-deficiency, phlegm-dampness, dampness-heat, blood-stasis, qi-depression, and special diathesis [22, 23].

Covariate assessment

Data on sociodemographic factors (e.g., age, sex, smoking, alcohol use), medical history, family history, and lifestyle were collected via a validated structured questionnaire administered by trained researchers. Smoking status was classified as "never" or "current/former," with smokers defined as those who had consumed more than 100 cigarettes (five packs) in their lifetime. Alcohol consumption was defined as drinking at least once per week for six months within the past year, versus abstinence. Physical measurements including height, weight, BMI, WC, and hip circumference (HC) were obtained by trained examiners, and waist-to-hip ratio (WHR) was calculated as WC divided by HC, with abnormal WHR defined as ≥0.9 for men and ≥0.85 for women.

Fasting venous blood samples (≥8 hours) were collected for biochemical analysis. Diabetes mellitus (DM) was defined as a prior DM diagnosis at the community or hospital level, or current use of antidiabetic medication [24, 25]. Hypertension was defined similarly as a prior diagnosis or ongoing antihypertensive therapy [26]. Dyslipidemia was diagnosed according to the 2016 Chinese guidelines if any of the following were observed: total cholesterol (TC) ≥6.2 mmol/L, TG ≥2.3 mmol/L, HDL-C <1.0 mmol/L, or LDL-C ≥4.1 mmol/L [27, 28].

Statistical analysis

All data were double-entered and verified using EpiData 3.0 (www.epidata.dk), then organized into an Excel™ database (Microsoft, Redwood, WA, USA). Categorical variables were summarized as frequencies or percentages, while continuous variables were presented as mean ± standard deviation (SD). Between-group comparisons were conducted using the chi-square test for categorical variables and Student's t-test for continuous variables. Multivariable logistic regression models were used to examine the association between TCMC and MAFLD, with subgroup and interaction analyses conducted to explore potential effect modifications by sex, age, BMI, and WHR.

Sensitivity analyses were performed to assess the robustness of the findings. Participants were stratified by the presence of phlegm-dampness constitution (PDC), and a "synthetic sample" was created using propensity score-based weights, followed by inverse probability of treatment weighting (IPTW) to adjust for covariates [29]. Weighted logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between PDC and MAFLD. Covariate balance after weighting was evaluated using standardized mean differences (SMD) and variance ratios [30–32], with SMD <0.1 generally considered negligible and SMD <0.25 acceptable, while variance ratios close to 1 or <2 indicate adequate balance.

All analyses were performed using SPSS 25.0 (IBM, Armonk, NY, USA) and SAS 9.4 (SAS Institute, Cary, NC, USA), and a two-sided $P < 0.05$ was considered statistically significant.

Results and Discussion

Baseline participant characteristics

Table 1 presents the baseline profile of the 7,085 participants. The study population included 2,961 men (41.8%) and 4,124 women (58.2%), with a mean age of 71.35 ± 5.58 years. MAFLD was identified in 1,408 individuals (19.9%). Compared with participants without MAFLD, those with MAFLD were more likely to be female and to have hypertension, dyslipidemia, and abnormal WHR. Significant differences were also observed between the MAFLD and non-MAFLD groups in sex, age, smoking status, alcohol consumption, WHR, hypertension, diabetes, and lipid abnormalities ($P < 0.05$ or $P < 0.001$).

Table 1. Characteristics of participants with MAFLD at baseline.

Characteristic	MAFLD			*P*
	Total	No	Yes	
Total	7085 (100.0)	5677 (80.1)	1408 (19.9)	
Age, years, (mean ± SD)	71.35 ± 5.58	71.57 ± 5.69	70.47 ± 4.99	<0.001*
Gender (n, %)				<0.001*
male	2961 (41.8)	2545 (44.8)	416 (29.5)	
female	4124 (58.2)	3132 (55.2)	992 (70.5)	
Tobacco smoking (n, %)				<0.001*
no	5332 (75.3)	4167 (73.4)	1165 (82.7)	
yes	1753 (24.7)	1510 (26.6)	243 (17.3)	
Alcohol consumption (n, %)				<0.001*

