1/ Hey #NephTwitter! 👋
We're back with a fresh #Xtorial
@ISNkidneycare

This **review article** in @*KIReports* looks at the MASLD - CKD axis, summarising epidemiology, mechanisms, screening, and therapy.

Key idea: this is not just coexistence, but shared biology.

https://pubmed.ncbi.nlm.nih.gov/41726005/

KI REPORTS
KIReports.org
REVIEW

The Metabolic Dysfunction–Associated Steatotic Liver Disease–CKD Axis: Intersecting Pathways and Opportunities for Early Intervention

Check for updates

Sriram Sriperumbuduri[1], Prathab Balaji Saravanan[2], Gaurav Gupta[1] and Arun J. Sanyal[3]

[1]Division of Nephrology, Virginia Commonwealth University Health System, Richmond, Virginia, USA; [2]School of Medicine, Virginia Commonwealth University, Richmond, Virginia, USA; and [3]Division of Gastroenterology and Hepatology, Virginia Commonwealth University Health System, Richmond, Virginia, USA

Chronic kidney disease (CKD) and metabolic dysfunction–associated steatotic liver disease (MASLD) are highly prevalent, overlapping conditions with significant health burdens. CKD affects > 650 million people worldwide and is a leading cause of morbidity and mortality, whereas MASLD affects nearly one-third of adults worldwide and increases risks of cardiovascular disease, kidney disease, and cancer. This review synthesizes epidemiologic and mechanistic evidence linking MASLD and CKD, with attention to clinical implications, screening, and management strategies. Studies consistently demonstrate a higher prevalence of CKD among patients with MASLD, with greater risk in those with advanced disease such as metabolic dysfunction–associated steatohepatitis and fibrosis. Shared mechanisms, including insulin resistance; systemic inflammation; renin-angiotensin-aldosterone system activation; and metabolic risk factors such as obesity, hypertension, and diabetes, contribute to kidney injury in this population. The coexistence of MASLD and CKD underscores the need for multidisciplinary approaches to care. Early identification of CKD in patients with MASLD, combined with aggressive management of metabolic risk factors, may improve outcomes. Further research is needed to refine screening strategies, clarify pathophysiologic pathways, and optimize treatment for this growing patient population.

Kidney Int Rep (2026) **11**, 103757; https://doi.org/10.1016/j.ekir.2025.103757
KEYWORDS: CKD; GLP-1 agonists; liver disease; MASLD; RAASi; SGLT2i

2/ Our #Xtorial is by Akshaya J @DrAkshayaJ, adult nephrologist from @CMCNephrology - No COI

#MedTwitter #nephtwitter @ISNkidneycare #XTwitter

Check out #KIReportsCommunity educational #blogposts at www.kireportscommunity.org. FOLLOW US at @KIReports

QUIZ:

🧵Quick clinical scenario before we start:

A 46-year-old man with T2DM, HTN, BMI 24 kg/m², mildly elevated ALT, and ultrasound showing fatty liver has:

• eGFR 82 ml/min/1.73m²
• Urine ACR 120 mg/g

Would you:
A) Reassure, kidney function is “normal”
B) Screen and follow for CKD progression
C) Refer only if creatinine rises
D) Ignore because he is not obese

