Metabolic Kidney Disease: A New Concept in the Interaction Between Obesity, Prediabetes, Diabetes and Liver Dysfunction

Articoli originali

Jorge Rico Fontalvo[1,2,6], Rodrigo Daza Arnedo[3,6], María Raad Sarabia[4], Javier Jiménez[5], Juan Montejo-Hernández[2,6], Tomas Rodríguez-Yánez[7], María José Soler[8], Maria Teresa Sciarrone-Alibrandi[9], Rodolfo Fernando Rivera[10]

Jorge Rico Fontalvo

1. Facultad de Medicina, Departamento de Nefrología, Universidad Simón Bolívar de Barranquilla, Barranquilla, Colombia
2. Departamento médico, IPS Nephromedicall Medellín, Medellín, Colombia
3. IPS Caminos Cartagena, Cartagena, Colombia
4. Facultad de Medicina, Departamento de Medicina Interna, Universidad del Sinú, Cartagena, Colombia
5. Facultad de Medicina, Universidad Militar Nueva Granada, Bogotá, Colombia
6. Asociación Colombiana de Nefrología e HTA (ASOCOLNEF), Bogotá, Colombia
7. Facultad de Medicina, Departamento de Medicina Interna, Universidad de Cartagena, Cartagena, Colombia
8. Servicio de Nefrología, Hospital Universitario Vall de Hebron, Barcelona, España
9. Struttura Complessa Nefrologia e Dialisi, IRCCS Ospedale San Raffaele di Milano, Italia
10. Struttura Complessa Nefrologia e Dialisi, Ospedale Pio XI, Desio, ASST Brianza, Italia

Corresponding author:
Rodolfo Rivera,
E-mail: md.rfrivera@gmail.com

ABSTRACT

Metabolic abnormalities such as obesity, insulin resistance, prediabetes, type 2 diabetes and metabolic dysfunction-associated steatotic liver disease (MASLD) increasingly contribute to chronic kidney disease (CKD). Although often treated as separate entities, these conditions share common mechanisms – including glomerular hyperfiltration, adipokine imbalance, chronic low-grade inflammation, endothelial dysfunction and lipid accumulation – that initiate and sustain renal injury long before classical CKD becomes clinically evident.

The concept of Metabolic Kidney Disease (MKD) offers a unified framework that captures the continuum of renal involvement across the metabolic spectrum. Obesity- and prediabetes-related MKD frequently precede diabetic kidney disease, while MASLD – according to updated EASL-EASD-EASO guidelines – is a multisystem disorder with direct renal consequences. Mixed metabolic phenotypes further intensify metabolic stress, accelerating progression toward CKD.

Recognising MKD has important clinical implications. Expanded screening strategies may identify early renal alterations in individuals with metabolic vulnerability who are not targeted by traditional CKD criteria. Integrating metabolic evaluation into nephrology practice may facilitate earlier, more holistic interventions and ultimately improve cardio-renal outcomes.

KEYWORDS: Obesity, Type 2 diabetes, Prediabetes, Chronic Kidney Disease, Liver dysfunction, Cardiorenal metabolic syndrome, Albuminuria, Glomerular hyperfiltration

List of Abbreviations:

ACR – Albumin-to-creatinine ratio
AGEs – Advanced glycation end-products
AKI – Acute kidney injury
CKD – Chronic Kidney Disease
CKM – Cardiovascular-kidney-metabolic syndrome
CRMS – Cardio-renal-metabolic syndrome
DKD – Diabetic kidney disease
eGFR – Estimated glomerular filtration rate
GLP-1 RA – Glucagon-like peptide-1 receptor agonist
HbA1c – Glycated haemoglobin
IL-6 – Interleukin 6
MASLD – Metabolic dysfunction–associated steatotic liver disease
MKD – Metabolic kidney disease
NAFLD – Non-alcoholic fatty liver disease (former term for MASLD)
NF-κB – Nuclear factor kappa-light-chain-enhancer of activated B cells
ORG – Obesity-related glomerulopathy
PKC – Protein kinase C
RAAS – Renin–angiotensin–aldosterone system
ROS – Reactive oxygen species
SGLT2 – Sodium–glucose cotransporter 2
T2DM – Type 2 diabetes mellitus
TGF-β – Transforming growth factor beta
TNF-α – Tumor necrosis factor alpha

Introduction

Cardiovascular diseases and other non-communicable conditions remain the leading cause of death worldwide, accounting for nearly 70% of global mortality [1]. Diabetes mellitus, arterial hypertension, obesity, and chronic kidney disease (CKD) constitute the most prevalent chronic conditions contributing to this burden. CKD affects an estimated 9-13% of the population, with prevalence increasingly driven by the global epidemics of diabetes and obesity [2, 3].

