Association of metabolic dysfunction-associated fatty liver disease with chronic kidney disease: a Chinese population-based study

Qian Hu a, Yao Chen b, Ting Bao a and Yan Huang a

a Health Management Center, West China Hospital of Sichuan University, Chengdu, China; b Department of Breast Surgery, West China Hospital, Sichuan University, Chengdu, China

ABSTRACT

Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) is a multisystem disorder, but its relationship with kidney injury remains controversial. This study aimed to evaluate MAFLD effects on the chronic kidney disease (CKD) prevalence in a general population in China.

Methods: In total, 15,010 individuals from the Health Management Center of West China Hospital from July 2020 to June 2021 were screened. Hepatic steatosis was defined as a median FibroScan controlled attenuation parameter (CAP) ≥ 240 dB/m using liver ultrasound transient elastography. CKD was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m² and/or the presence of albuminuria. The association of MAFLD with CKD was examined using logistic regression. Risk factors for CKD in different MAFLD subgroups were also investigated.

Results: A total of 8226 individuals were finally included. Of them, 4406 (53.6%) had MAFLD, and 592 (7.2%) had CKD. After propensity score matching (PSM), 5530 eligible subjects were selected (n = 2765 in each group). There was a higher CKD prevalence in subjects with MAFLD than in those without MAFLD (8.9% vs. 5.4%, p < 0.001). MAFLD was significantly associated with a higher CKD prevalence (OR 1.715, 95% CI 1.389 – 2.117, p < 0.001), although it was not an independent risk factor. The results indicated that age, diabetes mellitus (DM), overweight/obesity, hypertension, hyperuricemia, hypertriglyceridemia, remnant cholesterol (RC), and C-reactive protein (CRP) were independently associated with a higher CKD prevalence. In the subgroup analysis, hypertension, hyperuricemia, RC, and the nonalcoholic fatty liver disease fibrosis score (NFS) were independent risk factors for the prevalence of CKD in individuals with DM or prediabetes and MAFLD. Furthermore, hypertension, hyperuricemia, and body fat percentage (BFP) were independently associated with CKD in subjects with MAFLD without DM.

Conclusion: Individuals with MAFLD had a higher prevalence of CKD, whereas it was not an independent risk factor for CKD.

Abbreviations: MAFLD: Metabolic Associated Fatty Liver Disease; NAFLD: Nonalcoholic Fatty Liver Disease; DM: Diabetes Mellitus; CKD: Chronic Kidney Disease; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; CRP: High Sensitivity C-Reactive Protein; UACR: Urine Albumin Creatinine Ratio; BMI: Body Mass Index; GGT: γ-Glutamyl Transpeptidase; ALP: Alkaline Phosphatase; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; HbA1c: Hemoglobin A1c; FIB-4: Fibrosis 4; NFS: NAFLD Fibrosis Score; BFP: Body Fat Percentage; OR: Odds Ratio

Introduction

Nonalcoholic fatty liver disease (NAFLD) has become the most common cause of chronic liver disease and is characterized by accumulated fat in liver cells [1]. The prevalence of NAFLD has reached an alarming proportion, affecting nearly 25% of adults worldwide and 30% of adults in China [2]. Emerging evidence has established relationships between NAFLD and chronic kidney disease (CKD), cardiovascular disease (CVD), and diabetes [3,4].

Metabolic dysfunction-associated fatty liver disease (MAFLD), a new condition proposed by an international expert consensus in 2020 [5], better characterizes the role of metabolic disorders in fatty liver disease than NAFLD. Its diagnosis is based on three manifestations, including overweight/obesity, type 2 diabetes mellitus (T2DM) or metabolic dysfunction. Hence, the major
benefit of the MAFLD classification is that it reflects the notion that multiple metabolic factors promote hepatic steatosis and do not simply just coexist \[6\]. Therefore, early identification of those at high risk of metabolic disorders may contribute to the further prevention of MAFLD.

CKD has become a major health-threatening disease in the twenty-first century, affecting 15% of individuals worldwide; moreover, CKD gradually progresses to end-stage renal disease (ESRD), which imposes a substantial burden on human health and the social economy \[7\]. Accordingly, there is an urgent need to identify more specific biomarkers and search for new CKD interference targets. Previous studies have demonstrated that hypertension, DM, hyperuricemia, and obesity are associated with an increased risk of CKD \[8\]; however, whether MAFLD can differentiate individuals at high risk of CKD is still uncertain.

In this study, we aimed to evaluate the association between MAFLD and CKD in a Chinese population and investigate the risk factors for CKD in individuals with MAFLD.