This review explores why the answer may be more important than we think. 👀

#Xtorial #NephTwitter #KIReports

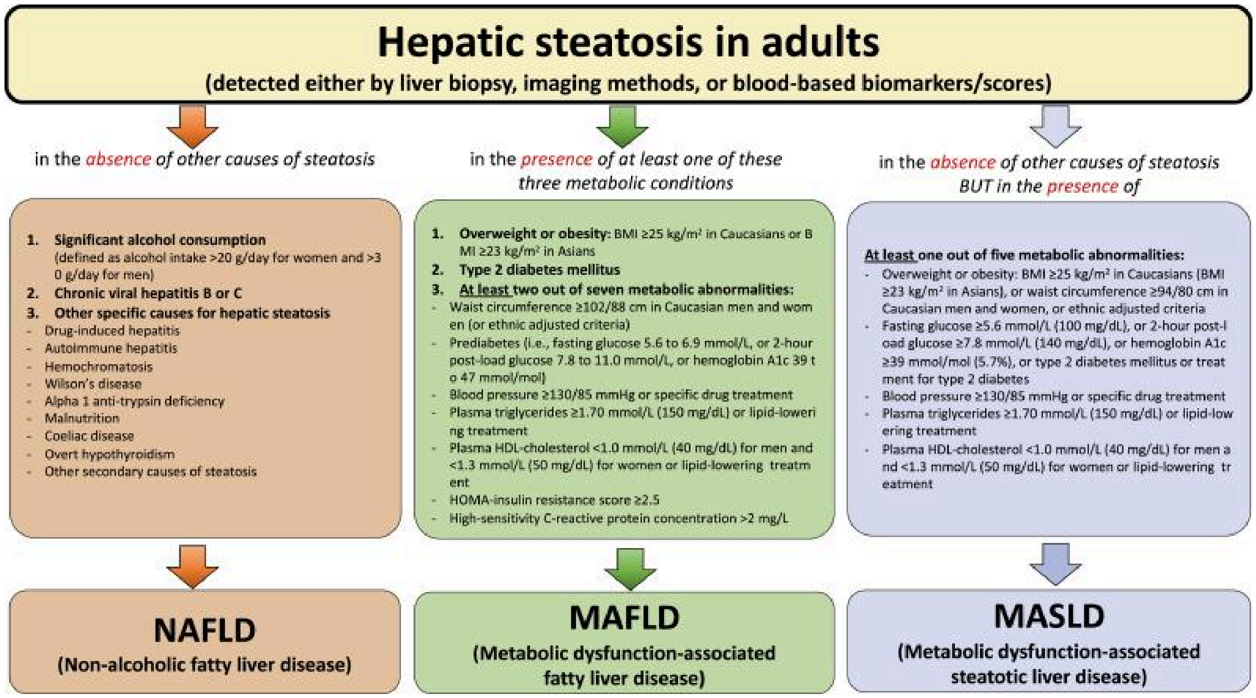
3/

What’s MASLD?

Steatotic liver disease (SLD) + one or more cardiometabolic risk factor(s) + absence of harmful alcohol intake.

Affects ~1/3 adults; There are ~700 million CKD patients globally.

Across studies, MASLD is associated with ~2× higher CKD risk, increasing further with disease severity.



4/

Disease stage matters:

• Simple steatosis → modest risk
• MASH → higher risk
• Advanced fibrosis → strongest predictor

Fibrosis consistently tracks with CKD incidence and progression.

5/

CKD prevalence in MASLD ranges widely (~20–55%).

Prospective data also show higher risk of incident CKD and even ESKD in MASLD populations.

