Cerdika: Jurnal Ilmiah Indonesia, 6 (7), July 2026
p-ISSN: 2774-6291 e-ISSN: 2774-6534
Available online at http://cerdika.publikasiindonesia.id/index.php/cerdika/index

Association Between Non-Alcoholic Fatty Liver Disease, Metabolic Dysfunction-Associated Fatty Liver Disease and the Risk of Chronic Kidney Disease in patients aged ≥18 years: A Systematic Review

Putu Ngurah Pradnya Wibawa*, Ni Putu Lia Juliantini, Ni Luh Putu Serly Ekayanti
UPTD Dawan II Community Health Center, Indonesia
Email: pradnyawibawa@yahoo.com*, liajuliantini26@gmail.com, serlyekayanti@gmail.com

Keywords:
Non-Alcoholic Fatty Liver Disease (NAFLD); Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD); Risk of Chronic Kidney Disease (CKD).

Abstract
Non-alcoholic fatty liver disease (NAFLD) is a chronic liver condition whose prevalence continues to rise in parallel with increasing rates of obesity, insulin resistance, and other metabolic disorders. NAFLD is also associated with extrahepatic conditions, including chronic kidney disease (CKD). This study aimed to determine whether there is an association between NAFLD and the incidence of CKD. This scoping review analyzed articles published between August 2016 and August 2026 from PubMed, ScienceDirect, and OpenAlex. The inclusion criteria comprised English-language cohort studies, case-control studies, and cross-sectional studies examining the association between NAFLD and the risk of CKD. Fifteen articles were selected following a rigorous screening process. The findings indicate a consistent and significant association between fatty liver disease—particularly metabolic dysfunction-associated fatty liver disease (MAFLD) and metabolic dysfunction-associated steatotic liver disease (MASLD)—and an increased risk of incident CKD. MAFLD appears to be a better predictor of chronic kidney disease (CKD) than the traditional NAFLD definition, primarily because it directly incorporates metabolic dysfunction. The terminology has evolved from non-alcoholic fatty liver disease (NAFLD) to metabolic dysfunction-associated fatty liver disease (MAFLD). This shift represents a change in diagnostic strategy from exclusion-based criteria (as in NAFLD) to inclusion-based criteria that prioritize metabolic dysfunction (including obesity and diabetes), which has been shown to be more effective in assessing the risk of developing CKD.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) represents a prevalent chronic liver condition globally, and its incidence is increasing in tandem with rising rates of obesity, insulin resistance, and metabolic syndrome. Current estimates suggest that NAFLD affects approximately 25–30% of adults worldwide, making it a significant public health concern (Lonardo et al., 2022). Moreover, the effects of NAFLD extend beyond the liver; it is strongly associated with extrahepatic conditions, including cardiovascular disease and chronic kidney disease (Adams et al., 2017; Kaya & Yilmaz, 2021; Targher & Byrne, 2017).

Chronic kidney disease (CKD), a progressive condition characterized by gradual deterioration of renal function, is a major contributor to global morbidity and mortality. The relationship between NAFLD and CKD has gained considerable attention in recent years, as both conditions share underlying pathophysiological mechanisms, including chronic inflammation, oxidative stress, and metabolic dysregulation (Mantovani et al., 2022).

The introduction of new terminology, such as Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD), has strengthened the link between metabolic dysfunction and the risk of CKD.

Recent investigations suggest that both non-alcoholic fatty liver disease (NAFLD) and

metabolic dysfunction-associated fatty liver disease (MAFLD) are associated with an increased risk of CKD, with no significant differences observed between them (Agustanti et al., 2023). This finding highlights the central role of metabolic mechanisms in the pathogenesis of both conditions.

The novelty of this study lies in its comprehensive synthesis of recent evidence comparing the predictive value of NAFLD and MAFLD/MASLD criteria for CKD risk. Unlike previous reviews that focused primarily on NAFLD, this systematic review specifically examines the transition from NAFLD to MAFLD and subsequently to MASLD, evaluating the clinical utility of these evolving diagnostic frameworks. Additionally, this review explores the role of liver fibrosis severity in modulating CKD risk and assesses the consistency of findings across different populations and study designs. By incorporating the most recent evidence, including studies published up to 2026, this review provides an up-to-date perspective on this rapidly evolving field. This comprehensive approach allows for a more nuanced understanding of the relationship between fatty liver disease and CKD and offers practical implications for clinicians and researchers.

Although the association between NAFLD, MAFLD, and CKD has been extensively documented, the precise causal pathways and their clinical significance remain incompletely understood. Consequently, a systematic review is warranted to evaluate the most current evidence regarding the association between NAFLD, MAFLD, and the risk of developing CKD.