**Methods**

**Study population**

This cross-sectional study analyzed the data of 15,010 Chinese individuals who underwent liver ultrasound transient elastography examinations at the Health Management Center of West China Hospital from July 2020 to June 2021. Of them, 6784 were excluded for the following reasons: (1) missing ultrasound data, (2) a history of liver surgery, (3) presence of a malignant tumor, (4) nonconformity to the diagnostic criteria of MAFLD \[5\], (5) missing C-reactive protein (CRP) data, (6) missing body composition analysis data, (7) incomplete clinical data, or (8) pregnancy (Figure 1). The inclusion criteria were as follows: (1) age ≥18 years old, (2) a diagnosis of MAFLD, and (3) comprehensive health checkup data. The related general information and clinical data of all eligible individuals were collected. Hepatic steatosis was defined as a median FibroScan controlled attenuation parameter (CAP) ≥240 dB/m using liver ultrasound transient elastography. Body composition analysis was performed with an InBody analyzer (InBody570) based on bioelectrical impedance technology. This study was approved by the Ethics Committee of West China Hospital of Sichuan University, and informed consent was obtained from all subjects.

**Diagnostic criteria for MAFLD**

The established 2020 criteria for MAFLD include evidence of hepatic steatosis plus one of the following:

![Figure 1](image_url) - The flowchart of the subjects included in this study. PSM: Propensity Score Matching.
overweight/obesity, type 2 DM, or the presence of metabolic disorder. Metabolic disorder was defined as evidence of no less than two of the following metabolic risk factors: (1) waist circumference $\geq 102/88$ cm in Caucasian men and women (or $\geq 90/80$ cm in Asian men and women); (2) blood pressure $\geq 130/85$ mmHg or related drug treatment; (3) plasma triglycerides $\geq 150$ mg/dl or related drug treatment; (4) plasma high-density lipoprotein cholesterol (HDL-C) $< 40$ mg/dl in men and $< 50$ mg/dl in women or related drug treatment; (5) prediabetes (i.e. fasting glucose level of 100–125 mg/dl, or 2-h post-load glucose level of 140–199 mg/dl or HbA1c 5.7–6.4%); (6) homeostasis model assessment of insulin resistance (HOMA-IR) score $\geq 2.5$; and (7) plasma high-sensitivity CRP level $> 2$ mg/L [5]. Overweight or obesity was defined as body mass index (BMI) $\geq 25$ kg/m$^2$ in Caucasians or BMI $\geq 23$ kg/m$^2$ in Asians. Diabetes mellitus (DM) in this study was defined as a history of diabetes or HbA1c $\geq 6.5$% [9], and prediabetes was defined as a level of HbA1c of 5.7–6.4%.

**Other diagnostic criteria**

CKD was defined as an estimated glomerular filtration rate (eGFR) $< 60$ mL/min/1.73 m$^2$ (CKD-EPI [10]) and/or the presence of albuminuria, defined as a urinary albumin-to-creatinine ratio (UACR) $\geq 30$ mg/g. Hypertension was defined as a history of hypertension or blood pressure $\geq 140/90$ mmHg. Hyperuricemia was defined as a blood uric acid level $\geq 420/360$ μmol/L in men and women. Remnant cholesterol was defined as total cholesterol (mmol/L) – low-density lipoprotein cholesterol (LDL-C) (mmol/L) – HDL-C (mmol/L) [11]. The fibrosis 4 (FIB-4) score and NAFLD fibrosis score (NFS) were used to assess the degree of liver fibrosis. Their formulas are as follows: FIB-4 = age (years) × AST(U/L)/(PLT(10$^9$/L) × ALT(U/L)$^{1/2}$), NFS = $-1.675 + 0.037 \times$ age(years)$+ 0.094 \times$ BMI(kg/m$^2$)$+ 1.13 \times$ impaired fasting glucose/diabetes (yes = 1, no = 0) + 0.99 × AST/ALT – 0.013 × platelet ($\times 10^9$/l) – 0.66 × albumin (g/dl) [12].

**Data collection**

The demographic and clinical information of subjects was collected at the time of physical checkup and included the following: (1) age, sex, ethnicity, height, weight, systolic/diastolic blood pressure, medical history, waist circumference, etc.; (2) HbA1c, blood uric acid, serum creatinine, eGFR, UACR, etc.; (3) LDL-C, HDL-C, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), etc.; and (4) CRP, body fat percentage (BFP) (overall body fat/body weight), basal metabolic rate, etc.

**Statistical analysis**

All calculations were performed using SPSS software (version 26.0, IBM Corp., Armonk, NY, USA). The included individuals were divided into two groups, namely, the MAFLD and non-MAFLD groups. Propensity score matching (PSM) with a caliper of 0.02 was used to match the following three variables in a 1:1 ratio between two groups: age, sex, and ethnicity. Continuous variables are expressed as means ± standard deviations (SDs) or medians with interquartile ranges (IQRs), and categorical data are presented as frequencies and percentages. The normality of the data was assessed using the Kolmogorov–Smirnov test. Differences between the two groups were calculated by Student’s t test, the Mann–Whitney U test, or the chi-square test, as appropriate. Logistic regression analysis was performed to identify risk factors for CKD. A two-sided $p < 0.05$ was considered statistically significant.