Table 1. Meta-analysis showing the association between MASLD and CKD

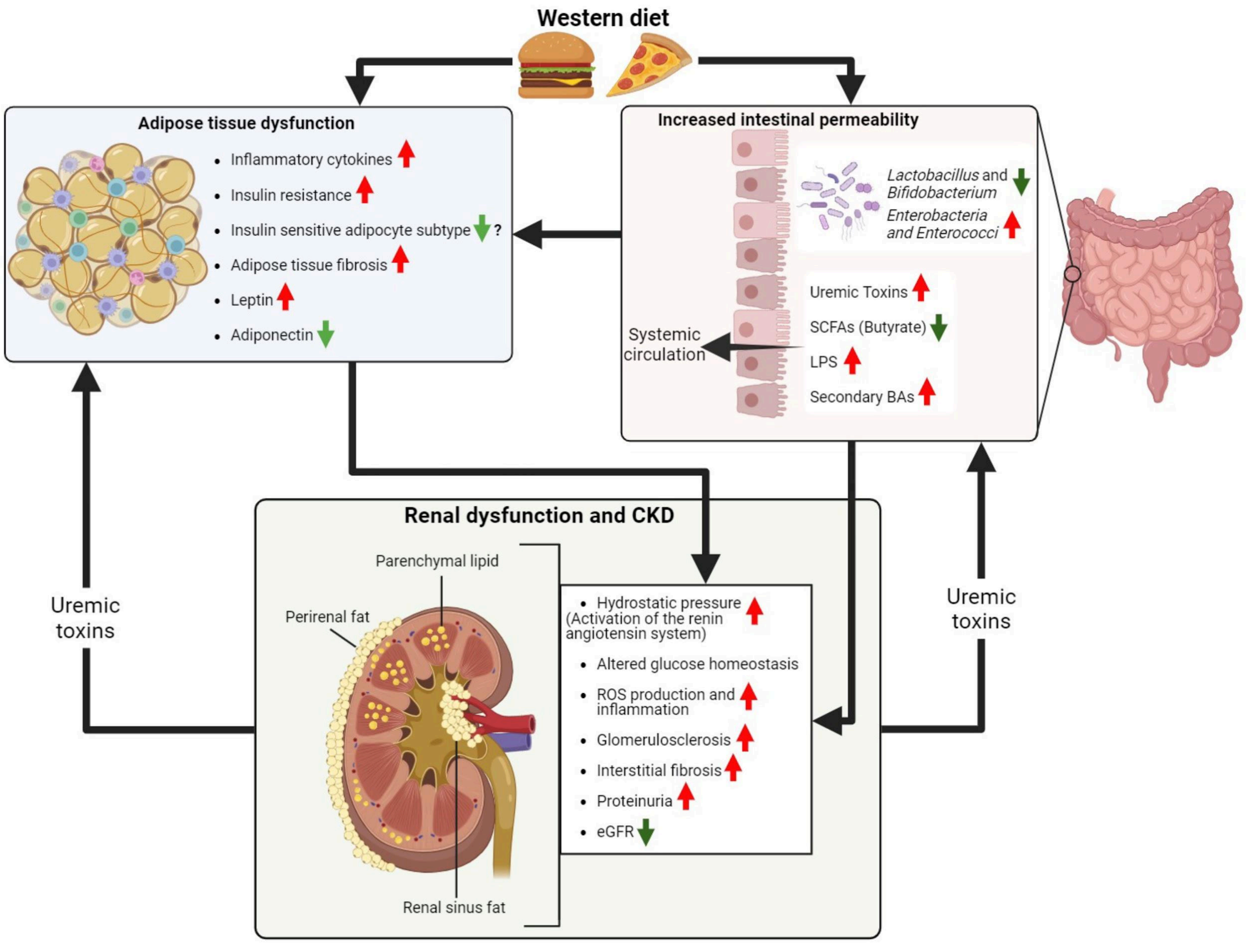
	Year	Author	Number and type of studies	Number of subjects	Outcome (Adjusted analysis)	Comments
1.	2014	Giovanni Musso *et al.*[6]	33 studies: 16 population based; 17 hospital-based (20 cross-sectional and 13 longitudinal)	63,902	(a) MASLD: OR: 2.12, 95% CI (1.69–2.66). Prevalence of CKD; HR: 2.12, 95% CI (1.42–3.17) for incident CKD (b) MASH: OR: 2.53, 95 % CI (1.58–4.05) Prevalence of CKD; HR: 3.29, 95% CI (2.30–4.71) for incident CKD (c) Advanced fibrosis: OR: 5.20, 95% CI (3.14–8.61) for prevalent CKD and HR: 3.29 (2.30–4.71) for incident CKD	MASH has a higher prevalence and incidence of CKD than simple steatosis. 13 studies (2205 participants) Defined as MASLD by liver histology
2.	2017	Mantovani *et al.*[7]	9 observational studies	96,595	(a) MASLD-Random effects HR 1.37, 95% CI (1.20–1.53) for incident CKD. (b) Severe MASLD (ultrasound and noninvasive fibrosis markers)- HR: 1.50, 95% CI (1.25–1.74) for incident CKD. Median follow-up: 5.2 yrs	40% increase in the risk of incident CKD. Subjects predominantly of Asian decent No biopsy proven studies were included
3.	2022	Mantovani *et al.*[8]	13 observational studies	1,222,032	MASLD: random effects. HR: 1.43, 95% CI: (1.33–1.54) for incident CKD. Median follow-up 9.7 yrs	1.45-fold risk of incident CKD stage ≥ 3

CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; MASH, metabolic dysfunction associated steatohepatitis; MASLD, metabolic dysfunction–associated steatotic liver disease; OR, odds ratio.

6/

Overlap with traditional risks (DM, HTN, obesity) is significant.

But MASLD-specific factors, especially fibrosis, remain independently associated with albuminuria and CKD risk.



7/

Mechanisms are shared and interconnected:

- Insulin resistance
- Systemic inflammation
- RAAS activation
- Oxidative stress
- Gut dysbiosis

Suggests a liver–kidney–CV axis rather than isolated disease.