In parallel, the prevalence of diabetes has doubled from 1990 to 2022, reaching over 828 million adults globally [4]. Similar trends are observed in Latin America and other regions, where obesity and metabolic dysfunction are now major determinants of cardiovascular and renal risk [5–10]. Importantly, mounting evidence indicates that kidney injury can arise before overt diabetes develops, occurring across the entire spectrum of metabolic disturbances, including obesity, prediabetes, insulin resistance, and metabolic dysfunction-associated steatotic liver disease (MASLD).

These interconnected processes form a continuum in which excess adiposity and adipose-tissue dysfunction induce systemic inflammation, endothelial injury, glomerular hyperfiltration, and neurohormonal activation. This "adipocentric" perspective has led to the recognition of the Cardio-Renal-Metabolic Syndrome (CRMS) as an integrated model encompassing cardiovascular, renal, and metabolic abnormalities [11–13].

Within this framework, the concept of Metabolic Kidney Disease (MKD) emerges as a unifying term describing kidney damage mediated primarily by metabolic dysfunction, even in the absence of sustained hyperglycaemia. MKD encompasses kidney injury associated with obesity, prediabetes, type 2 diabetes, MASLD, and mixed phenotypes. Its early recognition may be essential to interrupt disease progression and reduce cardiovascular and renal complications.

Importantly, metabolic dysfunction precedes and amplifies kidney injury across the entire continuum of adiposopathy, insulin resistance, impaired glucose tolerance, type 2 diabetes and MASLD, highlighting that renal damage often develops before overt hyperglycaemia becomes clinically detectable.

Cardio-Renal-Metabolic Syndrome (CRMS)

The Cardio-Renal-Metabolic Syndrome (CRMS) provides the essential pathophysiological context from which Metabolic Kidney Disease emerges. Evidence accumulated over the last decade shows that excess adiposity – particularly visceral and ectopic fat accumulation – drives a systemic inflammatory state that disrupts cardiovascular, renal, and metabolic homeostasis [14]. Rather than isolated diseases, these conditions form an interconnected continuum in which dysfunction in one organ system accelerates injury in the others.

The American Heart Association defines CRMS as a systemic disorder characterized by pathophysiological interactions between metabolic risk factors, CKD, and cardiovascular disease (CVD), leading to multiorgan dysfunction and increased cardiovascular events [12]. This framework emphasizes the bidirectional nature of these interactions: CVD increases the likelihood of renal dysfunction; CKD amplifies cardiovascular risk; and metabolic abnormalities – including adipose-tissue dysfunction, insulin resistance, and subclinical inflammation – drive both processes simultaneously [15–18].

Three major biological pathways underpin CRMS:

1. Chronic low-grade inflammation, mediated by adipose-derived cytokines such as IL6 and TNFα, promoting endothelial dysfunction, oxidative stress, and vascular injury.
2. Insulin resistance, contributing to altered podocyte signaling, increased sodium reabsorption, impaired nitric oxide bioavailability, and early glomerular hyperfiltration.
3. Neurohormonal activation, including heightened activity of the sympathetic nervous system and the renin–angiotensin–aldosterone system (RAAS), fostering vasoconstriction, hypertension, fibrosis, and progressive organ damage.

To support clinical stratification, the AHA proposes a staging system encompassing the entire spectrum of metabolic and cardiorenal dysfunction [12, 15]:

- Stage 0: No metabolic risk factors
- Stage 1: Excess or dysfunctional adiposity, including prediabetes
- Stage 2: Metabolic risk factors and/or moderate-to-high CKD risk
- Stage 3: Subclinical CVD with overlapping metabolic or renal risk
- Stage 4: Established CVD ± CKD (4a: without renal insufficiency; 4b: with renal insufficiency)

Within this continuum, the kidney is both target and mediator of metabolic injury. CRMS thus provides the conceptual foundation for MKD/ERM, clarifying how metabolic dysfunction – independent of glycaemic thresholds – initiates and amplifies renal injury.