no	5692 (80.3)	4464 (78.6)	1228 (87.2)	
yes	1393 (19.7)	1213 (21.4)	180 (12.8)	
Abnormal WHR (n, %)				<0.001*
no	1310 (18.5)	1232 (21.7)	78 (5.5)	
yes	5775 (81.5)	4445 (78.3)	1330 (94.5)	
BMI, kg/m^2 (n, %)				<0.001*
<23	2928 (41.3)	2768 (48.8)	160 (11.4)	
≥23	4157 (58.7)	2909 (51.2)	1248 (88.6)	
Hypertension (n, %)				<0.001*
no	3725 (52.6)	3156 (55.6)	569 (40.4)	
yes	3360 (47.4)	2521 (44.4)	839 (59.6)	
Diabetes mellitus (n, %)				<0.001*
no	6033 (85.2)	4983 (87.8)	1050 (74.6)	
yes	1052 (14.8)	694 (12.2)	358 (25.4)	
Dyslipidemia (n, %)				<0.001*
no	4280 (60.4)	3722 (65.6)	558 (39.6)	
yes	2805 (39.6)	1955 (34.4)	850 (60.4)	
TC (mmol/L)	5.21 ± 1.10	5.16 ± 1.08	5.41 ± 1.15	<0.001*
TG (mmol/L)	1.77 ± 1.22	1.60 ± 0.98	2.47 ± 1.72	<0.001*
LDL-C (mmol/L)	3.13 ± 0.90	3.11 ± 0.90	3.22 ± 0.92	<0.001*
HDL-C (mmol/L)	1.42 ± 0.37	1.46 ± 0.38	1.24 ± 0.32	<0.001*
GLU (mmol/L)	5.67 ± 2.00	5.64 ± 1.98	5.77 ± 2.10	0.033*
TCMC (n, %)				
Gentleness				<0.001*
no	3609 (50.9)	2704 (47.6)	905 (64.3)	
yes	3476 (49.1)	2973 (52.4)	503 (35.7)	
Qi-deficiency				0.028*
no	6326 (89.3)	5046 (88.9)	1280 (90.9)	
yes	759 (10.7)	631 (11.1)	128 (9.1)	
Yang-deficiency				0.011*
no	6372 (89.9)	5080 (89.5)	1292 (91.8)	
yes	713 (10.1)	597 (10.5)	116 (8.2)	
Yin-deficiency				0.151
no	5711 (80.6)	4557 (80.3)	1154 (82.0)	
yes	1374 (19.4)	1120 (19.7)	254 (18.0)	
Phlegm-dampness				<0.001*
no	4427 (62.5)	3893 (68.6)	534 (37.9)	
yes	2658 (37.5)	1784 (31.4)	874 (62.1)	
Dampness-heat				0.717
no	6622 (93.5)	5303 (93.4)	1319 (93.7)	
yes	463 (6.5)	374 (6.6)	89 (6.3)	
Blood-stasis				0.054
no	6070 (85.7)	4841 (85.3)	1229 (87.3)	
yes	1015 (14.3)	836 (14.7)	179 (12.7)	
Qi-depression				0.004*
no	6578 (92.8)	5246 (92.4)	1332 (94.6)	
yes	507 (7.2)	431 (7.6)	76 (5.4)	
Special diathesis				0.602
no	6801 (96.0)	5446 (95.9)	1355 (96.2)	
yes	284 (4.0)	231 (4.1)	53 (3.8)	

MAFLD= Metabolic dysfunction-associated fatty liver disease; BMI= body mass index; WHR= waist-to-hip ratio; TC= total cholesterol; TG= triglycerides; LDL-C= low-density lipoprotein-cholesterol; HDL-C= high-density lipoprotein-cholesterol; GLU= fasting glucose; TCMC= traditional Chinese medicine constitution.
*$P < 0.05$.

Distribution of TCMC among MAFLD Patients

Table 1 presents the composition of Traditional Chinese Medicine Constitution (TCMC) types in individuals with MAFLD. Among the 1,408 affected participants, the phlegm-dampness constitution (PDC) was most prevalent, observed in 62.1% (n = 874), followed by the gentleness constitution in 35.7% (n = 503). Other TCMC types included yin-deficiency (18.0%, n = 254), blood-stasis (12.7%, n = 179), qi-deficiency (9.1%, n = 128), yang-deficiency (8.2%, n = 116), dampness-heat (6.3%, n = 89), qi-depression (5.4%, n = 76), and special diathesis (3.8%, n = 53). Comparisons with participants without MAFLD revealed statistically significant differences in the occurrence of gentleness, qi-deficiency, yang-deficiency, PDC, and qi-depression types ($P < 0.05$ or $P < 0.001$).