**Results**

**Characteristics of the participants**

A total of 8226 individuals were included in this study (Figure 1), with 4406 in the MAFLD group and 3820 in the non-MAFLD group. Of them, 592 (7.2%) had CKD, 704 (8.5%) had DM, 2770 (33.7%) had prediabetes and 5406 (65.7%) were overweight or obese. As shown in Table 1, before PSM, CKD was more prevalent in the MAFLD group than in the non-MAFLD group (9.3 vs. 4.8%, $p < 0.001$). This difference was maintained after PSM (8.9% in the MAFLD group vs. 5.4% in the non-MAFLD group, $p < 0.001$). Age and the percentage of males were significantly different between the two groups but were balanced after PSM.

Before PSM, the MAFLD group had a higher HbA1c level; higher BMI; larger waist circumference; higher BFP; higher basal metabolic rate; higher serum creatinine, total cholesterol, LDL-C, remnant cholesterol, CRP, ALT, AST, ALP, GGT levels; higher FIB-4 scores and NFS; lower eGFR; lower HDL-C level; and higher prevalence rates of CKD, DM, prediabetes, smoking, overweight/obesity, albuminuria, hyperuricemia, and hypertriglyceridemia than the non-MAFLD group.

After PSM, the MAFLD group still had a higher HbA1c level; higher BMI; larger waist circumference; higher BFP; higher basal metabolic rate; higher total cholesterol, LDL-C, remnant cholesterol, CRP, ALT, AST, ALP, and GGT levels; higher FIB-4 score and NFS; lower
### Table 1. Baseline characteristics before and after propensity score matching (PSM).

| Variates                  | Before PSM | After PSM | p value | p value |
|---------------------------|------------|-----------|---------|---------|
|                          | Non-MAFLD  | MAFLD     |         | MAFLD   |
|                          | (n = 3820) | (n = 4406) |         | (n = 2765) |
| Age (years)               | 47 (38.54) | 42 (49.55) | <0.001 | 48.90 ± 10.32 |
| Male (n, %)               | 1671 (43.7) | 3266 (74.1) | <0.001 | 1670 (60.4) |
| Chinese Han (n, %)        | 3678 (96.3) | 4214 (95.6) | 0.142  | 2653 (95.9) |
| DM (n, %)                 | 148 (3.9) | 556 (12.6) | <0.001 | 143 (5.2) |
| Prediabetes (n, %)        | 1019 (26.7) | 1751 (39.7) | <0.001 | 866 (31.3) |
| Smoking (n, %)            | 1002 (26.2) | 1756 (39.9) | <0.001 | 941 (34) |
| Overweight/obesity (n, %) | 1375 (36) | 4031 (91.5) | <0.001 | 1173 (42.4) |
| BMI (kg/m²)               | 22.06 (20.43-23.78) | 25.89 (24.34-27.77) | <0.001 | 22.52 (20.83-24.17) |
| Waist circumference (cm)  | 76 (70-82) | 89 (83-94) | <0.001 | 78.41 ± 8.471 |
| Body fat percentage (%)   | 0.269 (0.228-0.314) | 0.303 (0.266-0.345) | <0.001 | 0.26 (0.22-0.31) |
| Basal metabolic rate (kcal) | 1303.22 ± 172.78 | 1455.19 ± 184.52 | <0.001 | 1351 (1191-1484) |
| ALP (IU/L)                | 182 (4.8) | 410 (9.3) | <0.001 | 149 (5.4) |
| Albuminuria (n, %)        | 151 (4.0) | 386 (8.8) | <0.001 | 118 (4.3) |
| eGFR (ml/min/1.73 m²)     | 97.03 (86.65-105.86) | 94.29 (84.01-102.77) | <0.001 | 92.80 ± 13.96 |

**HDL-C level; and higher prevalence rates of CKD, DM, prediabetes, overweight/obesity, albuminuria, hyperuricemia, and hypertriglyceridemia than the non-MAFLD group. In contrast, after PSM, the MAFLD group had a higher eGFR and lower serum creatinine level than the non-MAFLD group. There were no differences observed in age, sex, ethnicity or smoking status between MAFLD and non-MAFLD groups.**

### Association between MAFLD and CKD after PSM

Logistic regression analysis was performed to reveal the relationship between MAFLD and CKD in subjects, as shown in **Table 2**. The univariate analyses showed that MAFLD, age, DM, prediabetes, hypertension, overweight/obesity, waist circumference, BFP, hyperuricemia, hypertriglyceridemia, HDL-C, remnant cholesterol, CRP, FIB-4 score, and NFS were significantly associated with an increased risk of CKD (p < 0.05). The covariates with a p value < 0.05 in the univariate analyses were entered into the multivariate logistic regression model. After adjustment for the above covariates, age (OR 1.025, 95% CI 1.011-1.04, p = 0.001), DM (OR 2.526, 95% CI 1.828–3.492, p < 0.001), hypertension (OR 2.651, 95% CI 2.117-3.319, p < 0.001), overweight/obesity (OR 0.718, 95% CI 0.519–0.993, p = 0.045), hyperuricemia

