Obesity Facts

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Prevalence and Risk Factors of Metabolic Dysfunction-Associated Fatty Liver Disease with Renal Insufficiency in Overweight/Obese Adults

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Keywords
Metabolic dysfunction-associated fatty liver disease · Renal insufficiency · Overweight and obesity · Fibrosis

Abstract
Introduction: The prevalence of metabolic dysfunction-associated fatty liver disease (MAFLD) with renal insufficiency in recent years and the association between MAFLD and renal insufficiency are not entirely clear, especially in overweight/obesity. The aim of this study was to analyze the prevalence and risk factors of MAFLD with renal insufficiency in overweight/obese adults. ***Methods:*** Individuals who attended checkup at the Second Affiliated Hospital of Xi'an Jiaotong University from 2016 to 2021 were included. The prevalence of MAFLD with renal insufficiency (estimated glomerular filtration rate ≤90 mL/min/1.73 m^2) in overweight/obesity was estimated. Propensity score-matched analysis, univariate and multivariate analyses were used to determine the risk factors for MAFLD with renal insufficiency. ***Results:*** From 2016 to 2021, the prevalence of MAFLD in overweight/obesity reached its highest of 44.7% in 2017 and its lowest of 36.9% in 2018; and 33.9% in 2021 and 21.8% in 2019 is the highest and lowest prevalence of MAFLD with renal insufficiency, respectively. MAFLD was more common in men, old individuals, and persons with a higher body mass index (BMI) and was characterized by significant renal insufficiency. MAFLD with renal insufficiency was more common in women, old individuals, and persons with a higher BMI and was characterized by significant metabolic dysfunction and liver fibrosis. Multivariable analysis showed that BMI, uric acid, and fibrosis (evaluated with noninvasive liver fibrosis score [fibrosis-4]) were independent risk factors for MAFLD with renal insufficiency. ***Conclusion:*** The prevalence of MAFLD with renal insufficiency in overweight/obese adults is quite high in the last 5 years. BMI, uric acid, and fibrosis are independent risk factors for MAFLD with renal insufficiency.

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Introduction

Nonalcoholic fatty liver disease (NAFLD) has become the most prevalent liver disease worldwide. It affects 25–30% of the global population and significantly increases the risk of cirrhosis, liver failure, and hepatocellular carcinoma [1]. Currently, there are no approved drugs for NAFLD [2]. To better understand the disease and advance research, in 2020, the international community of hepatologists reached a consensus to rename NAFLD as metabolic dysfunction-associated fatty liver disease (MAFLD). The diagnostic criteria for MAFLD are based on the presence of hepatic steatosis (documented either by imaging, blood biomarkers/scores, or liver histology) combined with one of the following three conditions: overweight or obesity (defined as body mass index [BMI] ≥25 kg/m^2 in Caucasians or BMI ≥23 kg/m^2 in Asians), type 2 diabetes mellitus, or metabolic dysfunction [3–5]. In contrast to NAFLD, MAFLD is a definitive diagnosis that does not require the exclusion of alcohol consumption and other comorbid liver diseases (e.g., viral hepatitis) [6]. MAFLD places more emphasis on metabolic dysfunction than NAFLD, identifying a group with higher number of comorbidities and a worse prognosis [7, 8]. More than 2.2 billion people worldwide are overweight or obese, which has become a global health problem. Overweight/obesity lead to the development of the metabolic syndrome and various comorbidities, including MAFLD, type 2 diabetes, hypertension, hyperlipidemia, cardiovascular disease, chronic kidney disease (CKD), obstructive sleep apnea, osteoarthritis, and malignancy [9, 10]. The prevalence of overweight/obesity correlates with the prevalence and severity of MAFLD, and epidemiological data suggest that obese people make up the majority of the MAFLD population [11, 12]. Overweight/obesity is associated not only with simple steatosis but also with progressive liver disease including steatohepatitis, cirrhosis, and liver cancer [13]. Finally, overweight/obesity is not only associated with all-cause mortality but also increase liver-related mortality in patients with NAFLD [13, 14]. Therefore, the new definition of MAFLD includes overweight/obesity as one of the three major diagnostic criteria. With the redefinition of NAFLD, there is a need to reevaluate the epidemiology, mechanisms, treatment, and management of MAFLD. The relationship between MAFLD and various metabolic disorders including insulin resistance, diabetes, hyperlipidemia, and hyperuricemia has been fairly well studied [15, 16]. However, relatively few studies have been conducted on MAFLD and renal insufficiency, especially in overweight/obese populations, and it is not fully understood what characteristics of MAFLD are more likely to result in renal insufficiency. Meanwhile, there is a lack of information on trends in the prevalence of MAFLD with renal insufficiency in large-scale populations. Based on the strong relationship between overweight/obesity and MAFLD as well as CKD [9, 10], this study aimed to establish the prevalence, clinical characteristics, and risk factors of MAFLD with renal insufficiency in overweight/obese adults in a large population, thus providing a basis for the management of MAFLD with renal insufficiency.

Materials and Methods

Study Subjects and Data Collection

This cross-sectional study included individuals who had health checkups performed at the Second Affiliated Hospital of Xi'an Jiaotong University from January 2016 to December 2021. The study was approved by the Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University. Consent was obtained from the health checkup subjects for the use of their examination data. Figure 1 shows the flowchart for the inclusion and exclusion of subjects in the study. We used only data from 2021 in our analysis of risk factors for MAFLD and MAFLD with renal insufficiency because the same individuals on physical examination may exist in different years. Subjects with complete information on BMI, sex, age (≥18 years), and results of the abdominal ultrasound were included in the prevalence trend analysis. Subjects with complete data on sex, age, BMI, abdominal ultrasound, platelet count, systolic blood pressure (SBP), diastolic blood pressure (DBP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), total bilirubin (TBIL), fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), uric acid (UA), blood urea nitrogen (BUN), and serum creatinine (Scr) were included in the analysis of clinical characteristics.