METHOD

Study Design

This study was a systematic review aimed at identifying, evaluating, and qualitatively synthesizing scientific evidence on the relationship between non-alcoholic fatty liver disease (NAFLD), metabolic dysfunction-associated fatty liver disease (MAFLD), and chronic kidney disease (CKD).

The review applied the PICO framework, focusing on adults aged ≥18 years. The exposures were NAFLD and MAFLD, while the comparison group consisted of individuals without NAFLD or MAFLD. The outcome of interest was the incidence of CKD as reported in the included studies.

The literature search, conducted in February 2026, used a structured and comprehensive search strategy to ensure the inclusion of relevant, high-quality studies. This study relied on secondary data derived from previously published peer-reviewed articles selected based on predefined inclusion criteria aligned with the study objectives.

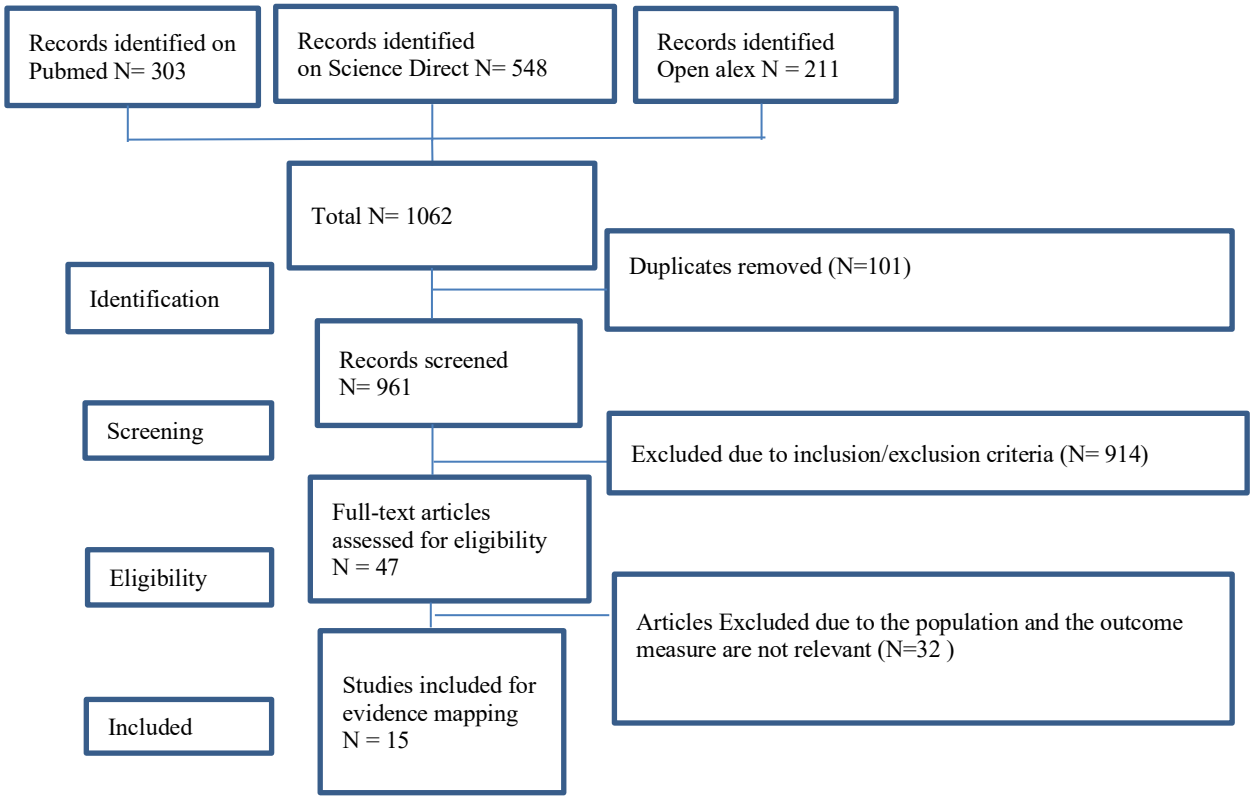
Data Sources and Search Strategy

A systematic literature search was conducted across three electronic databases: PubMed, ScienceDirect, and OpenAlex. The search strategy employed a combination of keywords and Boolean operators as follows: ("Non-alcoholic Fatty Liver Disease"[Mesh] OR "Fatty Liver"[Mesh] OR NAFLD[tiab] OR "nonalcoholic fatty liver"[tiab] OR "non-alcoholic fatty liver"[tiab] OR NASH[tiab] OR "nonalcoholic steatohepatitis"[tiab]) AND ("Renal Insufficiency, Chronic"[Mesh] OR "Kidney Failure, Chronic"[Mesh] OR "Chronic Kidney Disease"[tiab] OR CKD[tiab] OR "chronic renal disease"[tiab] OR "renal insufficiency"[tiab]). The search was limited to articles published in English and within the last 10 years.