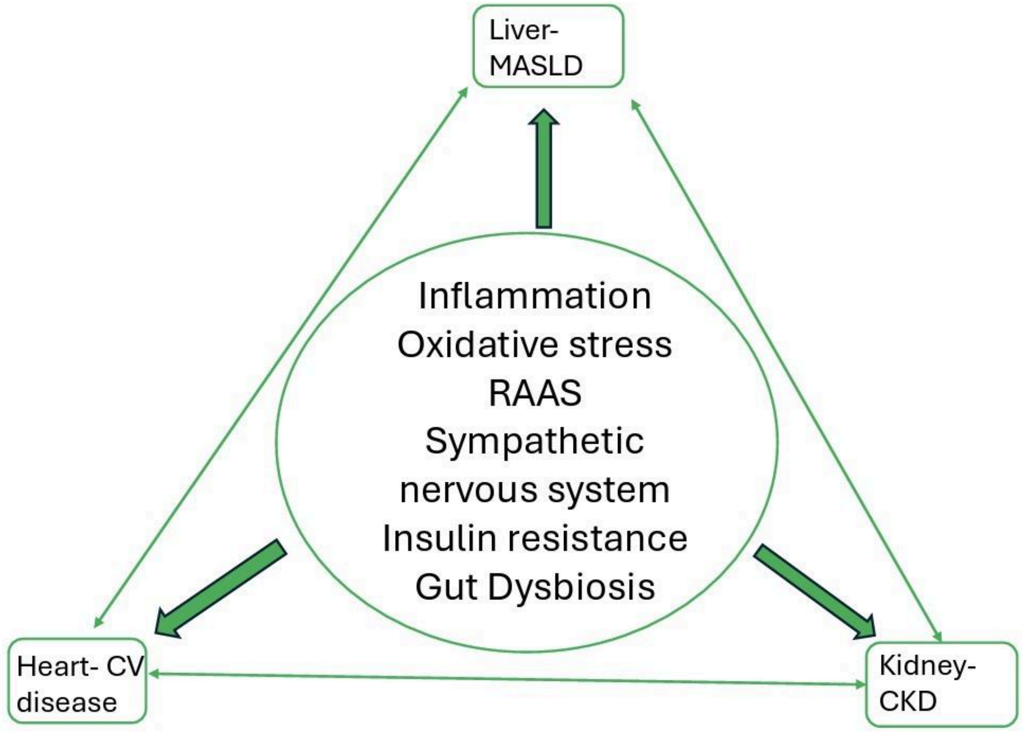
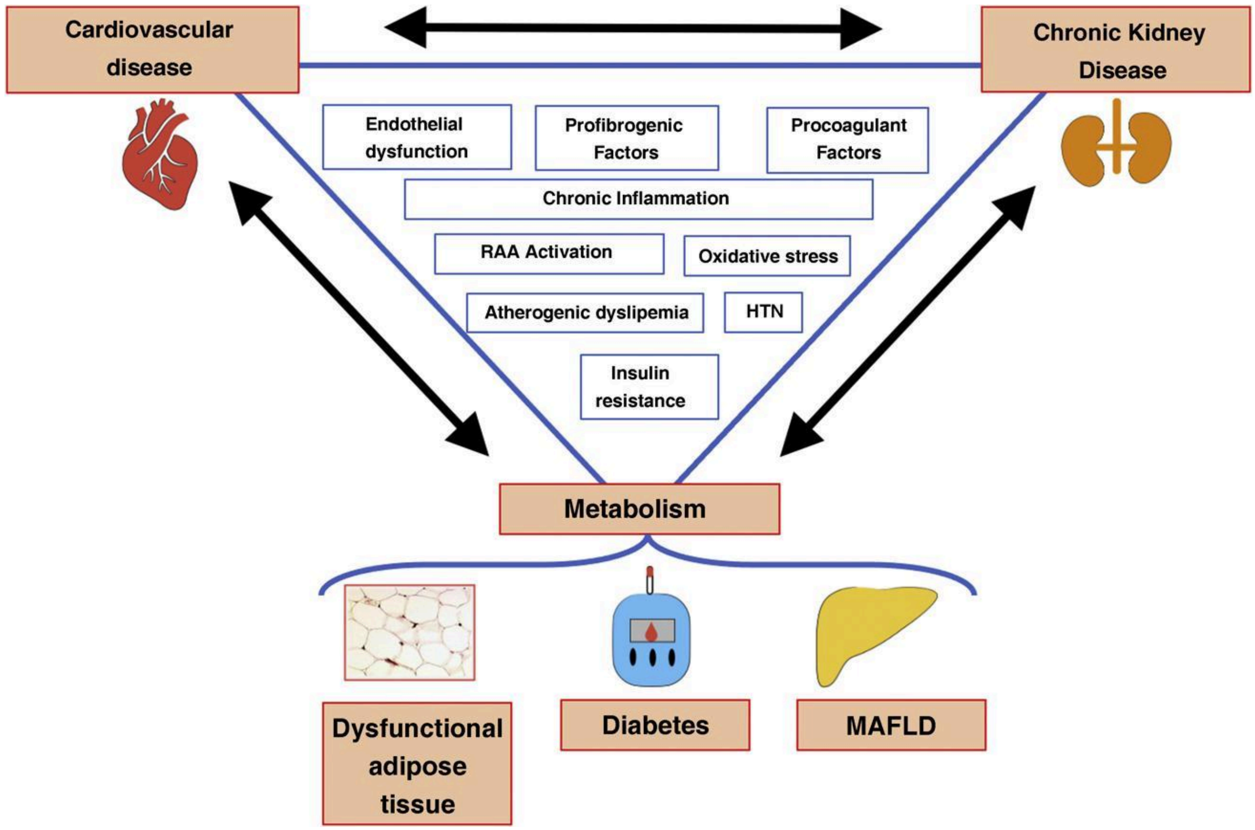