Definition and Concept of Metabolic Kidney Disease (MKD/ERM)

Metabolic Kidney Disease (MKD), or *Enfermedad Renal Metabólica* (ERM), is an emerging and evolving concept that seeks to integrate the entire spectrum of renal injury associated with metabolic dysfunction. Rather than representing a single disease or a traditional histopathological entity, MKD reflects a continuum of pathophysiological alterations in which adipose-tissue dysfunction, insulin resistance, and chronic low-grade inflammation converge to drive early and progressive kidney damage. This view departs from classical models focused exclusively on hyperglycaemia or hypertension, and instead places the metabolic milieu – especially dysfunctional adiposity – at the centre of renal injury [13, 19] (Figure 1).

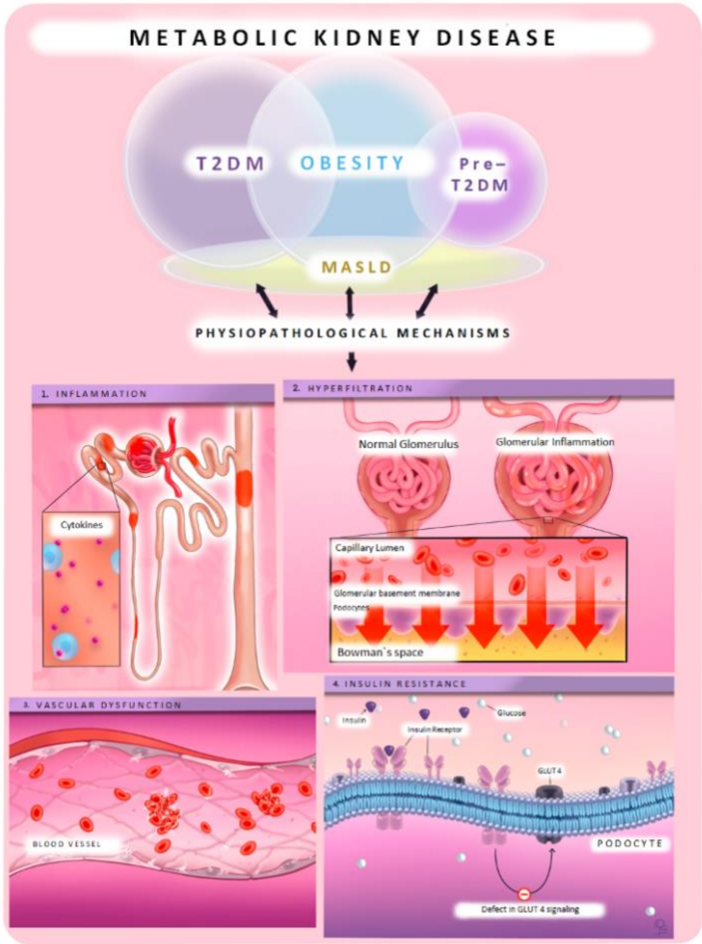

Figure 1. Common pathophysiological mechanisms in metabolic kidney disease (MKD). 1. Inflammation: increased cytokine and adipokine signalling leading to endothelial dysfunction, tissue remodelling, and fibrosis. 2. Hyperfiltration: intraglomerular hypertension and haemodynamic stress, contributing to podocyte injury and glomerulosclerosis. 3. Endothelial dysfunction: impaired nitric oxide bioavailability leading to altered autoregulation and vascular stiffness. 4. Insulin resistance: disrupted insulin signalling in target tissues (e.g., podocytes, hepatocytes) promoting metabolic stress, lipotoxicity, and apoptosis.

Adipose-tissue dysfunction plays a pivotal mechanistic role. Excess visceral fat promotes secretion of proinflammatory cytokines (TNF-α, IL-6), dysregulated adipokines (reduced adiponectina, elevated leptina), increased oxidative stress, and activation of the renin–angiotensin–aldosterone system (RAAS). These mechanisms favour afferent arteriolar vasodilation, intraglomerular hypertension, podocyte stress, and alterations in glomerular permeability. Over time, these changes contribute to hypertrophy of glomerular structures, expansion of mesangial matrix, tubulointerstitial inflammation, and ultimately to a decline in glomerular filtration [20–24]. This continuum perspective aligns with current evidence, emphasizing that renal alterations frequently emerge during early metabolic imbalance, well before traditional diagnostic criteria for diabetes or CKD are met.