Association between TCMC and MAFLD

The relationship between TCMC types and MAFLD was explored using multivariable logistic regression, treating MAFLD status as the outcome variable and the nine constitution types as predictors **(Table 2)**. In the unadjusted model considering only constitution types, PDC showed a strong positive association with MAFLD (OR = 3.15; 95% CI: 2.72–3.66; $P < 0.001$). After adjusting for demographic factors (sex, age), lifestyle factors (smoking, alcohol), anthropometric measures (BMI, WHR), and metabolic conditions (hypertension, diabetes, dyslipidemia), the PDC remained significantly associated with higher odds of MAFLD (OR = 1.78; 95% CI: 1.50–2.11; $P < 0.001$). Interestingly, the qi-depression constitution demonstrated a protective effect, showing a significant inverse relationship with MAFLD in the fully adjusted model (OR = 0.64; 95% CI: 0.48–0.86; $P = 0.003$). No other TCMC types were significantly linked to MAFLD after full adjustment.

Table 2. Multivariable logistic regression analysis of MAFLD and TCM constitution.

TCMC	Crude model		Minimally adjusted model		Fully adjusted model	
	OR (95%CI)	***P***	**OR (95%CI)**	***P***	**OR (95%CI)**	***P***
Gentleness	0.773 (0.655–0.914)	0.003*	0.780 (0.659–0.920)	0.004*	0.873 (0.728–1.047)	0.142
Qi-deficiency	0.833 (0.639–1.038)	0.103	0.883 (0.706–1.105)	0.278	0.830 (0.654–1.052)	0.123
Yang-deficiency	0.826 (0.660–1.034)	0.096	0.774 (0.616–0.972)	0.027	0.920 (0.721–1.174)	0.501
Yin-deficiency	0.873 (0.734–1.037)	0.121	0.880 (0.739–1.047)	0.151	0.887 (0.737–1.067)	0.202
Phlegm-dampness	3.153 (2.715–3.662)	<0.001*	3.351 (2.878–3.903)	<0.001*	1.776 (1.496–2.108)	<0.001*
Dampness-heat	1.032 (0.793–1.344)	0.813	1.053 (0.805–1.377)	0.707	1.028 (0.774–1.366)	0.846
Blood-stasis	0.784 (0.650–0.946)	0.011*	0.818 (0.676–0.989)	0.038*	0.888 (0.726–1.086)	0.247
Qi-depression	0.732 (0.559–0.960)	0.024*	0.639 (0.486–0.841)	0.001*	0.643 (0.481–0.860)	0.003*
Special diathesis	0.921 (0.669–1.269)	0.616	0.945 (0.683–1.308)	0.734	1.002 (0.712–1.412)	0.989

TCMC: Traditional Chinese medicine constitution; OR: odds ratio; CI: confidence interval.
Crude model: included only the nine TCMC types.

Minimally adjusted model: accounted for the nine TCMC types along with sex and age.
Fully adjusted model: controlled for the nine TCMC types as well as sex, age, smoking status, alcohol intake, BMI, abnormal WHR, hypertension, diabetes, and dyslipidemia.
*$P < 0.05$.

Subgroup analysis of PDC and MAFLD

The subgroup analysis **(Figure 2)** demonstrated that the phlegm-dampness constitution (PDC) was consistently positively associated with MAFLD across most factor levels, with the exception of alcohol consumption and participants with normal WHR. The link between PDC and MAFLD was stronger in men than in women, with adjusted odds ratios of 2.04 (95% CI: 1.47–2.84) versus 1.70 (95% CI: 1.39–2.08), and a significant interaction effect ($P_{interaction} = 0.003$). Similarly, the association was more pronounced among individuals who smoked

tobacco compared with non-smokers, with adjusted ORs of 2.11 (95% CI: 1.39–3.21) versus 1.75 (95% CI: 1.45–2.12), and a significant interaction ($P_{interaction} = 0.006$).