Diagnostic Criteria

The diagnostic criteria for MAFLD are based on evidence of hepatic steatosis (detected by abdominal ultrasound) combined with overweight/obesity (BMI ≥23 kg/m^2). Additional diagnostic criteria include elevated SBP (≥130 mm Hg), elevated DBP (≥85 mm Hg), elevated FBG (≥5.6 mmol/L), elevated TG (≥1.7 mmol/L), elevated TC (≥5.2 mmol/L), reduced HDL-C (<1.0 mmol/L for men and <1.3 mmol/L for women), elevated LDL-C (≥3.1 mmol/L), elevated UA (≥416 μmol/L for men and ≥357 μmol/L for women), and elevated ALT (>40 IU/L). The fibrosis-4 (FIB-4) index, a noninvasive tool to predict fibrosis, was calculated as follows: FIB-4 = age (years) × AST (IU/L)/square root of platelet count (10^9/L) × ALT (IU/L). In accordance with the AGA guidelines [17], fibrosis in MAFLD was classified as no significant fibrosis (FIB-4 <1.3), uncertain risk of significant liver fibrosis (1.3≤ FIB-4 <2.67), and high risk of significant fibrosis (FIB-4 ≥2.67). FIB-4 ≥1.3 was used as a threshold in the analysis of impact of fibrosis on MALFD with renal insufficiency. Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation [18, 19]:

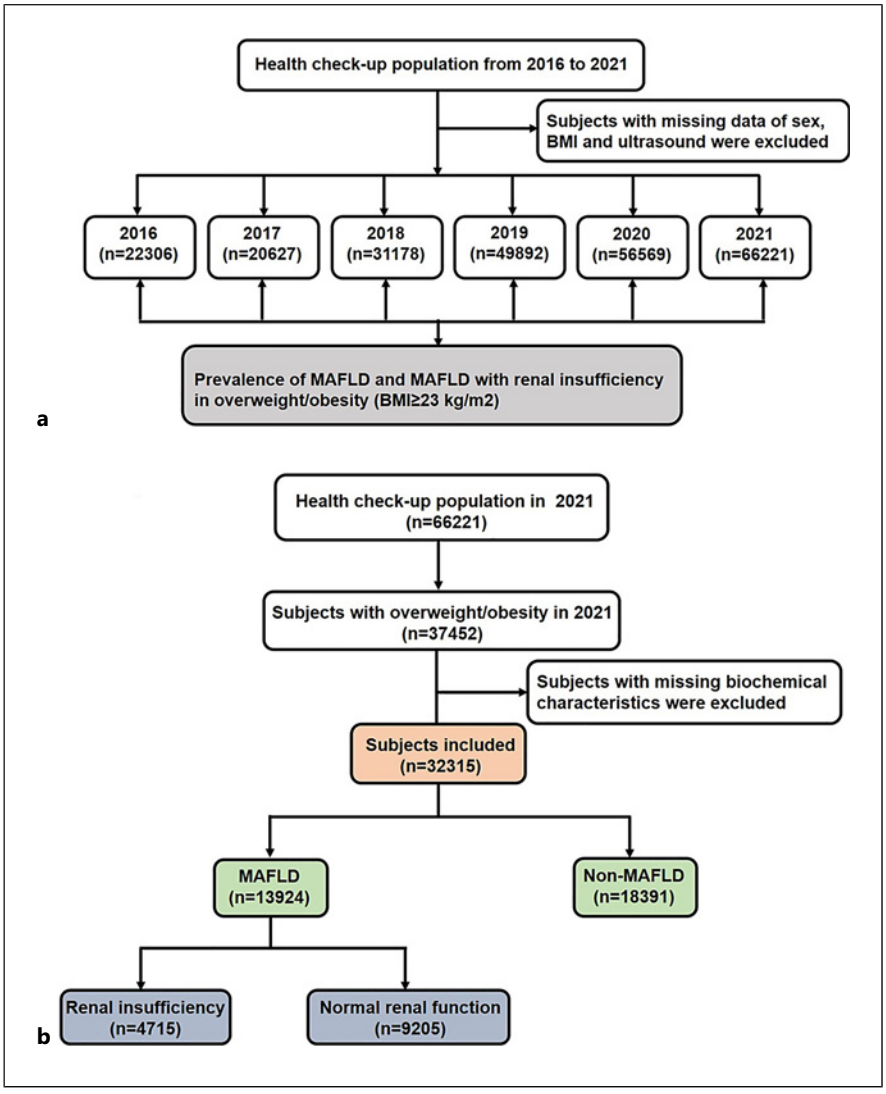

Fig. 1. Study flow diagram. **a** Study flow diagram for prevalence of MAFLD and MAFLD with renal insufficiency in overweight/obesity. **b** Study flow diagram for risk factors of MAFLD with renal insufficiency in overweight/obesity.

eGFR = 141 × min (Scr/κ, 1)α × max (Scr/κ, 1) −1.209 × 0.993Age × 1.018 (if female), where κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1. Renal insufficiency was defined as eGFR ≤90 mL/min/1.73 m^2.

Statistical Methods

Statistical analysis was performed using SPSS 23.0 software (SPSS Inc., Chicago IBM Corporation). Propensity score matching (PSM) was used to match the sex and age differences. Count data were expressed as *n* (%), and the χ^2 test was used. A nonparametric test was used for the comparison of rank data. All non-normally distributed measurement data were expressed as medians and interquartile ranges, M (P25-P75), and the Mann-Whitney U test was used. Binary multivariate logistic regression was used to analyze the independent risk factors for MAFLD and MAFLD with renal insufficiency. Spearman correlation analysis was used to analyze the correlation between BMI and eGFR, with the r value being the correlation coefficient. $p < 0.05$ was considered statistically significant.