Figure 1. Figure illustrating the major factors contributing to the pathophysiology of CKD MASLD and CV disease. CKD- chronic kidney disease; CV disease- cardiovascular disease; MASLD- metabolic dysfunction associated steatotic liver disease; RAAS- renin angiotensin aldosterone system.



8/
Interesting signal: "lean MASLD" also carries CKD risk.

Lean MASLD is defined by meeting criteria for MASLD despite having a normal BMI -

- **BMI <23 kg/m² in Asian populations**
- **BMI <25 kg/m² in non-Asian populations)**

Visceral adiposity (Bioimpedance) > Central adiposity (Waist Circumference) > BMI in mediating kidney outcomes.

9/
Noninvasive fibrosis markers may also help identify kidney risk in MASLD.

A meta-analysis of 21 studies (~3 lakh patients) showed FIB-4, NFS, and APRI correlate with incident CKD. Even simple indices like the Fatty Liver Index predicted long-term CKD risk.

Interesting newer data: AI-derived qFibrosis changes correlated with eGFR decline over time. #NephTwitter #Xtorial #KIReports

Table 2. Predictive utility of non-invasive liver fibrosis markers for CKD risk in MASLD

Fibrosis marker	Risk of incident CKD	Comments
FIB-4	High FIB-4 score increases risk. OR: 2.51, 95% CI: 1.87–3.37 Higher FIB-4 (> 2.67) vs. lower FIB-4 (< 1.30)- OR: 3.53, 95% CI: 2.12–5.90	Regression analysis influenced by hypertension, MASLD, and BMI
NFS	High NFS increases risk. OR: 2.49, 95% CI: 1.89–3.30 Higher NFS score (> 0.676) vs. lower NFS score (< −1.455). OR: 3.43, 95% CI: 2.06–5.72	–
APRI	High APRI score (≥ 0.5) vs. low APRI (< 0.5). OR: 1.40, 95% CI: 1.14–1.72	–

10/
Clinical implication: screen CKD in MASLD

Suggested approach:
• Serum creatinine/eGFR
• Urine ACR
• ± cystatin C in extremes of muscle mass

Annual monitoring is reasonable, with closer follow-up in advanced fibrosis.

FIB-4/NFS may help stratify risk

KFRE can guide nephrology referral and earlier risk-modifying therapy.