MKD as an Integrative Clinical Framework

The strength of the MKD concept lies in its ability to integrate metabolic phenotypes that traditionally have been described separately. Obesity, prediabetes, type 2 diabetes, MASLD, and their combinations share physiopathological pathways that converge on the kidney. Although the magnitude and temporal sequence of injury may differ, the kidney responds to metabolic stress in a largely stereotyped manner: early glomerular hyperfiltration, podocyte maladaptation, endothelial dysfunction, and progressive fibrosis.

This integrative framework does not negate existing terminology, such as Diabetic Kidney Disease (DKD) or CKD associated with metabolic syndrome, but rather seeks to connect them. DKD remains essential for describing renal injury in established diabetes. However, it does not encompass patients with obesity or prediabetes who show similar physiopathological patterns. Likewise, CKD associated with metabolic syndrome often remains an epidemiological description rather than a mechanistic one. MKD proposes a unifying perspective, highlighting the central role of metabolic dysfunction – whether hepatic, adipose, or pancreatic – in initiating and sustaining renal damage. Given its high prevalence and strong metabolic basis, MASLD should be formally recognised as a key determinant of renal vulnerability within the MKD spectrum, warranting systematic screening even in non-diabetic individuals.

Clinical Implications

Recognizing MKD as a distinct and broader clinical construct may help clinicians identify high-risk individuals who would not be screened under current CKD guidelines. It may also encourage early therapeutic interventions targeting adipose-tissue inflammation, insulin resistance, and metabolic stress before overt renal dysfunction becomes evident. Ultimately, MKD promotes a shift from reactive nephrology to a more preventive, metabolically informed approach, consistent with contemporary cardio-renal-metabolic frameworks.

Comparable patterns of early metabolic stress and altered body composition have been reported in kidney conditions characterised by organomegaly, where malnutrition and sarcopenia may develop despite preserved eGFR [25, 26], particularly in women due to the higher prevalence of hepatomegaly [27–29].

Furthermore, persistent inflammatory activation is a hallmark across CKD phenotypes. Evidence from anemia management [30], intravenous iron stewardship [31], and uremic toxin–driven vascular injury [32] highlights how metabolic and inflammatory disturbances can converge to amplify renal vulnerability, mirroring several mechanisms central to MKD.

Clinical Subtypes of Metabolic Kidney Disease

Metabolic Kidney Disease encompasses a spectrum of renal manifestations arising from distinct but interrelated metabolic disturbances. Although these conditions share common physiopathological

G Ital Nefrol 2026 - ISSN 1724-5990 - © 2026 Società Italiana di Nefrologia - Anno 43 Volume 1 – DOI: 10.69097/43-01-2026-06

pathways – such as insulin resistance, adipose-tissue dysfunction, chronic inflammation, and endothelial injury – each metabolic phenotype imprints a characteristic pattern of renal involvement (Figure 2). In the following sections, we describe the major clinical subtypes of MKD, highlighting their specific mechanisms, histopathological features, and implications for early detection and progression.

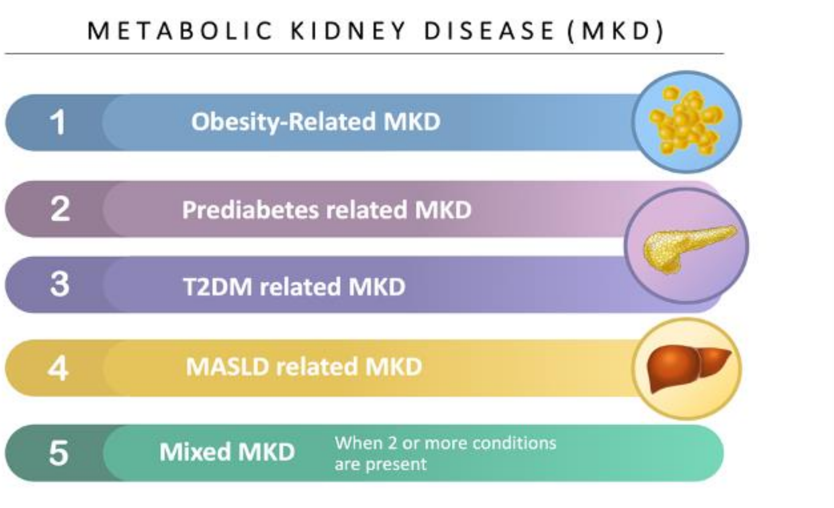

Figure 2. Proposed classification of metabolic kidney disease (MKD). Subtypes include obesity-related MKD, prediabetes-related MKD, T2DM-related MKD, MASLD-related MKD, and mixed MKD.