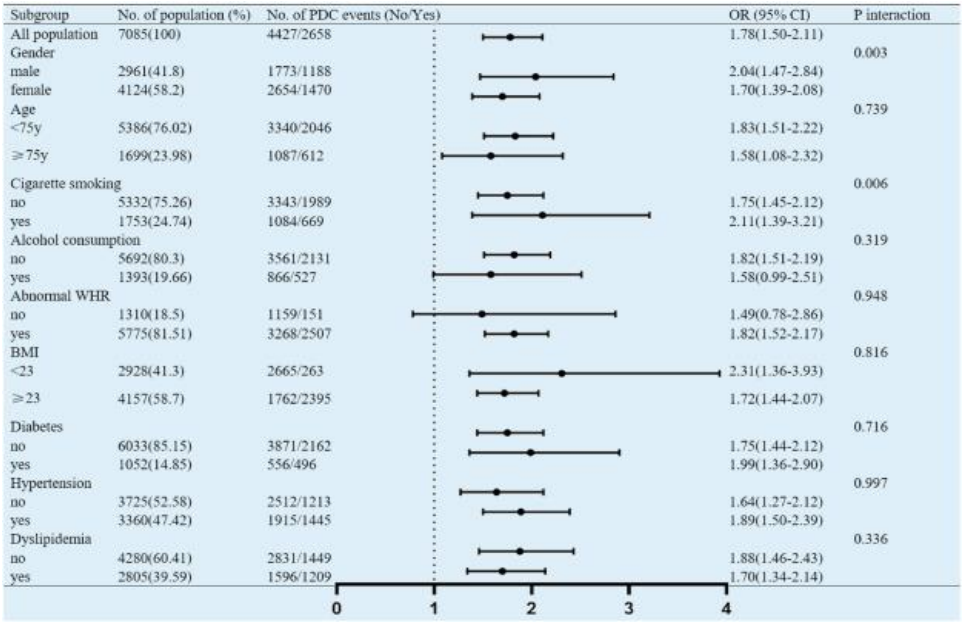

Figure 2. Subgroup analysis MAFLD: Metabolic dysfunction-associated fatty liver disease; PDC: phlegm-dampness constitution; BMI: body mass index; WHR: waist-to-hip ratio; OR: odds ratio; CI: confidence interval; $P_{interaction}$: interaction test within subgroup analysis to investigate the relationship between the PDC and MAFLD separately in a population with different levels of confounding factors (e.g., gender, age, tobacco smoking). The interaction between the phlegm-dampness constitution with each confounding factor was examined.

Sensitivity analysis

Participants were first classified based on the presence or absence of the phlegm-dampness constitution (PDC). Covariates adjusted using inverse probability of treatment weighting (IPTW) derived from the propensity score included potential confounders such as age, sex, smoking, alcohol use, BMI, WHR, hypertension, diabetes mellitus, dyslipidemia, and the remaining eight TCMC types. After weighting, the standardized mean differences (SMDs) for all matched covariates were below 0.1 or 0.2 between the PDC and non-PDC groups, indicating adequate balance. Following adjustment for these confounders, weighted logistic regression yielded an odds ratio (OR) of 1.78 (95% CI: 1.42–2.24) for the association between PDC and MAFLD **(Table 3)**, consistent with the findings from the fully adjusted multivariable logistic regression model.

Table 3. Association of the phlegm-dampness constitution with MAFLD after IPTW matching.

After IPTW	Phlegm-dampness constitution			
	No	**Yes**	**OR (95%CI)**	***P***
MAFLD (n, %)	618 (14.8)	641 (20.1)	1.78 (1.42–2.24)	0.002*

MAFLD: Metabolic dysfunction-associated fatty liver disease; IPTW: inverse probability of treatment weighting; OR: odds ratio; CI: confidence interval.

*$P < 0.05$.

Various TCMC types have been linked to specific health conditions [7, 9], highlighting their potential value in the early detection and prevention of disease.

Our study identified a significant relationship between the phlegm-dampness constitution (PDC) and MAFLD. A higher proportion of individuals with the PDC had MAFLD compared with those without it. Even after adjusting for multiple confounders—including age, sex, smoking, alcohol use, BMI, WHR, hypertension, diabetes, dyslipidemia, and the remaining eight TCMC types—multivariable logistic regression confirmed a positive association between PDC and MAFLD. These results align with previous findings reported by Liang *et al*. and Zhu *et al*. [16, 33].

Environmental factors may contribute to the high prevalence of PDC in certain regions. For instance, the Lingnan area's warm and humid climate, frequent rainfall, complex terrain, and proximity to the sea create conditions

conducive to phlegm and dampness, making PDC a common TCMC type in this population. PDC has been recognized as a high-risk factor for chronic metabolic disorders, including hyperlipidemia, diabetes, and NAFLD [14, 34, 35], and is often described as the "common soil" underlying endocrine, nutritional, and metabolic diseases [35]. From the TCM perspective, MAFLD develops primarily due to the interplay between PDC and impaired liver and spleen function, as phlegm-dampness can disrupt their normal physiological activities [36].