Results

Prevalence of MAFLD with Renal Insufficiency in Overweight/Obese Adults in 2016–2021

From 2016 to 2021, 246,793 health checkups (133,331 males, 113,462 females) were included. The prevalence of overweight/obesity in total reached the highest of 62.3% in 2019 and the lowest of 51.6% in 2017; in yearly overweight/obesity, the prevalence of MAFLD reached its highest of 44.7% in 2017 and its lowest of 36.9% in 2018; and 33.9% in 2021 and 21.8% in 2019 is the highest and lowest prevalence of renal insufficiency in MAFLD, respectively. The prevalence of both overweight/obesity and MAFLD was significantly higher in men than in women ($p < 0.001$) (Fig. 2a, b). However, the prevalence of MAFLD with renal insufficiency was significantly higher in women than in men ($p < 0.001$) (Fig. 2c).

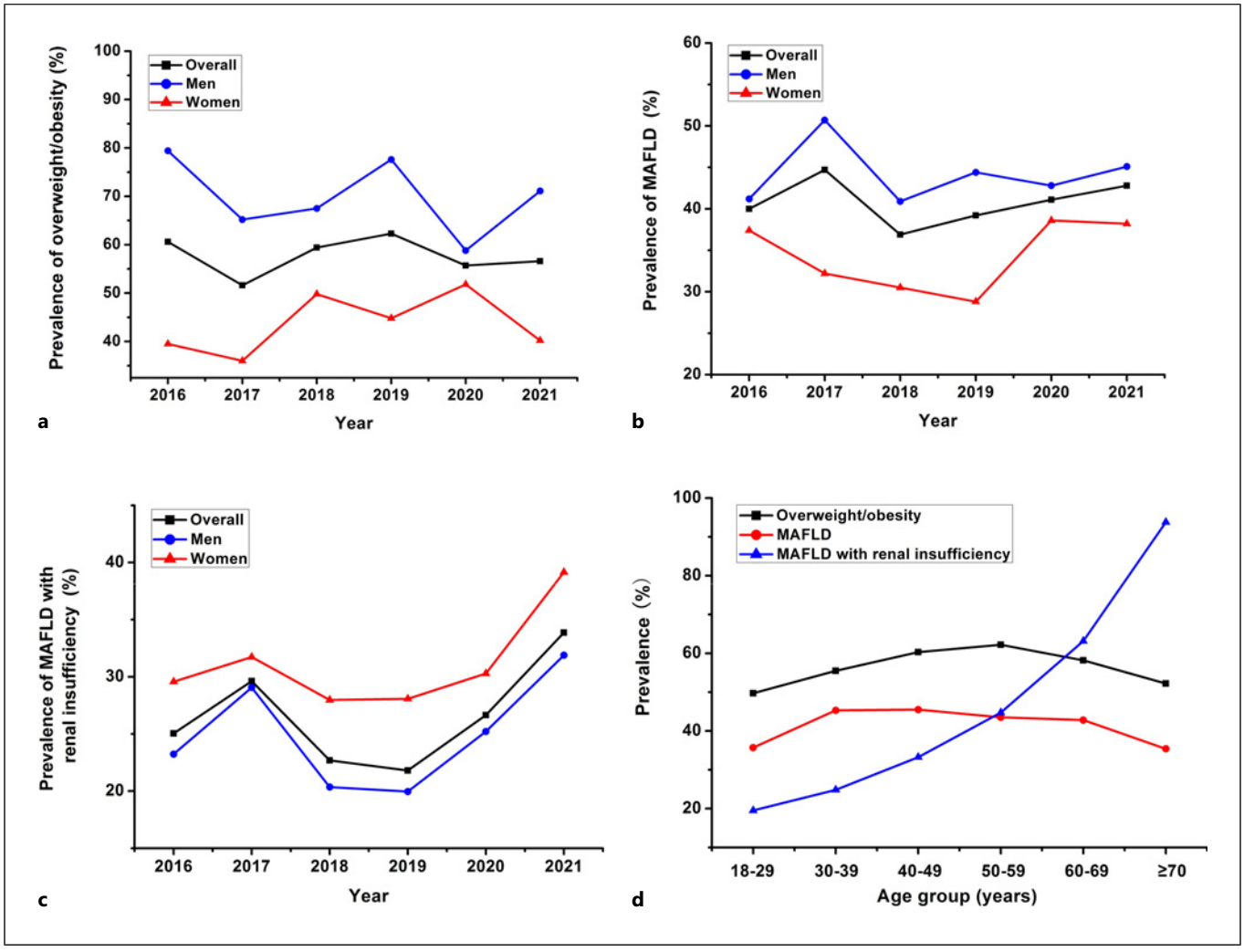

Fig. 2. Prevalence of MAFLD with renal insufficiency in 2016–2021. **a** Prevalence of overweight/obesity in 2016–2021. **b** Prevalence of MALFD in overweight/obesity in 2016–2021. **c** Prevalence of MALFD with renal insufficiency in overweight/obesity in 2016–2021. **d** Prevalence of overweight/obesity, MAFLD, and MAFLD with renal insufficiency in different age-groups in 2021.

Prevalence of MAFLD with Renal Insufficiency at Different Ages in 2021

We analyzed the prevalence of MAFLD with renal insufficiency at different ages using data from 2021. Health checkups in 2021 were divided into six age-groups: 18–29 years old, 30–39 years old, 40–49 years old, 50–59 years old, 60–69 years old, ≥70 years old. The prevalence of overweight/obesity, MAFLD, and MAFLD with renal insufficiency differed by age-groups. The prevalence of overweight/obesity is highest in the 50–59 age-group (62.2%), and the prevalence of MAFLD in overweight/obesity is highest in the 40–49 age-group (45.5%). However, the prevalence of MAFLD with renal insufficiency showed an increasing trend with age (Fig. 2d).