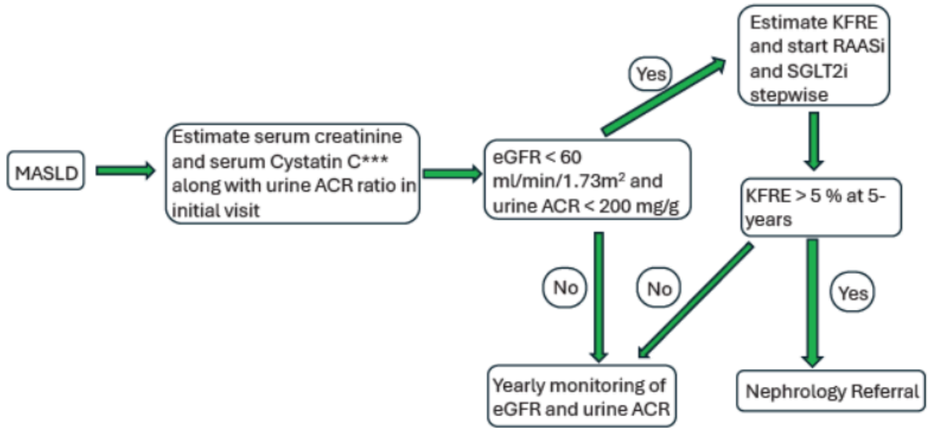


Figure 2. Figure showing proposed CKD screening for patients with MASLD. eGFR, estimated glomerular filtration rate;

11/

In CKD patients, MASLD should be suspected with:
• Steatosis on imaging
• Unexplained AST/ALT elevation
• ≥2 metabolic risk factors
• Family history of MASLD cirrhosis

Consider liver US during routine CKD evaluation

Hepatology referral if steatosis/fibrosis is identified.

Early identification → start GLP-1RA or resmetirom.

However the cost of Resmetirom ($4,116 for a month) is prohibitive

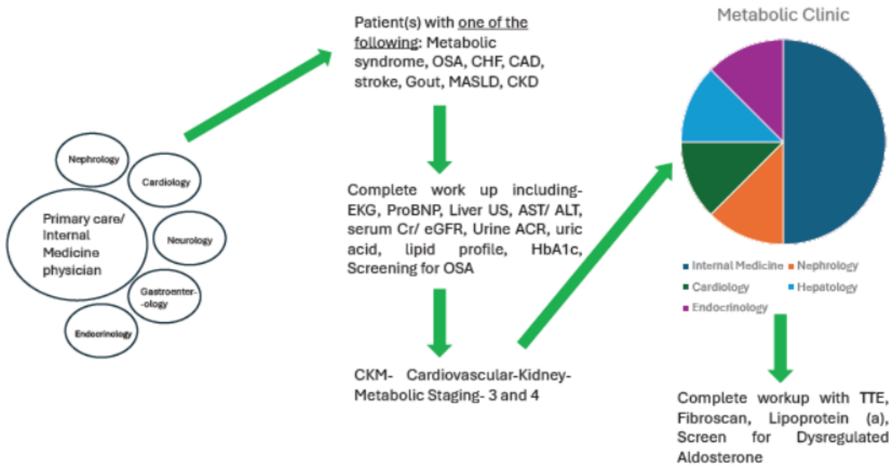


Figure 3. Figure showing the referral criteria and flow of metabolic clinic. ALT, alanine aminotransferase; AST, aspartate aminotransferase;

12/
Lifestyle intervention remains the foundation of MASLD management.

Most guidelines recommend structured diet + exercise aimed at weight reduction:
• 7–10% weight loss in obesity
• 3–5% even in non-obese MASLD

Associated with lower hepatic fat and improved fibrosis markers. #Xtorial #NephTwitter

13/
Mediterranean-style and plant-based dietary patterns appear beneficial in both MASLD and CKD.

Reported benefits include:
• Reduced steatosis & insulin resistance
• Lower BP and albuminuria
• Slower eGFR decline
• Reduced metabolic acidosis

Exercise (aerobic + resistance) also improves insulin sensitivity and cardiometabolic parameters. #KIReports

14/
SGLT2 inhibitors continue to show overlap across the liver–kidney axis.

In MASLD studies:
• Reduced hepatic fat & fibrosis markers
• Lower CV and CKD events

In CKD trials (CREDENCE, DAPA-CKD, EMPA-KIDNEY):
• Slower CKD progression

• Reduced albuminuria
• Lower HF hospitalization and mortality

Benefits extend even to non-diabetic CKD. #NephTwitter

Table 3. Table showing therapeutic role of SGLT2 inhibitors, GLP-1 receptor agonists, RAAS inhibitors, and MRAs in CKD and MASLD