Molecular studies further support the metabolic risk associated with PDC. Whole-genome DNA methylation profiling revealed that individuals with PDC exhibit differential gene expression enriched in multiple metabolic pathways compared with those with a gentleness constitution, suggesting heightened susceptibility to metabolic disorders [37]. Emerging research on mechanisms such as DNA methylation, RNA regulation, and gut microbiota has demonstrated that PDC is associated with insulin resistance, oxidative stress, elevated free fatty acids, disturbances in energy metabolism, endocrine imbalances, genetic factors, and impaired glucose and lipid metabolism [38–40]. These findings collectively underscore the close connection between PDC and MAFLD development.

Subgroup and interaction analyses indicated that men with PDC and individuals with PDC who smoked tobacco had a higher likelihood of developing MAFLD. Consistent with previous meta-analyses, MAFLD risk is elevated in populations with higher BMI, hypertension, diabetes, dyslipidemia, advanced fibrosis scores, and male sex [3, 5]. Several studies also suggest a positive association between tobacco use and NAFLD, although the mechanisms remain unclear [41–43]. Additionally, tobacco smokers are approximately 1.8 times more likely to exhibit PDC than non-smokers [44]. This pattern may reflect behavioral tendencies in men, who are more likely to smoke, consume alcohol, and prefer greasy or salty diets, thereby promoting phlegm and dampness accumulation [45]. While the precise mechanisms underlying the interaction of PDC with sex and smoking in MAFLD development remain to be fully elucidated, TCMC principles emphasize that biased constitutions can be modified and lifestyle interventions may mitigate disease progression. Experimental evidence further supports this, showing that phlegm-resolving treatments can reduce liver injury in NAFLD and non-alcoholic steatohepatitis models [46, 47]. Currently, no definitive treatment exists for MAFLD due to the incomplete understanding of its underlying mechanisms [48], making a healthy lifestyle the cornerstone for preventing early disease progression [49]. Traditional Chinese Medicine Constitution (TCMC) assessment provides valuable insights into disease susceptibility, progression, and prognosis [38]. Specifically, examining the phlegm-dampness constitution (PDC) offers a meaningful entry point to study metabolic dysregulation [42, 50]. Individuals with PDC are prone not only to metabolic disorders but also to cardiovascular and cerebrovascular conditions [51], indicating an elevated baseline risk for metabolic abnormalities regardless of other comorbidities [38]. Consequently, integrating TCMC evaluation with assessments of disease susceptibility enables early identification of high-risk individuals, facilitating preventive interventions, slowing disease progression, and supporting targeted treatment strategies. Based on our findings, individuals with PDC—particularly men or those who smoke—should receive prioritized monitoring for MAFLD. Lifestyle modification and dietary adjustments aimed at correcting PDC could serve as effective preventive and therapeutic measures for chronic metabolic diseases, including MAFLD.

The robustness of our findings was further confirmed through sensitivity analyses using inverse probability of treatment weighting (IPTW) based on propensity scores, which indicated that our results were stable and reliable. This study has several limitations. First, its cross-sectional design prevents causal inference, allowing only identification of associations between PDC and MAFLD. Second, self-reported data on lifestyle factors such as smoking and alcohol consumption may be subject to recall bias. Third, MAFLD diagnosis was based on abdominal ultrasonography rather than liver biopsy, limiting our ability to assess disease severity. Future research should include histological validation and employ multicenter, large-scale, standardized epidemiological studies to strengthen the evidence. Additionally, cohort studies or mechanistic investigations are needed to clarify the causal pathways linking PDC to MAFLD, including the potential modifying roles of sex and tobacco use.

Conclusion

Our study confirmed a significant positive association between PDC and MAFLD, with the relationship being more pronounced in men and tobacco smokers. In contrast, a negative correlation was observed between the qi-depression constitution and MAFLD, challenging some traditional TCM assumptions. These findings underscore the importance of targeted interventions in older adults identified with PDC—particularly males and smokers—within routine health assessments under programs such as China's Traditional Chinese Medicine Management

Plan for the Elderly. Correcting PDC and reducing tobacco use may help prevent the onset and progression of MAFLD.

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Conflict of Interest: None

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