### Data are presented as the mean ± SD, the median with interquartile range, or counts and percentages.

DM: diabetes mellitus; HbA1c, glycosylated hemoglobin; BMI: body mass index; eGFR: estimated glomerular filtration rate; CKD: chronic kidney disease; ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: γ-glutamyl transpeptidase; FIB-4: fibrosis-4; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; CRP: C-reactive protein; NFS: NAFLD fibrosis score.

---

**A two-tailed p < 0.05 was considered statistically significant.**
MAFLD (n, %) 2519 (49.1) 246 (62.3) 1.715 (1.389-2.117) <0.001 0.972 (0.739-1.277) 0.837
Age (years) 48 (42-56) 54 (47-60) 1.047 (1.037-1.058) <0.001 1.025 (1.011-1.04) 0.001
Male (n, %) 3092 (60.2) 245 (62) 1.078 (0.874-1.332) 0.478
DM (n, %) 378 (7.4) 102 (25.8) 5.323 (4.046-7.004) <0.001 2.526 (1.828-3.492) <0.001
Prediabetes (n, %) 1857 (36.2) 146 (37) 1.551 (1.225-1.964) <0.001 1.096 (0.851-1.410) 0.478
Hypertension (n, %) 1098 (21.4) 199 (50.4) 3.733 (3.034-4.597) <0.001 2.651 (2.117-3.319) <0.001
Smoking (n, %) 1687 (32.9) 126 (31.9) 0.957 (0.769-1.192) 0.697
Overweight/obesity (n, %) 3362 (65.6) 290 (73.4) 1.457 (1.157-1.834) 0.001 0.718 (0.519-0.993) 0.045
Waist circumference (cm) 83 (76-89) 86 (79-94) 1.042 (1.031-1.053) <0.001 1.013 (0.998-1.029) 0.098
Body fat percentage (%) 0.287 (0.243-0.334) 0.309 (0.261-0.353) 73.225 (15.12-354.627) <0.001 2.42 (0.327-17.929) 0.387
Hyperuricemia (n, %) 1110 (21.6) 141 (35.7) 2.021 (1.645-2.482) <0.001 1.332 (1.024-1.732) 0.033
Hypertriglyceridemia (n, %) 1823 (35.5) 208 (52.7) 2.021 (1.645-2.482) <0.001 1.332 (1.024-1.732) 0.033
HDL-C (mmol/L) 1.25 (1.05-1.5) 1.15 (0.95-1.42) 0.461 (0.332-0.640) <0.001 0.908 (0.595-1.387) 0.656
LDL-C (mmol/L) 3.03 (2.5-3.55) 3.01 (2.45-3.67) 0.978 (0.861-1.110) 0.726
Remnant cholesterol (mmol/L) 0.52 (0.37-0.73) 0.65 (0.45-0.95) 1.618 (1.415-1.850) <0.001 1.259 (1.076-1.474) 0.004
CRP (>2mg/L) 2621 (51) 257 (65.1) 1.786 (1.442-2.212) <0.001 1.30 (1.027-1.645) 0.029
FIB-4 score 1.11 (0.76-1.63) 1.38 (0.96-2.03) 1.28 (1.176-1.394) <0.001 1.034 (0.925-1.157) 0.554
NFS score −2.17 (−2.99−1.38) −1.58 (−2.47−0.70) 1.510 (1.385-1.647) <0.001 1.116 (0.988-1.261) 0.076

Data are presented as the mean ± SD, the median with interquartile range, or counts and percentages.

DM: diabetes mellitus; FIB-4: fibrosis-4; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; CRP: C-reactive protein; NFS: NAFLD fibrosis score.

* A two-tailed p < 0.05 was considered statistically significant.

Additionally, we explored the prevalence of different FIB-4 scores and NFS in subjects with and without CKD. As shown in Figure 3, FIB-4 scores of 1, 2, and 3 accounted for 46, 42, and 12%, respectively, in the CKD group and 61, 32, and 7%, respectively, in the non-CKD group. Moreover, NFS of 1, 2, and 3 accounted for 54, 43, and 4%, respectively, in the CKD group and 73, 26, and 1%, respectively, in the non-CKD group. Accordingly, the individuals with CKD had
higher fibrosis scores than those without CKD ($p < 0.001$).