Medication class	Indications in CKD	Benefits in CKD and MASLD	Key clinical points (side effects / monitoring)
SGLT2 inhibitors	Diabetic kidney disease; proteinuric CKD with eGFR ≥ 20 ml/min per 1.73 m^2	Slows CKD progression, reduces albuminuria; decreases hepatic steatosis and inflammation	Risk of genital mycotic infections, volume depletion, and rare euglycemic ketoacidosis; monitor kidney function, especially with diuretic use
GLP-1 receptor agonists	Diabetes with ASCVD risk; obesity in CKD	Promotes weight loss, improves glycemic control; reduces liver fat and improves aminotransferases	GI symptoms (nausea, vomiting), contraindicated in gastroparesis; some agents require subcutaneous administration, which may affect adherence
RAAS inhibitors (ACEi/ARB)	Hypertension, proteinuric CKD, heart failure	Reduces proteinuria, slows CKD progression; improves insulin sensitivity, potentially mitigating MASLD progression	Monitor for hyperkalemia, AKI, and cough (with ACEi); routine serum creatinine and potassium monitoring recommended, especially after initiation or dose escalation
MRAs (spironolactone, eplerenone, finerenone)	Resistant hypertension; Proteinuric CKD; Heart failure with reduced ejection fraction	Reduce proteinuria, antiinflammatory and antifibrotic effects; finerenone shown to improve kidney and CV outcomes in DKD; may reduce hepatic fibrosis in MASLD	Risk of hyperkalemia, especially with impaired kidney function or concurrent RAAS inhibitors; monitor potassium and kidney function closely; endocrine side effects with spironolactone (e.g., gynecomastia)

15/
GLP-1 receptor agonists also show emerging benefits in MASLD + CKD.

Semaglutide/liraglutide studies demonstrated:
• Higher MASH resolution
• Reduced liver fat and inflammation
• CV protection
• Slower eGFR decline and lower kidney risk in FLOW/SELECT

Table 4. Table comparing the salient features of Select and Flow trials

	SELECT trial[58]	FLOW trial[59]
Population	Aged ≥ 45 yrs, pre-existing CV disease, BMI ≥ 27 kg/m^2, nondiabetics	Type 2 diabetes mellitus, CKD: eGFR of 50–75 ml/min per 1.73 m^2 and urine ACR of 300–5000 mg/g or eGFR of 25 to < 50 ml/min per 1.73 m^2 and urine ACR > 100 and < 5000 mg/g
Intervention	Once-weekly subcutaneous semaglutide 2.4 mg or placebo	Once-weekly subcutaneous semaglutide 1 mg or placebo
Outcome Definitions	Primary CV end point was composite of death from CV causes, nonfatal myocardial infarction, or nonfatal stroke	Major kidney disease event: composite of the onset of kidney failure (dialysis, transplantation, or an eGFR < 15 ml/min per 1.73 m^2), ≥ 50% reduction in the eGFR from baseline, (or) death from kidney-related or CV causes
Effect Sizes	Decreased risk of outcome among users of semaglutide; HR: 0.80; 95% CI: 0.72–0.90	Decreased risk of outcome among users of semaglutide; HR: 0.79; 95% CI: 0.66–0.88
Comments	Among users of Semaglutide, the incidence of the prespecified main composite kidney end point (death from kidney disease, initiation of CKRT, onset of persistent eGFR < 15 ml/min per 1.73 m^2, persistent ≥ 50% reduction in eGFR or onset of persistent macroalbuminuria) was lower (HR: 0.78; 95% CI: 0.63–0.96)[58]	Among users of Semaglutide, there was a lower rate of eGFR decline (HR: 0.82; 95% CI: 0.68–0.98) and all-cause mortality (HR: 0.80; 95% CI: 0.67–0.95)

ACR, albumin-to-creatinine ratio; BMI, body mass index; CI, confidence interval; CV, cardiovascular; BMI, body mass index; CKRT, continuous kidney replacement therapy; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HR, hazard ratio.

Signals appear strongest before advanced cirrhosis develops. #Xtorial

16/
Other pathways under study:
• Finerenone and MRAs
• RAAS blockade
• Bariatric surgery
• Gut microbiome modulation

Emerging therapies targeting lipid metabolism (e.g., THR-β agonists like resmetirom) show promise in MASH.

17/
Takeaway from this review:

MASLD and CKD are linked through shared metabolic and inflammatory pathways.

Early identification + integrated management may be key to altering outcomes.

https://pubmed.ncbi.nlm.nih.gov/41726005/

#NephTwitter