Clinical Characteristics and Risk Factors of MAFLD in Overweight/Obese Adults

Compared with non-MAFLD, MAFLD was more commonly seen in men, old subjects, and subjects with a high BMI. All clinical characteristics were compared before and after PSM for gender and age. Compared with the non-MAFLD group, the MAFLD group had more severe metabolic dysfunction (a higher percentage of the population had elevated SBP, DBP, FBG, TG, TC, LDL-C, and UA and reduced HDL-C), more prevalent liver damage (increase in ALT, AST, ALP, GGT, and TBIL), and renal injury (elevation of BUN with Scr and reduction in eGFR) (Table 1). Multivariable regression analysis showed that male sex, high BMI, elevated SBP,

Table 1. Demographic and biochemical characteristics of MAFLD and non-MAFLD groups in overweight/obese adults in 2021

Characteristics	Before PSM			After PSM with gender and age		
	non-MAFLD (*n* = 18,391)	MAFLD (*n* = 13,924)	*p* value	non-MAFLD (*n* = 13,728)	MAFLD (*n* = 13,728)	*p* value
Gender (male), *n* (%)	12,283 (66.8)	10,136 (72.8)	<0.001	9,948 (72.5)	9,948 (72.5)	–
Age, years	39 (31, 51)	40 (32, 51)	<0.001	39 (32, 51)	40 (32, 51)	0.505
BMI, kg/m^2	25.55 (24.17, 27.61)	27.74 (25.6, 30.52)	<0.001	25.45 (24.16, 27.37)	27.71 (25.63, 30.47)	<0.001
Metabolic abnormalities						
Elevated SBP, *n* (%)	5,994 (32.6)	6,669 (47.9)	<0.001	4,488 (32.7)	6,577 (47.9)	<0.001
Elevated DBP, *n* (%)	5,258 (28.6)	6,377 (45.8)	<0.001	4,012 (29.2)	6,273 (45.7)	<0.001
Elevated FBG, *n* (%)	3,487 (19.0)	5,109 (36.7)	<0.001	2,835 (20.7)	5,044 (36.7)	<0.001
Elevated TG, *n* (%)	4,795 (26.1)	8,319 (59.7)	<0.001	3,671 (26.7)	8,188 (59.6)	<0.001
Elevated TC, *n* (%)	2,866 (15.7)	3,486 (25.0)	<0.001	2,211 (16.1)	3,433 (25.0)	<0.001
Reduced HDL-C, *n* (%)	5,048 (25.6)	6,022 (43.2)	<0.001	3,306 (24.1)	5,942 (43.3)	<0.001
Elevated LDL-C, *n* (%)	4,691 (25.5)	5,042 (36.2)	<0.001	3,675 (26.8)	4,976 (36.2)	<0.001
Elevated UA, *n* (%)	3,795 (20.6)	5,477 (39.3)	<0.001	2,533 (18.5)	5,411 (39.4)	<0.001
Liver function						
ALT, IU/L	18 (15, 23)	24 (19, 33)	<0.001	19 (15, 24)	24 (19, 33)	<0.001
AST, IU/L	18 (14, 23)	24 (19, 35)	<0.001	19 (15, 23)	24 (19, 34)	<0.001
ALP, IU/L	74 (63, 88)	79 (67, 94)	<0.001	74 (62, 88)	79 (67, 94)	<0.001
GGT, U/L	18 (13, 27)	31 (21, 47)	<0.001	18 (13, 28)	31 (21, 47)	<0.001
TBIL, μmol/L	11.9 (9, 15.5)	11.9 (9.1, 15.6)	0.206	11.8 (9, 15.4)	11.9 (9.1, 15.6)	0.032
Renal function						
BUN, mmol/L	4.6 (3.9, 5.4)	4.62 (3.96, 5.45)	<0.001	4.6 (3.9, 5.4)	4.62 (3.96, 5.46)	0.001
SCr, μmol/L	79.3 (69.1, 88.0)	80.9 (72.2, 88.75)	<0.001	79.2 (69.5, 88)	80.9 (72.1, 88.8)	<0.001
eGFR, mL/min/1.73 m^2	97.6 (84.8, 102)	97.1 (85.2, 107.7)	0.001	98.6 (87.1, 109.4)	97.1 (85.1, 107.7)	<0.001
eGFR <90, *n* (%)	34.1 (6,284/18,391)	33.9 (4,715/13,924)	0.565	4,198 (30.5)	4,672 (34.0)	<0.001
eGFR <60, *n* (%)	1.7 (321/18,391)	1.9 (258/13,924)	0.471	229 (1.7)	254 (1.9)	0.251

Elevated SBP: ≥130 mm Hg. Elevated DBP: ≥ 85 mm Hg. Elevated FBG: ≥5.6 mmol/L. Elevated TG: ≥1.7 mmol/L. Elevated TC: ≥5.2 mmol/L. Reduced HDL-C: <1.0 mmol/L for men and <1.3 mmol/L for women. Elevated LDL-C: ≥3.1 mmol/L. Elevated UA: ≥416 μmol/L for men and ≥357 μmol/L for women.

elevated DBP, elevated FBG, elevated TG, reduced HDL-C, elevated LDL-C, and elevated UA were all independent risk factors for the development of MALFD (Fig. 3a).