Inclusion Criteria

The inclusion criteria were defined as follows: (1) Population: adult and elderly individuals (≥18 years), (2) Exposure: NAFLD and MAFLD diagnosed using valid methods (ultrasound, CT scan, MRI, biopsy, or validated clinical criteria), (3) Outcome: incidence of CKD, (4) Study design: cohort, case-control, and cross-sectional studies, (5) Articles published in English, (6) Publications within the last 10 years, and (7) Availability of full-text articles.

In the first step of the article search (identification), 1062 publications were located using three data sources: PubMed, Science Direct, and Open Alex. Of these, 548 were from Science Direct, 303 were from PubMed, and 211 were from Open Alex. There were 961 items left after the filtering procedure eliminated 101 duplicates. The second step, "screening," examined article names for abstracts and literature review relevancy. Articles that didn't fit the requirements were removed. 914 articles were removed after 47 were discovered with titles that satisfied the requirements. Articles from scoping reviews, systematic reviews, and meta-analyses were excluded as part of the "eligibility" process. Additionally, free full text articles that addressed association between non-alcoholic fatty liver disease (NAFLD) and the risk of chronic kidney disease and that satisfied the criteria within the previous ten years (February 2016–February 2026) were reviewed. Finding the number of papers that best fit the inclusion and exclusion criteria and complemented the goals of this scoping study was the last phase, referred to as the "inclusion" step. 15 items satisfied all standards, while the remaining 32 were removed. The flowchart below (Figure 1) details the outcomes of the article selection procedure.



The flowchart below (Figure 1) details the outcomes of the article selection procedure.

RESULTS AND DISCUSSION

Table 1. Association Between Non-Alcoholic Fatty Liver Disease (NAFLD) and the Risk of Chronic Kidney Disease

No	Author (Year)	Title and Study Design	Aim	Result	Conclusion
1	Kwon et al. (2023)	MAFLD and NAFLD in the prediction of incident chronic kidney disease **Study Design:** Cohort study	The study aimed to evaluate whether metabolic dysfunction-associated fatty liver disease or non-alcoholic fatty liver disease better predicts the risk of developing incident chronic kidney disease	• The study included 21,713 adults who were followed for a median of 5.3 years, during which 912 participants (4.2%) developed CKD. • Participants in the MAFLD-only group (HR 1.97) and the combined group (meeting both MAFLD and NAFLD criteria; HR 1.50) showed a significantly increased risk of CKD. • In contrast, the NAFLD-only group (meeting NAFLD criteria but not MAFLD) did not show an increased risk of CKD (HR 1.06). • The risk of CKD was also significantly higher in MAFLD subgroups with the following conditions: ○ Overweight/obesity (HR 2.94) ○ Diabetes (HR 2.20) ○ Excessive alcohol consumption (HR 2.71) ○ Viral hepatitis (HR 2.38) • Subgroup analysis further showed that individuals with lean MAFLD had an increased risk of CKD, whereas individuals with lean NAFLD did not demonstrate a higher risk.	• The shift in definition from NAFLD to MAFLD enables the identification of a greater number of individuals at risk of developing CKD. • The risk of CKD is not increased in individuals with NAFLD who do not meet MAFLD criteria or who are not overweight/obese. This study highlights that the increased risk of CKD in patients with fatty liver who have excessive alcohol consumption or viral hepatitis should not be overlooked, as these groups are included within the MAFLD definition.
2	Chen et al. (2020)	The correlation between fatty liver disease and chronic kidney disease **Study Design:** cross-sectional study	The study aimed to assess the association between non-alcoholic fatty liver disease and chronic kidney disease and evaluate the role of liver fibrosis	• ut of a total of 29,797 subjects, NAFLD and CKD were identified in 44.5% and 20.2% of the population, respectively. • nitial findings showed that subjects with NAFLD had a higher proportion of CKD compared to those without NAFLD (24.1% vs 17.1%). • owever, multivariate analysis indicated that NAFLD, as a whole, was not an independent risk factor for CKD (OR 1.015; p = 0.630). • urther analysis revealed that advanced liver fibrosis (defined by NAFLD-FS > 0.676) had a strong and independent	• (AFLD in general is not a risk factor for CKD; however, patients with NAFLD and advanced liver] fibrosis have a significantly higher risk of developing CKD. •] he degree of liver fibrosis, rather than the mere presence of fatty liver, is the key determinant of CKD] risk. • herefore, patients with NAFLD and advanced fibrosis