**Risk factors for CKD in subjects with DM or prediabetes and MAFLD**

Among 1474 individuals with DM or prediabetes and MAFLD, 169 (11.47%) had CKD. The results of the multivariate logistic regression analysis indicated that hypertension (OR 3.429, 95% CI 2.401–4.896, $p < 0.001$), hyperuricemia (OR 1.495, 95% CI 1.035–2.158, $p = 0.032$), remnant cholesterol (OR 1.305, 95% CI 1.068–1.595, $p = 0.009$), and NFS (OR 1.359, 95% CI 1.141–1.617, $p = 0.001$) were independent risk factors for CKD after adjustment for age, overweight/obesity, waist circumference, BFP, hypertriglyceridemia, HDL-C, CRP, and the FIB-4 score (Table 3).

**Risk factors for CKD in subjects with DM or prediabetes without MAFLD**

Among 1009 individuals with DM or prediabetes without MAFLD, 79 (7.83%) had CKD. The results of the multivariate logistic regression analysis suggested that age (OR 1.036, 95% CI 1.003–1.069, $p = 0.034$), hypertension (OR 2.393, 95% CI 1.447–3.959, $p = 0.001$), hyperuricemia (OR 2.036, 95% CI 1.147–3.616, $p = 0.015$), hypertriglyceridemia (OR 1.804, 95% CI 0.953–3.412, $p = 0.07$), remnant cholesterol (mmol/L) (OR 1.233, 95% CI 0.629–2.42, $p = 0.542$), CRP (mg/L) (OR 1.6, 95% CI 0.974–2.626, $p = 0.063$), FIB-4 score (OR 1.135, 95% CI 0.907–1.421, $p = 0.269$), NFS score (OR 1.139, 95% CI 0.901–1.439, $p = 0.276$) were independent risk factors for CKD after adjustment for overweight/obesity, waist circumference, BFP, hypertriglyceridemia, HDL-C, CRP, the FIB-4 score, the NFS, and remnant cholesterol (Table 4).

**Risk factors for CKD in subjects with MAFLD without DM**

Among 2428 subjects with MAFLD without DM, 170 (7.0%) had CKD. The results of the multivariate logistic regression
regression analysis showed that hypertension (OR 3.246, 95% CI 2.319–4.542, \( p < 0.001 \)), hyperuricemia (OR 1.503, 95% CI 1.059–2.133, \( p = 0.023 \)), and BFP (OR 34.849, 95% CI 1.549–784.001, \( p = 0.025 \)) were independently associated with CKD after adjustment for age, overweight/obesity, waist circumference, hypertriglyceridemia, HDL-C, CRP, the FIB-4 score, the NFS, remnant cholesterol, and prediabetes (Table 5).

### Discussion

In this study, we retrospectively analyzed the relationship between MAFLD and CKD. A total of 8226 subjects met the inclusion criteria, and 592 (7.2%) subjects with CKD were included. Our results demonstrated that subjects with MAFLD had a higher prevalence of CKD than those without MAFLD before and after PSM. The logistic regression analysis indicated that MAFLD was significantly associated with CKD, although it was not an independent risk factor. The results also showed that age, diabetes, overweight/obesity, hypertension, hyperuricemia, hypertriglyceridemia, remnant cholesterol, and CRP were independent risk factors for CKD. We performed subgroup analyses and observed that hypertension, hyperuricemia, remnant cholesterol, and the NFS were independent risk factors for prevalence CKD in individuals with MAFLD and DM or prediabetes. Furthermore, hypertension, hyperuricemia, and BFP were independently associated with CKD in individuals with MAFLD without DM. In particular, hypertension and hyperuricemia were significantly associated with CKD in all subgroups.

The association of chronic renal injury with NAFLD has been extensively investigated over the years [13], but studies on the association of CKD with MAFLD are limited. The results of Deng et al. based on the dataset of the National Health and Nutrition Examination Survey (NHANES) 2017–2018 [12] in the United States, showed that MAFLD was not associated with CKD after adjustment for age, sex, and race, whereas the FIB-4 score was an independent risk factor for CKD. In addition, the study by Sun et al. based on the dataset of the NHANES 1988–1994, indicated that MAFLD was not independently associated with prevalent CKD (eGFR < 60 mL/min/1.73 m\(^2\), OR 1, 95% CI 0.89–1.13, \( p = 0.970 \)) after adjustment for sex, age, ethnicity, alcohol intake, and preexisting diabetes [14].

In this study, we found that MAFLD was significantly related to the increased prevalence of CKD even after adjustment for age, sex and ethnicity, although it was not an independent risk factor after adjustment for additional clinical variables. In addition, we observed that the NFS was an independent risk factor for CKD in subjects with MAFLD with DM or prediabetes (OR 1.359, 95% CI 1.141–1.617, \( p = 0.001 \)), similar to the results of Sun et al. [14]. Furthermore, a recent 4.6-year cohort study in China demonstrated that MAFLD increased the incident risks of CKD and CVD [15]. In addition, we also found that MAFLD patients with CKD had a higher degree of cirrhosis than those without CKD (data not shown), which was consistent with the results of Ciardullo et al. [16] These findings suggested that MAFLD and its related metabolic disorders might play important roles in the development and progression of CKD, and potential treatments might benefit both CKD and MAFLD.