Obesity-Related- Metabolic Kidney Disease

Obesity represents one of the most consistent and well-established metabolic risk factors for the development and progression of kidney disease. Far from being a passive -energy storage compartment, adipose tissue – -particularly visceral fat accumulation – functions as an active endocrine and immunometabolic organ capable of modulating systemic inflammation, insulin sensitivity, oxidative stress, haemodynamics, and neurohormonal signalling [33–37]. These perturbations exert direct and indirect effects on renal structure and function, forming the basis of obesity-related- metabolic kidney disease.

From a haemodynamic standpoint, obesity is characterized by increased renal plasma flow, afferent arteriolar vasodilation, and elevated intraglomerular pressure. These early adaptations, largely mediated by hyperinsulinaemia, enhanced tubular sodium–glucose reabsorption, and heightened RAAS and sympathetic nervous system activity, culminate in glomerular hyperfiltration [36–38]. Persistent hyperfiltration contributes to enlargement of glomerular tuft volume and sets the stage for podocyte hypertrophy, detachment, and loss – events central to the initiation of proteinuria and progressive glomerulosclerosis.

Adipokines are central mediators of renal injury in obesity. Elevated leptin levels promote proliferation of mesangial cells, collagen deposition, and activation of profibrotic pathways, whereas reduced adiponectin impairs endothelial integrity and increases susceptibility to inflammation and oxidative stress [22, 37]. In parallel, secretion of cytokines such as IL6 and TNFα from dysfunctional adipose tissue fuels systemic lowgrade inflammation, promoting renal endothelial dysfunction, altered nitric oxide bioavailability, and microvascular injury.

Histopathological studies have described a recognizable phenotype in obesity-related kidney disease, known as obesity-elated glomerulopathy (ORG). Biopsies commonly reveal glomerulomegaly, mesangial expansion, podocyte -foot process widening, increased extracellular matrix deposition, thickening of the glomerular basement membrane, and variable degrees of

tubulointerstitial inflammation and fibrosis [38–42]. Although traditionally considered a benign or slowly progressive condition, recent data suggest that ORG may lead to significant proteinuria and decline in kidney function, especially when metabolic risk factors coexist or remain uncontrolled.
Importantly, obesity also amplifies the impact of other metabolic abnormalities – prediabetes, MASLD, dyslipidaemia, and hypertension – enhancing their deleterious effects on the kidney. This synergistic behaviour explains why obesity serves not only as a primary driver of MKD but also as a critical component in mixed metabolic phenotypes.
The recognition of obesity-related MKD underscores the need for early clinical identification of renal stress in individuals with overweight or obesity, even in the absence of diabetes or overt CKD. Given the potential reversibility of early haemodynamic changes and the benefits of weight reduction, pharmacological metabolic modulation, and lifestyle interventions, early detection represents a crucial opportunity for prevention and disease-modifying therapy.