No	Author (Year)	Title and Study Design	Aim	Result	Conclusion
				association with an increased risk of CKD (OR 2.284; p < 0.001). • he prevalence of NAFLD also increased in parallel with the progression of CKD to more advanced stages.	should undergo CKD screening and receive appropriate management if diagnosed.
3	Mantovani et al. (2024)	MASLD, hepatic steatosis and fibrosis are associated with the prevalence of chronic kidney disease and retinopathy in adults with type 1 diabetes mellitus **Study Design:** cross-sectional study	The study aimed to evaluate the association of metabolic dysfunction-associated steatotic liver disease and fibrosis with chronic kidney disease and retinopathy	• his study included 1,409 adult outpatients with type 1 diabetes mellitus. • atients with MASLD and significant fibrosis (n = 93) showed a much higher prevalence of CKD (36.6%) and diabetic retinopathy (51.1%) compared to: • ASLD without fibrosis (CKD 14.0%; retinopathy 34.2%) • ndividuals without steatosis (CKD 13.4%; retinopathy 26.3%) • fter adjusting for sex, duration of diabetes, HbA1c, hypertension, and medication use, patients with MASLD and significant fibrosis had a 1.76-fold higher risk of CKD compared to individuals without steatosis. • atients with MASLD without fibrosis had a 1.49-fold higher risk of retinopathy compared to individuals without steatosis. • he results remained consistent even after excluding individuals with moderate alcohol consumption from the analysis.	• on-invasive detection of MASLD and liver fibrosis in patients with type 1 diabetes mellitus can help identify individuals at high risk of chronic microvascular complications, particularly CKD. • he severity of liver disease (fibrosis) shows a stronger association with CKD, whereas the presence of steatosis is more closely related to retinopathy.
4	Kasim et al. (2020)	Correlation Between Non-Alcoholic Fatty Liver Disease and Chronic Kidney Disease **Study Design:** This case-control study	The study aimed to determine the correlation between non-alcoholic fatty liver disease and chronic kidney disease	• his study included 134 subjects who were equally divided into NAFLD and non-NAFLD groups (67 subjects each). • ubjects with NAFLD had a significantly higher proportion of eGFR < 60 ml/min/1.73 m² compared to the non-NAFLD group (40.3% vs 16.4%; p = 0.002). • tage 3 CKD was found significantly more frequently in the NAFLD group (37.3%) compared to the non-NAFLD group (9%; p = 0.001). • n contrast, the non-NAFLD group had	• his study concluded that NAFLD has a significant correlation with the occurrence of CKD. • atients with NAFLD tend to have lower kidney function (eGFR < 60 ml/min/1.73 m²) and more advanced stages of CKD (stage 3) compared to individuals without fatty liver.

No	Author (Year)	Title and Study Design	Aim	Result	Conclusion
				a higher proportion of stage 1 and 2 CKD. • o statistically significant association was found between NAFLD and the occurrence of proteinuria (p = 0.051), although A3-grade proteinuria appeared to be more common in the NAFLD group.	
5	Ono et al. (2025)	Metabolic dysfunction-associated steatotic liver disease can be a possible predictive factor of incident chronic kidney disease **Study Design:** cohort study	The study aimed to evaluate metabolic dysfunction-associated steatotic liver disease as an independent predictor of chronic kidney disease	• his study included 15,873 participants based on health check-up data from Asahi University Hospital, Japan. • he highest incidence of CKD was observed in individuals with MASLD, at 9.5%. • ultivariate analysis demonstrated that MASLD was significantly associated with an increased risk of CKD (OR 1.37; 95% CI 1.12–1.67; p = 0.002). • ther significant predictors of CKD included age (OR 1.04) and baseline estimated glomerular filtration rate (eGFR) (OR 0.88). • ardiometabolic risk factors, rather than alcohol consumption, played a more prominent role in CKD development. For instance, the MASLD group with increased alcohol intake (MetALD) did not show a significant association with incident CKD (OR 1.10; p = 0.67).	This study demonstrates that MASLD is a significant independent risk factor for the development of CKD. Early identification and appropriate management of MASLD are essential to reduce or prevent the increasing incidence of CKD in the future.
6	Gurun et al. (2024)	Increased risk of chronic kidney disease and mortality in a cohort of people diagnosed with metabolic dysfunction associated steatotic liver disease with hepatic fibrosis **Study Design:** cohort study	The study aimed to assess the impact of liver fibrosis on chronic kidney disease and mortality	• his study included 2,046 individuals with MASLD, consisting of 1,448 (70.8%) without fibrosis and 598 (29.2%) with fibrosis. • he analysis showed that liver fibrosis was significantly associated with an increased risk of CKD (adjusted Relative Risk/aRR = 1.31; p = 0.021). • here was a clear increase in mortality risk among individuals with liver fibrosis (adjusted Hazard Ratio/aHR = 2.30). • he highest mortality risk was observed in individuals with both fibrosis and CKD (aHR = 5.07; p < 0.001) compared to those without either condition.	Liver fibrosis is an independent risk factor for CKD in patients with MASLD. In addition, the combination of liver fibrosis and CKD significantly increases the risk of mortality. Therefore, screening of kidney function (such as eGFR and uACR) is strongly recommended as part of liver health monitoring in individuals with MASLD and fibrosis.