Clinical Characteristics and Risk Factors of MAFLD with Renal Insufficiency

Compared with MAFLD with normal renal function, MAFLD with renal insufficiency was more frequently seen in women, older individuals, and individuals with higher BMI. Also, more pronounced metabolic dysfunction and more severe fibrosis were present in the MAFLD with the renal insufficiency group (Table 2). However, the transaminases in the MAFLD with renal insufficiency group were instead lower than those in the normal renal function group. These results are consistent before and after using PSM with sex and age. Multivariable regression analysis revealed that BMI, elevated UA, and fibrosis were independent risk factors for MAFLD with renal insufficiency (Fig. 3b). Also, we found that elevated ALT was also a risk factor for MAFLD with renal insufficiency after multivariate analysis, which was different from the univariate analysis. Further analysis revealed that BMI and eGFR have a negative correlation ($r = -0.533$, $p < 0.001$, Fig. 4a). We also analyzed the distribution of eGFR after MAFLD was divided into groups with and without elevated UA, groups with and without elevated ALT, and groups with different FIB-4 values. The results found that the prevalence of renal insufficiency was higher in the elevated UA group, higher FIB-4 group, and non-elevated ALT group (Fig. 4b–d).

Discussion

According to the Global Burden of Disease project, a total of 2.2 billion people worldwide are overweight/obese. The latter group includes 107.7 million children

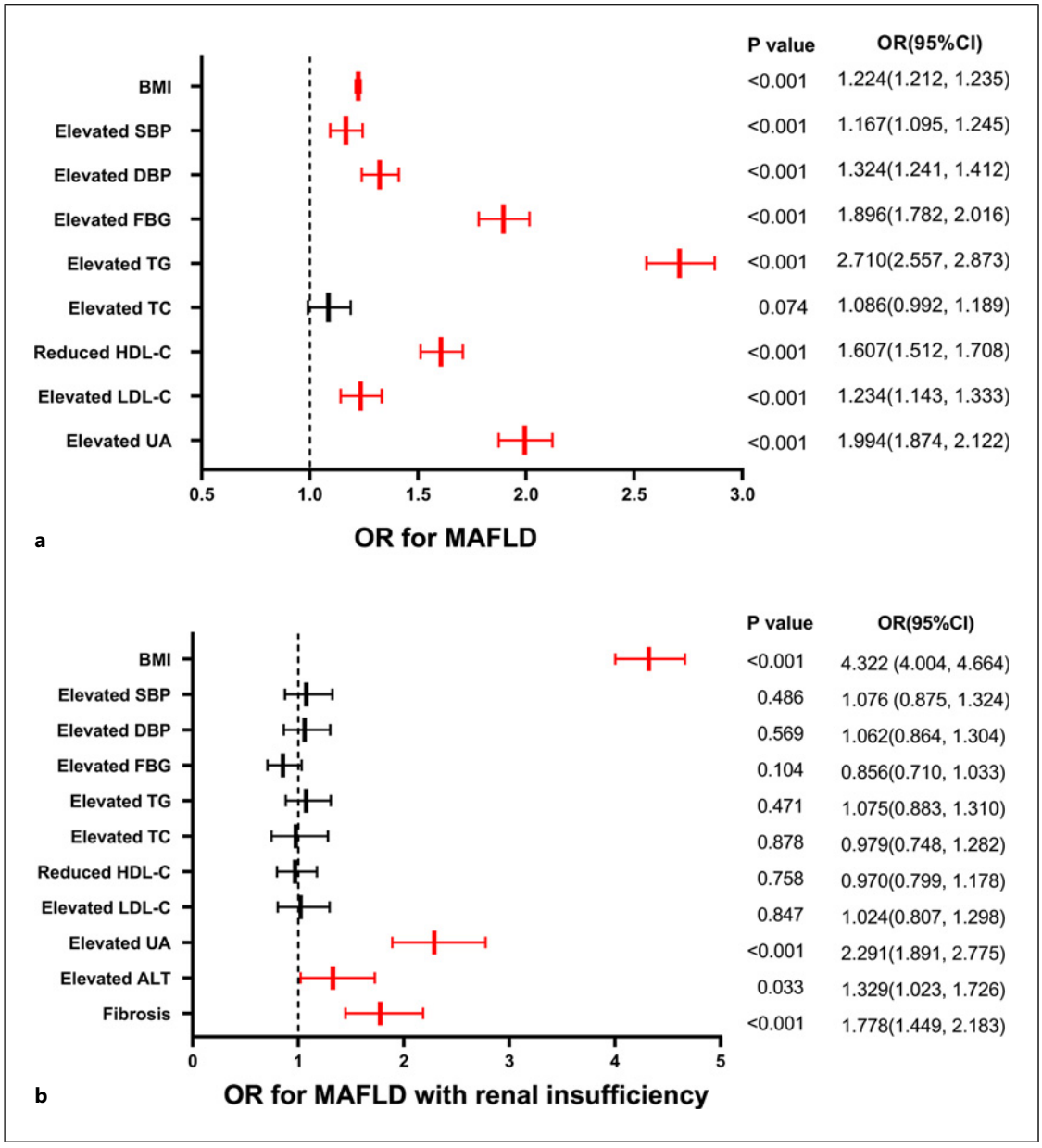

Fig. 3. Logistic regression analysis of the risk factors for MAFLD (**a**) and MAFLD with renal insufficiency (**b**).

and 603.7 million adults, with an overall prevalence of obesity being 5.0% and 12.0%, respectively [20]. The most recent data show that more than half of Chinese adults are overweight (34.3%) or obese (16.4%). This corresponds to 600 million overweight/obese people, the highest number in any country. Over the past 30 years, overweight/obesity rates have increased in all age-groups, by an average of about 2.5 times [21]. Both globally and in China, there are sex, age, and geographical differences in the prevalence of overweight and obesity, which are mainly related to genetics, hormones, work stress, lifestyle, and diet [20]. The data also showed that the prevalence of overweight/obesity is higher among adult men than women. Our study showed that the prevalence of overweight/obesity in total reached the highest of 62.3% in 2019 and the lowest of 51.6% in 2017, and the prevalence was significantly higher in males than in females. Further analysis indicated that the prevalence of overweight/obesity differed by