Remnant cholesterol is defined as triglyceride-rich lipoprotein cholesterol and is calculated as total cholesterol minus HDL-C and LDL-C. Recent studies have confirmed that remnant cholesterol, not HDL-C or LDL-C, is significantly associated with an increased risk of CVD [17,18]. A higher level of remnant cholesterol was also related to the prevalence of CKD in a general middle-aged population [19] and was predictive of all-cause, cardiovascular-related, and cancer-related mortality in individuals with MAFLD [20]. In our study, we demonstrated that remnant cholesterol was independently related to an increased risk of CKD in all subjects after PSM, as well as in individuals with MAFLD with DM or prediabetes, which suggests that elevated serum remnant cholesterol might contribute to the development of CKD in subjects with MAFLD. According to these findings, screening and evaluation of remnant cholesterol can more accurately identify a high risk of CKD and prevent prevalent CKD. Further studies are needed to elucidate the value of remnant cholesterol monitoring in MAFLD management.

CKD is characterized by a state of low-grade inflammation [21], and visceral adipose tissue (VAT) is related to microinflammation [22,23]. Emerging evidence has indicated that VAT is a better predictor of the

### Table 5. Risk factors for CKD in MAFLD subjects without DM (170/2428).

| Variates          | Odds ratio (95% CI) | \( p^* \) value |
|-------------------|--------------------|-----------------|
| Age (y)           | 1.014 (0.993-1.036) | 0.188           |
| Hypertension      | 3.246 (2.319-4.542) | <0.001          |
| Overweight/obesity| 0.778 (0.431-1.403) | 0.404           |
| Hyperuricemia     | 1.503 (1.059-2.133) | 0.023           |
| Hypertriglyceridemia | 1.225 (0.833-1.801) | 0.303           |
| Remnant cholesterol (mmol/L) | 1.239 (0.952-1.612) | 0.111           |
| CRP (>2mg/L)      | 1.287 (0.89-1.862)  | 0.18            |
| Prediabetes       | 1.073 (0.769-1.499) | 0.025           |
| Body fat percentage (%) | 34.849 (1.549-784.001) | 0.025          |
| FIB-4 score       | 1.037 (0.876-1.228) | 0.67            |
| NFS score         | 1.09 (0.909-1.307)  | 0.353           |

CRP: C-reactive protein; FIB-4: fibrosis-4; NFS, NAFLD fibrosis score.

* A two-tailed \( p < 0.05 \) was considered statistically significant.
development of CKD than BMI [24,25]. Recently, Tsai et al. [26] reported that a higher BFP and higher high-sensitivity (hs) CRP level were related to renal dysfunction in a general population. In this study, we also observed that CRP was an independent risk factor for CKD in the general population, and BFP was significantly associated with the prevalence of CKD in subjects with MAFLD without DM. In addition, the BFP was positively correlated with CRP \((r = 0.217, \ p < 0.001)\). These findings indicate that BFP may play an important role in renal injury in individuals with MAFLD with metabolic abnormalities, though this remains to be confirmed in additional studies.

Age, hypertension, DM, obesity, and dyslipidemia are common risk factors for CKD progression [27,28]. As predicted, the above covariates were also independently associated with the increased prevalence of CKD in this study, and several studies have shown that hypertension might be an important factor linking MAFLD and CKD [29]. The value of hyperuricemia in predicting CKD development in the general population is still controversial; however, it has been shown to be related to an increased prevalence of CKD in individuals with NAFLD and MAFLD [12,30]. We also found that hyperuricemia was significantly related to CKD in all individuals and subgroups, with a 2.036-fold higher risk than that in controls.

DM has become the major cause of CKD and ESRD in both developed and developing countries [31–33], and nearly 30–40% of affected individuals will develop renal injury [34]. In this study, we demonstrated that DM was an independent risk factor for CKD in the general population, similar to the results of Deng et al. based on the dataset of the NHANES 2017–2018 [12]. Interestingly, before PSM, individuals with MAFLD had a lower eGFR than those without MAFLD; however, the eGFR was higher in the MAFLD group than in the non-MAFLD group after PSM. This variation was most likely due to MAFLD-related metabolic dysfunction, such as DM and obesity, which contributed to glomerular hyperfiltration after adjustment for age, sex, and ethnicity. A similar reverse pattern was observed in the study by Deng et al. [12].