Prediabetes-Related Metabolic Kidney Disease

Prediabetes represents an intermediate metabolic state between normoglycaemia and overt diabetes, characterised by impaired fasting glucose, impaired glucose tolerance, or elevated glycated haemoglobin according to current diagnostic criteria [43]. Although traditionally viewed as a precursor stage with modest clinical implications, accumulating evidence indicates that prediabetes is not a benign condition. Rather, it constitutes a metabolically active and pathophysiologically relevant state capable of inducing early renal injury through mechanisms that parallel, but do not require, sustained hyperglycaemia [44–46].
Several epidemiological studies have demonstrated a consistent association between prediabetes and an increased risk of incident CKD, reduced eGFR, and elevated albuminuria. In a prospective cohort exceeding 7,000 individuals with nearly nine years of follow-up, both impaired glucose tolerance and elevated HbA1c were independently associated with new-onset CKD, with hazard ratios ranging from 1.13 to 1.39 [44]. These findings have been confirmed by larger population-based analyses, including the REACTION study involving more than 250,000 Chinese adults, where prediabetes was identified as an independent predictor of CKD, particularly among men [47]. Meta-analyses reinforce this association, suggesting that even modest elevations in glucose metabolism confer a measurable increase in renal risk [46].
From a mechanistic perspective, renal injury in prediabetes is driven primarily by insulin resistance, hyperinsulinaemia, and intermittent postprandial hyperglycaemia. These alterations impair podocyte insulin signalling, reduce nephrin expression, and promote cytoskeletal instability, rendering podocytes more vulnerable to detachment and apoptosis [45, 48]. Concurrently, increased proximal tubular sodium-glucose reabsorption diminishes sodium delivery to the macula densa, blunting tubuloglomerular feedback and favouring afferent arteriolar vasodilation – enhancing glomerular hyperfiltration in a pattern similar to early diabetic kidney disease [45, 48].
Oxidative stress also plays a central role. Elevated production of reactive oxygen species, accumulation of advanced glycation end-products, and activation of protein kinase C pathways contribute to endothelial dysfunction, mesangial expansion, and increased glomerular permeability [48]. These changes manifest clinically as low-grade albuminuria and may precede overt abnormalities in eGFR.
Despite this growing evidence, prediabetes is not currently included among the recommended indications for CKD screening in most clinical guidelines [49]. Given the substantial prevalence of prediabetes worldwide and its clear association with early renal injury, incorporating individuals with prediabetes into CKD risk stratification strategies could facilitate earlier detection of kidney involvement and prompt implementation of preventive interventions.

Diabetes-Related Metabolic Kidney Disease

Type 2 diabetes mellitus (T2DM) remains the most common metabolic condition associated with chronic kidney disease worldwide, and diabetic kidney disease (DKD) continues to represent a major cause of end-stage kidney disease [50]. However, within the conceptual framework of Metabolic Kidney Disease, diabetes-related renal injury is understood not as an isolated entity, but as the intensification and culmination of metabolic disturbances that often originate much earlier – during obesity, insulin resistance, and prediabetes. This perspective highlights the continuity of metabolic stress across the glycaemic spectrum and underscores the shared mechanisms that unite DKD with other MKD subtypes.

Hyperglycaemia initiates and amplifies several interrelated pathways that contribute to renal damage. Among the earliest alterations is glomerular hyperfiltration, driven by increased proximal tubular sodium-glucose reabsorption mediated by SGLT2. This reduces solute delivery to the macula densa, blunts tubuloglomerular feedback, and promotes afferent arteriolar vasodilation, thereby increasing intraglomerular pressure [51]. Persistent hyperfiltration accelerates podocyte hypertrophy and detachment – lesions central to the development of albuminuria.

Glucotoxicity exerts direct cellular effects. Chronic exposure to elevated glucose levels induces oxidative stress, mitochondrial dysfunction, and accumulation of advanced glycation end-products (AGEs). These processes trigger mesangial expansion, altered extracellular matrix turnover, and thickening of the glomerular basement membrane [52, 53]. Importantly, lipotoxicity – driven by elevated circulating free fatty acids and ectopic lipid accumulation – amplifies these pathways by promoting endoplasmic reticulum stress, inflammation, and apoptosis in podocytes and tubular cells [54].

Inflammatory and fibrotic pathways further contribute to disease progression. Activation of protein kinase C (PKC), nuclear factor-κB (NF-κB), and transforming growth factor-β (TGF-β) promotes epithelial–mesenchymal transition, interstitial fibrosis, and glomerulosclerosis [55]. These processes often evolve silently for years before clinical manifestations appear, explaining why many patients show evidence of renal structural injury even at the time of diabetes diagnosis.

Although DKD has traditionally been described as a distinct clinical entity, MKD emphasizes that diabetes-related renal injury represents a continuum of metabolic renal stress, rather than a binary state emerging only after hyperglycaemia surpasses diagnostic thresholds. This broader view aligns with epidemiological observations showing that albuminuria, reduced eGFR, and microvascular injury can be detected in a significant proportion of individuals with newly diagnosed diabetes or even during the prediabetic phase.