Table 2. Demographic and biochemical characteristics of MAFLD with renal insufficiency in overweight/obese adults in 2021

Characteristics	Before PSM			After PSM with gender and age		
	renal insufficiency (*n* = 4,715)	normal renal function (*n* = 9,209)	*p* value	renal insufficiency (*n* = 3,924)	normal renal function (*n* = 3,924)	*p* value
eGFR, mL/min/1.73 m^2	79.9 (72.2, 85.4)	101.0 (95.5, 107.4)	<0.001	80.7 (73.5, 85.8)	101.0 (95.5, 107.4)	<0.001
Scr, μmol/L	90.0 (81.4, 97.1)	72.0 (63.0, 79.6)	<0.001	91.5 (84.0, 98.1)	72.0 (63.0, 79.6)	<0.001
Gender (male), *n* (%)	3,232 (68.5)	7,704 (83.7)	<0.001	2,354 (60.0)	2,354 (60.0)	–
Age, years	47 (36, 57)	45 (35, 54)	<0.001	44 (35, 56)	45 (35, 54)	0.673
BMI, kg/m^2	31.3 (29.4, 34.2)	25.8 (24.7, 26.9)	<0.001	31.4 (29.4, 34.3)	25.8 (24.7, 26.9)	<0.001
Metabolic abnormalities						
Elevated SBP, *n* (%)	2,474 (52.5)	4,195 (45.5)	<0.001	1,980 (50.5)	1,774 (45.2)	<0.001
Elevated DBP, *n* (%)	2,245 (47.6)	4,132 (44.9)	0.002	1,864 (47.5)	1,747 (44.5)	<0.001
Elevated FBG, *n* (%)	1,830 (38.8)	3,279 (35.6)	<0.001	1,431 (36.5)	1,712 (43.6)	<0.001
Elevated TG, *n* (%)	2,938 (62.3)	5,381 (58.4)	<0.001	2,433 (62.0)	2,216 (56.5)	<0.001
Elevated TC, *n* (%)	1,263 (26.8)	2,223 (24.1)	0.001	1,022 (26.0)	977 (24.8)	<0.001
Reduced HDL-C, *n* (%)	2,534 (53.7)	3,488 (37.9)	<0.001	2,008 (51.2)	1,646 (41.9)	<0.001
Elevated LDL-C, *n* (%)	1,778 (37.7)	3,264 (35.4)	0.008	1,465 (37.3)	1,428 (36.4)	<0.001
Elevated UA, *n* (%)	2,459 (52.1)	3,018 (32.7)	<0.001	2,072 (52.8)	1,033 (26.3)	<0.001
ALT, IU/L	23 (18, 30)	24 (19, 35)	<0.001	23 (18, 30)	24 (19, 35)	<0.001
Elevated ALT, *n* (%)	492 (10.3)	1,651 (17.9)	<0.001	433 (11.0)	644 (16.4)	<0.001
FIB-4	1.13 (0.80, 1.58)	0.84 (0.59, 1.20)	<0.001	1.06 (0.77, 1.50)	0.84 (0.59, 1.20)	<0.001
Fibrosis (FIB-4 ≥1.3), *n* (%)	1,836 (38.9)	1,850 (20.1)	<0.001	1,278 (32.6)	817 (20.8)	<0.001
FIB-4 <1.3, *n* (%)	2,879 (61.1)	7,359 (79.9)	<0.001	2,541 (64.8)	3,097 (78.9)	<0.001
1.3≤ FIB-4 <2.67, *n* (%)	1,623 (34.4)	1,715 (18.6)		1,236 (31.5)	765 (19.5)	
FIB-4 ≥2.67 (%), *n* (%)	213 (4.5)	135 (1.5)		147 (3.7)	62 (1.6)	

Elevated SBP: ≥130 mm Hg. Elevated DBP: ≥ 85 mm Hg. Elevated FBG: ≥5.6 mmol/L. Elevated TG: ≥1.7 mmol/L. Elevated TC: ≥5.2 mmol/L. Reduced HDL-C: <1.0 mmol/L for men and <1.3 mmol/L for women. Elevated LDL-C: ≥3.1 mmol/L. Elevated UA: ≥416 μmol/L for men and ≥357 μmol/L for women. Elevated ALT: >40 IU/L.

age-groups. The prevalence of overweight/obesity has been shown to correlate with the prevalence and severity of NAFLD. According to the latest name change recommendations, MAFLD is diagnosed based on imaging suggestive of hepatic steatosis with the presence of overweight/obesity (BMI ≥25 kg/m^2 in Caucasians or BMI ≥23 kg/m^2 in Asians). A meta-analysis of 116 relevant studies including 2,667,052 cases [22] showed that the global prevalence of MAFLD in the overweight/obese population was 50.7%, with a higher prevalence in men (59.0%) than in women (47.5%). The same meta-analysis showed that the prevalence of MAFLD in China was 51.5% and was higher in the middle-aged (56.3%) than in the young and old population. In our study, the prevalence of MAFLD in yearly overweight/obesity reached its highest of 44.7% in 2017 and its lowest of 36.9% in 2018, with the value significantly higher in males than in females. The prevalence of MAFLD in overweight/obesity is highest in the 40–49 age-group. These findings are consistent with age differences in the prevalence of obesity/overweight and reconfirm the link between MAFLD and overweight/obesity. Overall, our results showed a slightly lower prevalence of overweight/obese MAFLD than previous studies, but the sex- and age-dependent differences were generally consistent with the current study [23].