Liver–kidney crosstalk in MAFLD includes alterations in the renin-angiotensin system (RAS), insulin resistance and activated protein kinase (AMPK) activation, impaired antioxidant defenses, and excessive dietary fructose intake, which affects kidney injury by altering lipogenesis and inflammatory responses [35,36]. Moreover, the insulin resistance involved in MAFLD can in turn aggravate lipid metabolism disorders, forming a vicious cycle. Imbalances in inflammatory cytokines [37], the activation of oxidative stress [36,38], and insulin resistance [39,40], the involvement of the RAAS system [41], production of hypoapoditcinemia and atherogenic dyslipidemia [40] and disruption of the intestinal barrier resulting from gut dysbiosis [42,43], increases in uremic toxins and secondary bile acids, and decreases in short-chain fatty acids are considered to be the common pathophysiological mechanisms linking MAFLD and CKD [44].

To date, rare large studies on the pharmacological or non pharmacological treatment of MAFLD patients with CKD have been reported [35]. However, because MAFLD and CKD share several common risk factors (e.g. obesity, insulin resistance, dyslipidemia, hypertension, and dysglycemia) and pathogenetic pathways, current management of MAFLD patients with CKD focuses on lipid and glucose lowering, blood pressure control, and weight loss [35]. Several studies have shown that sodium-glucose cotransporter-2 (SGLT2) inhibitors, peroxisome proliferator-activated receptor (PPAR) agonists, farnesoid X nuclear receptor (FXR) agonists, thyroid hormone receptor \(\beta\) (TR \(\beta\)) agonists and proprotein convertase subtilisin-kex in type 9 (PCSK9) inhibitors may be promising agents for the treatment of MAFLD patients with CKD [35,45]. Additionally, modulation of gut microbial components and mesenchymal stem cells (MSCs)-based therapy may be novel therapeutic strategies for MAFLD and CKD [46,47].

Several limitations in this study should be noted. First, it was a cross-sectional study in a single Chinese center, of which the findings might only apply to the Chinese population, and the diagnosis of CKD was based on a single examination of eGFR and UACR rather than several tests over three months. Second, the diagnostic criteria for overweight/obesity in China are BMI >24 kg/m\(^2\), which is different from the criteria ‘BMI >23 kg/m\(^2\)’ in this study. This might have a certain impact on the generalization of the results of this study in China. Third, given the limitation of datasets, some diagnostic indicators involved in MAFLD were unavailable, including the HOMA-IR score, hs-CRP level, the specific type of diabetes, the duration of diabetes, drinking status, hepatitis B virus infection or other liver disease. Fourth, the drug information of the subjects was lacking. Hence, we did not take therapeutic interventions into account, and other confounding factors, such as alcohol consumption, might affect the development of CKD. Fifth, the hepatic steatosis in this study was diagnosed based on FibroScan controlled attenuation parameter (CAP) \(\geq 240\) dB/m using liver ultrasound transient elastography, which may miss mild
fatty liver, and biopsy data, which are specifically useful to assess liver fibrosis, were unavailable in this study.

In summary, our study demonstrated that MAFLD might affect the development of CKD, though it is not an independent risk factor. Further studies are needed to identify the role of MAFLD in the trajectory of CKD and whether it could alter the overall prognosis of CKD. In addition, given that individuals with MAFLD might be more prone to chronic kidney damage, more attention should be given to identifying those at high risk of metabolic disorders; this information will be helpful in further advancing the clinical management of MAFLD and CKD.

Acknowledgments
The authors thank all the study participants for their cooperation.

Ethics approval and consent to participate
The Ethics Committee of the West China Hospital of Sichuan University provided authorization for our study. Written informed consent was obtained from each participant.

Author contributions
QH, YC, and YH designed and conducted the study, QH, YC, and TB participated in data collection, analysis and interpretation. The manuscript was prepared by QH and YC. All authors have read and approved the final manuscript.

Disclosure Statement
No potential conflict of interest was reported by the author(s).

Funding
This research was funded by the 1.3.5 Project for Disciplines of Excellence, West China Hospital, Sichuan University [ZYJC21056].