No	Author (Year)	Title and Study Design	Aim	Result	Conclusion
				• he lowest median life expectancy was found in the group with both fibrosis and CKD (64.0 years), while the highest was observed in those without either condition (82.2 years).	
7	Liang et al. (2022)	Association of metabolic dysfunction-associated fatty liver disease with diabetes, chronic kidney disease, and cardiovascular disease **Study Design:** cohort study	The study aimed to evaluate the association of metabolic dysfunction-associated fatty liver disease with metabolic and cardiovascular outcomes	• his community-based cohort study included 6,873 participants with a mean follow-up period of 4.6 years. • he prevalence of MAFLD was 46.7%, which was higher than that of NAFLD (40.3%). • uring the follow-up period, the incidence of MAFLD reached 27.0%. • AFLD was significantly associated with an increased risk of several conditions compared to individuals without fatty liver: ○ iabetes: Risk Ratio (RR) 2.08 (95% CI 1.72–2.52) ○ KD: RR 1.64 (95% CI 1.39–1.94) ○ ardiovascular disease: Hazard Ratio (HR) 1.44 (95% CI 1.15–1.81) • he MAFLD criteria also identified additional subgroups (e.g., individuals with excessive alcohol consumption or HBV infection) who had a higher risk of developing diabetes compared to individuals without fatty liver. However, these subgroups did not show a significant association with the incidence of CKD or cardiovascular disease during the study period.	Both MAFLD and NAFLD were significantly associated with an increased risk of developing CKD in the future. Patients with MAFLD had a 1.64-fold higher risk (RR 1.64; 95% CI 1.39–1.94) of developing CKD compared to individuals without fatty liver. A similar risk was also observed in patients with NAFLD (RR 1.70).
8	Jang et al. (2018)	Nonalcoholic fatty liver disease accelerates kidney function decline in patients with chronic kidney disease **Study Design:** longitudinal cohort study	The study aimed to assess the effect of non-alcoholic fatty liver disease on kidney function decline	• his longitudinal cohort study included 1,525 patients with CKD, with a mean follow-up period of 6.5 years. • he baseline prevalence of NAFLD was 40.9%. • he annual decline in estimated glomerular filtration rate (eGFR) was significantly greater in patients with NAFLD (-0.79%) compared to those without NAFLD (0.30%). • n multivariable-adjusted models, the mean difference in the annual	NAFLD is an independent risk factor associated with the progression of CKD. These findings suggest that routine screening and management of NAFLD in patients with CKD are important to identify individuals at high risk for rapid kidney function decline.

No	Author (Year)	Title and Study Design	Aim	Result	Conclusion
				percentage decline in eGFR between patients with and without NAFLD was -1.06%. • faster decline in kidney function was associated with: ○ Higher NAFLD fibrosis score (NFS), particularly in the intermediate to high categories (difference -2.12%) ○ Lower baseline eGFR (<45 ml/min/1.73 m²) ○ Presence of proteinuria, smoking habits, and hypertension	
9	Huh et al. (2017)	The fatty liver index as a predictor of incident chronic kidney disease **Study Design:** prospective cohort study	The study aimed to evaluate fatty liver index as a predictor of chronic kidney disease	• his study included 4,761 adults in South Korea (aged 40–69 years) who did not have CKD at baseline. • uring a mean follow-up period of 10 years, 724 subjects (15.21%) developed CKD. • he risk of incident CKD increased significantly with higher FLI scores; individuals with FLI ≥ 60 (indicating NAFLD) had a 1.459-fold higher risk compared to those with FLI < 30 (adjusted hazard ratio 1.459; 95% CI 1.189–1.791; p = 0.0012). • dding FLI to traditional CKD risk factor models significantly improved the prediction of CKD incidence. • his improvement was measured by: ○ Net Reclassification Improvement (NRI) of 17% (p < 0.001) ○ Integrated Discrimination Improvement (IDI) of 0.002 (p = 0.046)	The fatty liver index is an independent risk factor for the development of CKD. Its use as a surrogate marker for NAFLD represents a simple and useful clinical tool that enhances risk stratification beyond traditional factors, thereby aiding in the prediction and prevention of kidney function decline.
10	Wei et al. (2023)	The role of metabolic dysfunction-associated fatty liver disease in developing chronic kidney disease **Study Design:** longitudinal cohort study	The study aimed to investigate the role of metabolic dysfunction-associated fatty liver disease in chronic kidney disease development	○ his study included 41,246 participants in China who underwent three or more health examinations. ○ total of 11,860 participants (28.8%) were diagnosed with MAFLD. ○ uring a follow-up period of 14 years (median 10 years), 5,347 participants (13%) developed incident CKD. ○ AFLD was identified as a significant independent risk factor for CKD, with a hazard ratio (HR) of 1.18 (95% CI	MAFLD plays an important role in the long-term development of CKD. These findings highlight the importance of routine kidney function assessment in patients with MAFLD, as well as the implementation of early intervention strategies to prevent CKD, particularly in younger male patients with metabolic