The prevalence of CKD is increasing globally with the increase in overweight/obesity, diabetes, hypertension, and aging. NAFLD has also been reported to affect the development of CKD. The prevalence of CKD ranged from approximately 20–55% among patients with NAFLD compared to 5–30% among their counterparts without NAFLD [24]. MAFLD places more emphasis on metabolic dysfunction than NAFLD. However, relatively few studies have been conducted on the prevalence trends on MAFLD with renal insufficiency, especially in overweight/obese populations. Marenao et al.'s study showed that MAFLD is independently associated with a new onset of CKD and

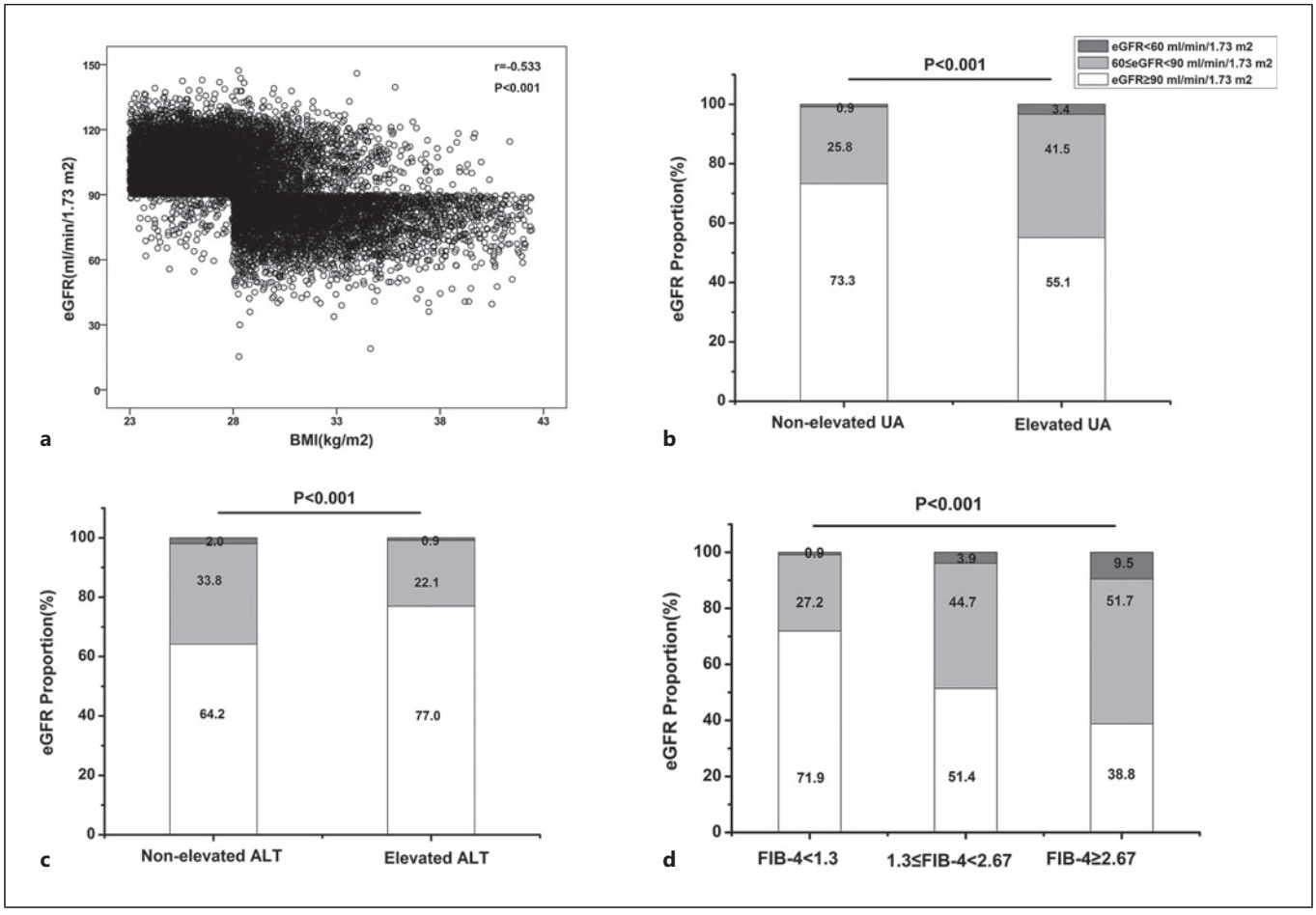

Fig. 4. eGFR proportion in different BMI, UA, ALT, and FIB-4. **a** Scatter plot of BMI and eGFR. **b** eGFR proportion in non-elevated and elevated UA groups. **c** eGFR proportion in non-elevated and elevated ALT groups. **d** eGFR proportion in different FIB-4 groups.

predicts the risk for development of CKD better than fatty liver or NAFLD [25]. One recent cross-sectional study found that MAFLD individuals had a lower eGFR and a greater prevalence of CKD (29.60% vs. 26.56%) than NAFLD individuals [19]. In our study, the prevalence of MAFLD with renal insufficiency (eGFR ≤90 mL/min/1.73 m^2) in yearly overweight/obesity reached its highest of 33.9% in 2021 and its lowest of 21.8% in 2019. The prevalence of MAFLD with renal insufficiency was significantly higher in women than in men, showing an increasing trend with age.