References
[1] Younossi Z, Tacke F, Arrese M, et al. Global perspectives on nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Hepatology. 2019;69(6):2672–2682.
[2] Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73–84.
[3] Zhang M, Lin S, Wang MF, et al. Association between NAFLD and risk of prevalent chronic kidney disease: why there is a difference between east and west? BMC Gastroenterol. 2020;20(1):139.
[4] Muzurović E, Peng CC, Belanger MJ, et al. Nonalcoholic fatty liver disease and cardiovascular disease: a review of shared cardiometabolic risk factors. Hypertension (Dallas, Tex: 1979). 2022;79(7):1319–1326.
[5] Eslam M, Newsome PN, Sarin SK, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. J Hepatol. 2020;73(1):202–209.
[6] Nan Y, An J, Bao J, et al. The Chinese society of hepatology position statement on the redefinition of fatty liver disease. J Hepatol. 2021;75(2):454–461.
[7] Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the global burden of disease study 2017. Lancet (London, England). 2020;395:709–733.
[8] Stevens PE, Levin A. Evaluation and management of chronic kidney disease: synopsis of the kidney disease: improving global outcomes 2012 clinical practice guideline. Ann Intern Med. 2013;158(11):825–830.
[9] 16. Diabetes advocacy: standards of medical care in diabetes-2019. Diabetes Care. 2019;42:182–183.
[10] Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604–612.
[11] Jansson Sigfrids F, Dahlström EH, Forsblom C, et al. Remnant cholesterol predicts progression of diabetic nephropathy and retinopathy in type 1 diabetes. J Intern Med. 2021;290(6):632–645.
[12] Deng Y, Zhao Q, Gong R. Association between metabolic associated fatty liver disease and chronic kidney disease: a Cross-Sectional study from NHANES 2017-2018. DMSO. 2021;14:1830–1833.
[13] Marcuccilli M, Chonchol M. NAFLD and chronic kidney disease. Int J Mol Sci. 2016;17(4):562.
[14] Sun DQ, Jin Y, Wang TY, et al. MAFLD and risk of CKD. Metabolism. 2021;115:154433.
[15] Liang Y, Chen H, Liu Y, 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(1):88–97.
[16] Ciardullo S, Ballabeni C, Trevisan R, et al. Liver fibrosis assessed by transient elastography is independently associated with albuminuria in the general United States population. Dig Liver Dis. 2021;53(7):866–872.
[17] Castañer O, Pintó X, Subirana I, et al. Remnant cholesterol, not LDL cholesterol, is associated with incident cardiovascular disease. J Am Coll Cardiol. 2020;76(23):2712–2724.
[18] Elshazy MB, Mani P, Nissen S, et al. Remnant cholesterol, coronary atheroma progression and clinical events in statin-treated patients with coronary artery disease. Eur J Prev Cardiol. 2020;27(10):1091–1100.
[19] Yan P, Xu Y, Miao Y, et al. Association of remnant cholesterol with chronic kidney disease in Middle-aged and elderly Chinese: a population-based study. Acta Diabetol. 2021;58(12):1615–1625.
[20] Huang H, Guo Y, Liu Z, et al. Remnant cholesterol predicts long-term mortality of patients with metabolic
dysfunction-associated fatty liver disease. J Clin Endocrinol Metab. 2022;107(8):e3295–e3303.

[21] Mihai S, Codrici E, Popescu ID, et al. Inflammation-related mechanisms in chronic kidney disease prediction, progression, and outcome. J Immunol Res. 2018; 2018:2180373.

[22] Srivastava N, Singh R, Alok K, et al. Variation of body fat percentage with special reference to diet modification in patients with chronic kidney disease: a longitudinal study. Saudi J Kidney Dis Transpl. 2014;25(4):793–800.

[23] Ramkumar N, Cheung AK, Pappas LM, et al. Association of obesity with inflammation in chronic kidney disease: a cross-sectional study. J Renal Nutr. 2004;14(4):201–207.

[24] Pinto-Sietsma SJ, Navis G, Janssen WM, et al. A central body fat distribution is related to renal function impairment, even in lean subjects. Am J Kidney Dis. 2003;41(4):733–741.

[25] Hanai K, Babazono T, Nyumura I, et al. Involvement of visceral fat in the pathogenesis of albuminuria in patients with type 2 diabetes with early stage of nephropathy. Clin Exp Nephrol. 2010;14(2):132–136.

[26] Tsai YW, Chan YL, Chen YC, et al. Association of elevated blood serum high-sensitivity C-reactive protein levels and body composition with chronic kidney disease: a population-based study in Taiwan. Medicine (Baltimore). 2018;97(36):e11896.

[27] Chen TK, Knicely DH, Grams ME. Chronic kidney disease diagnosis and management: a review. JAMA. 2019;322(13):1294–1304.

[28] Hager MR, Narla AD, Tannock LR. Dyslipidemia in patients with chronic kidney disease. Rev Endocr Metab Disord. 2017;18(1):29–40.

[29] Ciardullo S, Grassi G, Mancia G, et al. Nonalcoholic fatty liver disease and risk of incident hypertension: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2022;34(4):365–371.

[30] Bonino B, Leoncini G, Russo E, et al. Uric acid in CKD: has the jury come to the verdict? J Nephrol. 2020;33(4):715–724.

[31] Afkarian M, Zelnick LR, Hall YN, et al. Clinical manifestations of kidney disease among US adults with diabetes, 1988–2014. JAMA. 2016;316(6):602–610.

[32] Zhang L, Zhao MH, Zuo L, et al. China kidney disease network (CK-NET) 2016 annual data report. Kidney Int Suppl (2011). 2020;10(2):e97–e185.

[33] Zhang L, Long J, Jiang W, et al. Trends in chronic kidney disease in China. N Engl J Med. 2016;375(9):905–906.