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				1.11–1.26) after adjustment for multiple metabolic factors. ○ ased on sex, the risk of CKD in individuals with MAFLD was: • Male: HR 1.16 • Female: HR 1.32 ○ ubgroup analysis showed that the risk of CKD associated with MAFLD was stronger in males aged <60 years and in individuals with dyslipidemia.	comorbidities.
11	Park et al. (2025)	Non-Alcoholic Fatty Liver Disease and Its Association with Kidney and Cardiovascular Outcomes in Moderate to Advanced Chronic Kidney Disease **Study Design:** large cohort study	The study aimed to evaluate the association between fatty liver index and cardiovascular and kidney outcomes	• his study analyzed 816,857 individuals with an estimated glomerular filtration rate (eGFR) of 15–59 mL/min/1.73 m² over a median follow-up period of 7.7 years. • igher Fatty Liver Index (FLI) scores, as a marker of NAFLD, were associated with a stepwise increase in the risk of cardiovascular and renal events. • ompared to the low FLI group (<30), individuals with high FLI (≥60) had: ○ An adjusted hazard ratio of 1.36 for cardiovascular events ○ An adjusted hazard ratio of 1.24 for renal events • igh FLI was also associated with a 1.53-fold increased risk of all-cause mortality compared to the low FLI group. • Subgroup analysis showed that the association with cardiovascular events remained consistent, while the association with renal outcomes was significant in patients with eGFR 45–59, but not in those with eGFR 15–44.	A high FLI is a significant independent predictor of increased cardiovascular and renal event risk in patients with moderate to advanced CKD. NAFLD should be considered a comprehensive metabolic indicator reflecting the complex interplay between liver health, the cardiorenal system, and metabolic dysfunction in the CKD population.
12	Roderburg et al. (2023)	Non-alcoholic fatty liver disease is associated with an increased incidence of chronic kidney disease **Study Design:** cohort study	The study aimed to evaluate the incidence of chronic kidney disease in fatty liver disease patients	• his study included 92,225 patients with NAFLD and 92,225 matched controls without NAFLD. • ver a 10-year observation period, 19.1% of patients with NAFLD developed CKD compared to 11.1% in the non-NAFLD group ($p < 0.001$). • ox regression analysis showed a significant association, with a hazard ratio (HR) of 1.80 (95% CI 1.73–1.86). • his association was strongest in the	NAFLD significantly increases the risk of developing CKD in the adult population. It should be considered a systemic disease rather than an isolated liver condition. Therefore, the management of patients with NAFLD should involve a multidisciplinary approach, with a focus on the prevention and early

No	Author (Year)	Title and Study Design	Aim	Result	Conclusion
				younger age group (18–50 years), with an HR of 2.13. • he risk was also slightly higher in females (HR 1.85) compared to males (HR 1.74).	detection of CKD.
13	Nah et al. (2022)	Chronic kidney disease in nonalcoholic fatty liver disease at primary healthcare centers in Korea **Study Design:** cross-sectional study	The study aimed to determine prevalence and risk factors of chronic kidney disease in fatty liver disease	• his study analyzed 8,909 subjects, of whom 4,241 (47.6%) were diagnosed with NAFLD. • he prevalence of CKD in the NAFLD group was 12.4%, which was higher than in the non-NAFLD group (8.5%). • fter adjusting for age and metabolic status, NAFLD was independently associated with early-stage CKD (OR 1.27). • owever, NAFLD was not an independent risk factor for moderate to severe CKD; at these stages, advancing age and poor metabolic health appeared to be the dominant determinants. • A significant association was also observed between the degree of liver fibrosis (measured by magnetic resonance elastography) and the occurrence of CKD.	Overall, both NAFLD and liver fibrosis act as independent risk factors for CKD, particularly in the early stages of kidney impairment. Progression to more advanced CKD likely involves additional factors, including aging and metabolic dysfunction. Therefore, active CKD screening is recommended in individuals with NAFLD, especially among older adults and those with unfavorable metabolic profiles.
14	Hashimo to et al. (2022)	Metabolic associated fatty liver disease is a risk factor for chronic kidney disease **Study Design:** This study included both cross-sectional and cohort analyses	The study aimed to compare metabolic dysfunction-associated fatty liver disease with fatty liver disease without metabolic dysfunction	• n a cross-sectional study involving 27,371 participants, MAFLD was significantly associated with an increased risk of CKD (adjusted OR 1.83), whereas fatty liver without metabolic dysfunction showed no significant association (OR 1.02). • n a retrospective cohort study of 16,938 participants followed for a median of 4.6 years, MAFLD remained significantly associated with incident CKD (adjusted HR 1.30). • ndividuals with fatty liver but without metabolic dysfunction did not demonstrate an increased risk of CKD (HR 1.11). • AFLD was also associated with a higher risk of proteinuria (HR 1.95). • mong individuals with a baseline eGFR ≥75 mL/min/1.73 m², the risk of CKD	Overall, MAFLD appears to be an independent risk factor for the development of CKD, whereas fatty liver in the absence of metabolic dysfunction is not. These findings suggest that the MAFLD definition more accurately identifies individuals at higher risk for extrahepatic complications, including kidney disease.