Previous research documented that NAFLD is associated with metabolic syndrome components, such as obesity, insulin resistance, hyperglycemia, hypertension, and hyperlipidemia, and NAFLD was considered a hepatic manifestation of the metabolic syndrome [26]. Given the sex and age differences in the prevalence of MAFLD in the overweight and obese population, we utilized PSM for sex and age. We found that in comparison with the non-MAFLD group, the MAFLD group had a higher BMI and a significantly higher fraction of the population with elevated SBP, DBP, FBG, TG, TC, LDL-C, and UA and reduced HDL-C, before and after PSM. Further multivariable analysis found that male sex, high BMI, and elevated SBP, DBP, FBG, TG, LDL-C, and UA, as well as reduced HDL-C, were all independent risk factors for MALFD. In the overweight/obese populations, liver function indicators, including ALT, AST, ALP, GGT, and TBIL, were significantly higher in MAFLD patients than in non-MAFLD individuals. These data indicate the presence of liver dysfunction in MAFLD patients, which is consistent with previous studies pointing to NAFLD as the most common cause of unexplained liver function abnormalities [27].

Although NAFLD is a "multisystem" disease [28], the exact relationship between MAFLD and extrahepatic diseases, including CKD, is currently not entirely understood. Several recent studies (cross-sectional studies or cohort studies) identified a correlation between NAFLD and CKD, suggesting that NAFLD is a risk factor for the development of CKD and that the severity of NAFLD further increases the risk of CKD. The significant association between NAFLD and increased incidence of CKD persisted even after adjustment for age, sex, obesity, hypertension, type 2 diabetes, and other potential confounding factors [24, 29, 30]. A retrospective cohort analysis showed that the presence of NAFLD was associated with a nearly 50% increase in the risk of incident CKD over a follow-up period of 6.5 years [31]. Meta-analysis showed that the presence of advanced hepatic fibrosis was associated with a higher prevalence and incidence of CKD than either non-advanced fibrosis or simple steatosis, respectively [32]. Liver biopsy is the gold standard for assessing liver fibrosis in NAFLD/MAFLD; however, its invasiveness limits its routine availability. Sun DQ [29] found that liver fibrosis was independently associated with early kidney dysfunction in patients with biopsy-proven NAFLD. Thus, transient elastography-measured liver stiffness measurement can accurately identify those patients with NAFLD who are at risk of having early kidney dysfunction. Meanwhile, Eddowes P showed that noninvasive fibrosis scoring systems, especially FIB-4 and NFS-index, can be used to identify patients at risk of future liver-related events including CKD [33]. In comparison with NAFLD, MAFLD is a better predictor of CKD [19]. Our study identified an increase in BUN and Scr and a decrease in eGFR in MAFLD before and after using sex and age matching. Compared with the normal renal function group, MAFLD with renal insufficiency was more common in women, old individuals, and persons with a higher BMI and was characterized by significant metabolic dysfunction and liver fibrosis. Multivariable analysis showed that BMI, uric acid, and fibrosis (evaluated with noninvasive liver fibrosis score FIB-4) were independent risk factors for MAFLD with renal insufficiency. Further analysis found that BMI and eGFR have a negative correlation, which is consistent with previous study [34]. The FIB-4 index was used for noninvasive assessment of fibrosis in this study. The prevalence of renal insufficiency was higher in FIB-4 $\geq$2.67 versus 1.3$\leq$ FIB-4 <2.67 and FIB-4 <1.3 groups, which suggested that fibrosis may promote the development of renal insufficiency in MAFLD. This result also showed noninvasive fibrosis scoring systems FIB-4 can be used to identify patients at risk of renal insufficiency. Meanwhile, this study showed that the prevalence of renal insufficiency was higher in elevated UA groups versus non-elevated UA groups, which was not addressed in the previous study. This result suggested that UA rather than other metabolic abnormalities was more effective in identifying the risk of renal insufficiency. However, our results presented that the relationship between elevated ALT and renal insufficiency in MAFLD was uncertain, with opposite results presented in the univariate and multivariate analyses, and more research is needed to explore. The current literature supports the notion that renal insufficiency may be one of the extrahepatic diseases of MAFLD. However, whether renal insufficiency increases the risk of MAFLD or drives MAFLD progression is unclear and needs to be explored by more prospective research.

Our study was based on data from a large population undergoing health checkup, and the large sample size and the availability of extensive clinical data enabled adjusting for potential confounders. However, the study also had some limitations. First, this is a cross-sectional study in which the natural course of MAFLD and the causal relationship with metabolic characteristics and renal function could not be determined. Second, the diagnosis of MAFLD was based on ultrasonography, which is recommended as a first-line imaging method for MAFLD by the Association for the Study of the Liver [5]. However, ultrasonography may not be sensitive enough to detect the mild hepatic steatosis [35], and therefore, the actual prevalence of MAFLD and MAFLD with renal insufficiency may be higher. Third, some selection bias may be present since the population attending health screening tends to be more concerned about their health.

Conclusion

Our study found that there was a relatively high prevalence of MAFLD and MAFLD with renal insufficiency in overweight/obese adults in the last 5 years. Overweight/obese MAFLD was associated with significant metabolic dysfunction, liver and renal injury. Hypertension, hyperglycemia, dyslipidemia, and hyperuricemia were independent risk factors for the development of overweight/obese MAFLD. BMI, uric acid, and fibrosis (evaluated with noninvasive liver fibrosis score FIB-4) were independent risk factors for MAFLD with renal insufficiency. Our results emphasize the pandemic nature and the severity of overweight/obese

MAFLD with renal insufficiency that needs to be noticed by multidisciplinary specialists, health care practitioners, health policy-makers, and the public.

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Statement of Ethics

The study was approved by the Ethics Committee of the Second Affiliated Hospital of Xi'an Jiaotong University (2022036). Written informed consent was obtained for participation in this study.

Conflict of Interest Statement

The authors declared no conflict of interest.

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Author Contributions

Ameng Shi, Xiaoyan Guo, Xiaolan Lu, and Haitao Shi developed the conception and design of the study. Ameng Shi, Jiang Deng, and Juan Ma collected the data and wrote the manuscript. Longbao Yang, Xinxing Tantai, Qian Wang, and Danyan Chang performed the data analysis. Jinhai Wang revised the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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