No	Author (Year)	Title and Study Design	Aim	Result	Conclusion
				was notably higher in the MAFLD group (HR 1.57).	
15	Zhang et al. (2020)	Association between non-alcoholic fatty liver disease and risk of prevalent chronic kidney disease: differences between East and West	The study aimed to explain differences in fatty liver disease and chronic kidney disease association between populations	• his study included 60,965 participants, comprising 11,844 from the United States (NHANES III) and 51,229 from China. • he prevalence of NAFLD was higher in the United States (36.08%) compared to China (27.12%). • he proportions of CKD and advanced CKD were also higher in the United States (21.5% and 13.5%) than in China (9.1% and 4.0%). • nitial analyses showed an association between NAFLD and CKD in the Chinese cohort, but not in the U.S. cohort after adjustment for metabolic factors. • ubgroup analysis revealed that, after excluding advanced CKD cases, NAFLD became an independent risk factor for early-stage CKD (G1–G2) in both populations. • AFLD was not significantly associated with advanced CKD (G3–G5) after adjusting for metabolic factors.	Overall, NAFLD appears to increase the risk of CKD primarily at the early stages across different populations. Variations in previous findings may be explained by differences in the proportion of advanced CKD cases included in the analyses. While NAFLD contributes to early kidney injury, it may not be sufficiently strong as an independent driver of progression to advanced CKD without the influence of additional metabolic risk factors.

A Paradigm Shift in the Understanding of NAFLD and MAFLD

In recent years, fatty liver disease has emerged as a considerable global health concern. Internationally recognized experts have proposed a reclassification of this condition, designating it as Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD), a departure from its previous designation as Non-Alcoholic Fatty Liver Disease (NAFLD) (Kwon et al., 2023). This nomenclatural shift signifies more than a mere change in terminology; it reflects a substantial evolution in the clinical comprehension and diagnostic approach to the disease.

The primary difference between NAFLD and MAFLD is the criteria used to diagnose them. NAFLD is characterized as a diagnosis of exclusion, indicating that hepatic steatosis must be evident in the absence of other secondary etiologies (Kwon et al., 2023). To diagnose NAFLD, patients must not exhibit significant alcohol consumption (typically defined as >20 g/day for men and >10 g/day for women) and must show no indications of other liver diseases, such as viral hepatitis.

Conversely, MAFLD employs a more comprehensive and clinically focused methodology by emphasizing the patient's metabolic condition (Liang et al., 2022). MAFLD is diagnosed when liver fat accumulation is present alongside at least one of the following: overweight or obesity, type 2 diabetes, or signs of metabolic dysregulation (Kwon et al., 2023). This definition highlights metabolic dysfunction as a key factor in fatty liver disease, which

helps identify people at higher risk for related health problems.

The criteria for Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD) are notably broader, encompassing individuals with alcohol consumption or pre-existing liver ailments, provided there is demonstrable metabolic dysfunction (Kwon et al., 2023). This approach highlights the frequent co-occurrence of metabolic disturbances with other risk factors, which can synergistically exacerbate hepatic injury (Kwon et al., 2023).

For instance, people with hepatic steatosis who also have hepatitis B or drink too much alcohol can now be classified into MAFLD subgroups. In the past, these individuals would have been excluded from the NAFLD definition (Liang et al., 2022).

A growing body of research suggests that the MAFLD criteria are more effective at predicting extrahepatic complications, including chronic kidney disease (CKD) (Liang et al., 2022). Longitudinal investigations have demonstrated that individuals meeting the MAFLD criteria exhibit a significantly elevated likelihood of developing CKD compared to those with NAFLD but without metabolic dysfunction (Kwon et al., 2023). Indeed, the "NAFLD-only" subgroup—characterized by hepatic steatosis without metabolic abnormalities—typically does not present an increased risk of CKD (Kwon et al., 2023). These observations underscore that metabolic dysfunction, rather than the mere presence of hepatic fat, constitutes the primary driver of organ damage in fatty liver disease (Kwon et al., 2023).

In 2023, the term Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) was introduced to help reduce stigma and make disease classification more inclusive (Ono et al., 2025). For a diagnosis of MASLD, there must be at least one cardiometabolic risk factor. There are also subcategories, such as MetALD, which combines MASLD with moderate alcohol use (Ono et al., 2025).

NAFLD and MASLD as Risk Factors for CKD

1. Hormonal and Metabolic System Activity

The development of CKD is influenced by fatty liver disease through various systemic metabolic processes:

a. Activation of the Renin–Angiotensin System (RAS): Hepatic steatosis can initiate the activation of this system, which is crucial for regulating blood pressure and fluid equilibrium. Overactivation of the RAS can subsequently result in damage to the kidney's filtering units (Kwon et al., 2023).
b. Insulin resistance is a key factor linking fatty liver disease and chronic kidney disease (CKD), as shown by Hashimoto et al. (2022). This condition promotes sodium retention, activates the sympathetic nervous system, and disrupts natriuretic peptide pathways. These effects then contribute to the worsening of kidney function (Hashimoto et al., 2022).
c. Elevated blood glucose levels and increased lipid synthesis create a harmful metabolic environment. This environment can directly damage kidney cells and worsen kidney problems (Kwon et al., 2023).

2. Systemic Inflammation and Oxidative Stress

The liver, in addition to its function in lipid storage, actively participates in the immune response.

a. Release of Pro-inflammatory Mediators: Hepatic steatosis triggers the release of inflammatory cytokines, pro-oxidant substances, and profibrogenic mediators into the

bloodstream (Mantovani et al., 2024). Consequently, these elements can potentially induce vascular damage and structural alterations within the kidneys (Mantovani et al., 2024).

   b. Lipotoxicity, a condition where the liver accumulates too much fat, leads to the overproduction of very low-density lipoprotein (VLDL), which can cause atherogenic dyslipidemia (Wei et al., 2023). In addition, the buildup of oxidized lipids can damage the glomeruli and promote the growth of mesangial cells in the kidneys (Wei et al., 2023).

3. The Role of Adipokines and Genetic Factors
   a. Adipokine Dysregulation: Individuals afflicted with fatty liver disease frequently display an adipokine imbalance, characterized by diminished adiponectin concentrations and elevated fatty acid-binding protein 4 (FABP4) levels (Wei et al., 2023). This dysregulation exacerbates glomerular and tubulointerstitial damage, thereby precipitating a reduction in the estimated glomerular filtration rate (eGFR) (Wei et al., 2023).
   b. Genetic variations, specifically polymorphisms in genes like PNPLA3 and TM6SF2, are known to play a role in the shared development of liver and kidney diseases (Wei et al., 2023).
4. The gut, liver, and kidneys interact with each other in a two-way manner.
   a. Alterations in the gut microbiota and the subsequent compromise of the intestinal barrier observed in individuals afflicted with fatty liver disease may exert an influence on renal function. This phenomenon is mediated by the inter-organ communication facilitated by the release of biochemical signals (Wei et al., 2023).
   b. Synergistic Metabolic Dysfunction: Underlying metabolic abnormalities associated with MAFLD/MASLD—such as obesity and hypertension—act synergistically to accelerate kidney damage (Wei et al., 2023).

CONCLUSION

The nomenclature of fatty liver disease has evolved over time. It was originally termed non-alcoholic fatty liver disease (NAFLD), later redefined as metabolic dysfunction-associated fatty liver disease (MAFLD), and most recently updated to metabolic dysfunction-associated steatotic liver disease (MASLD). This reclassification represents a significant shift from the earlier exclusion-based definition of NAFLD to a more inclusive framework centered on metabolic dysfunction, such as obesity and diabetes. Consequently, this revised approach has demonstrated improved effectiveness in identifying individuals at risk of systemic complications.

Emerging evidence indicates a strong association between MAFLD and MASLD and an increased risk of chronic kidney disease (CKD). Individuals with MAFLD show a substantially higher likelihood of developing CKD compared with those without fatty liver disease or those classified under NAFLD without metabolic dysfunction. These findings underscore the central role of metabolic dysregulation in disease progression beyond hepatic involvement.

Fatty liver disease may contribute to renal impairment through multiple mechanisms, including activation of the renin–angiotensin system, insulin resistance, chronic systemic inflammation, oxidative stress, and adipokine imbalance. In addition, complex interactions

among the gut, liver, and kidneys—known as the gut–liver–kidney axis—further link hepatic and renal dysfunction.

The severity of liver disease, particularly hepatic fibrosis, is a key determinant of chronic kidney disease (CKD) risk, exerting a stronger influence than hepatic steatosis alone. The coexistence of liver fibrosis and CKD is associated with a significantly increased risk of mortality.

Given the systemic nature of fatty liver disease, clinicians should incorporate routine assessment of renal function in patients with MAFLD or MASLD. This includes evaluation of the estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (uACR). Early identification and management of metabolic risk factors are essential to slow the progression of renal dysfunction and improve long-term clinical outcomes.

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