Recognising diabetes-related MKD within this continuum has practical implications: it highlights the importance of early interventions targeting hyperglycaemia, insulin resistance, RAAS activation, and metabolic inflammation. Moreover, therapies such as SGLT2 inhibitors and GLP-1 receptor agonists – initially developed for glycaemic control – have demonstrated significant renal and cardiovascular protection precisely because they modulate many of these shared metabolic pathways.

MASLD-Related Metabolic Kidney Disease

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously termed non-alcoholic fatty liver disease (NAFLD), is now recognised as a multisystem metabolic disorder that extends well beyond the liver. The recent harmonized definitions and clinical practice guidelines issued jointly by EASL, EASD and EASO [56] underline the strong metabolic underpinnings of MASLD and its close association with insulin resistance, visceral fat accumulation, dyslipidaemia and systemic inflammation. This updated framework emphasizes that MASLD frequently coexists with other metabolic conditions and contributes to end-organ damage, including the kidney.

A growing body of evidence indicates that MASLD is independently associated with chronic kidney disease (CKD). A comprehensive and authoritative review by Bilson, [57] summarized epidemiological and mechanistic data supporting a strong association between MASLD and increased CKD risk, even after adjusting for obesity, diabetes and hypertension. These observations confirm that MASLD is not simply a marker of metabolic syndrome but a condition with its own pathophysiological impact on renal structure and function.

Mechanistically, MASLD promotes renal injury through multiple interconnected pathways. Hepatic steatosis triggers the release of hepatokines (e.g., fetuin-A) and other inflammatory mediators, which aggravate insulin resistance, endothelial dysfunction, and oxidative stress. These systemic disturbances impair glomerular autoregulation and increase susceptibility to hyperfiltration and podocyte stress. Disturbances in lipid metabolism characteristic of MASLD facilitate the accumulation of toxic lipid intermediates, contributing to mitochondrial dysfunction and activation of pro-fibrotic cascades within the kidney.

A further layer of complexity arises from genetic predisposition. Variants such as PNPLA3, TM6SF2 and MBOAT7 – well-established determinants of liver disease severity in MASLD – have been associated with increased renal vulnerability, suggesting shared metabolic and inflammatory pathways between hepatic steatosis and CKD [58]. These data reinforce the concept that renal involvement in MASLD is not solely a consequence of coexisting metabolic abnormalities, but reflects intrinsic pathobiological processes linked to the disease itself.

Meta-analytic data continue to support the association between MASLD and kidney dysfunction. The landmark systematic review by Musso and colleagues [59] remains a frequently cited foundational analysis demonstrating increased CKD prevalence and incidence among individuals with NAFLD. While older, its conclusions align with contemporary findings and highlight persistent mechanistic plausibility across diverse populations.

Recognizing MASLD as a distinct subtype within the broader spectrum of Metabolic Kidney Disease has important clinical implications. Given its high global prevalence and frequent underdiagnosis, incorporating MASLD into CKD risk stratification frameworks may facilitate earlier identification of renal involvement. Furthermore, therapeutic strategies targeting hepatic steatosis – such as GLP-1 receptor agonists, weight reduction and lifestyle interventions – may confer renal benefits even in the absence of overt diabetes. As recent guidelines emphasize [60, 61], a comprehensive approach addressing metabolic dysfunction across organ systems represents a crucial step toward improving long-term outcomes.

Mixed Metabolic Kidney Disease

Mixed Metabolic Kidney Disease represents the convergence of multiple metabolic derangements acting simultaneously on renal structure and function. In clinical practice, this phenotype is increasingly common, reflecting the overlap between obesity, insulin resistance, prediabetes, type 2 diabetes, hypertension, dyslipidaemia and MASLD. Rather than functioning as isolated risk factors, these conditions interact through shared mechanisms that amplify metabolic stress on the kidney, accelerating the transition from early functional changes to established chronic kidney disease [38].

From a pathophysiological standpoint, mixed MKD embodies a state in which haemodynamic, inflammatory, hormonal and lipid-related disturbances reinforce one another. Excess visceral fat accumulation fuels chronic low-grade inflammation and adipokine dysregulation, worsening insulin resistance and promoting hyperinsulinaemia [22]. In parallel, progressive impairments in glucose tolerance intensify tubular sodium-glucose reabsorption, stimulating afferent arteriolar vasodilation and glomerular hyperfiltration [45]. When MASLD coexists, the release of hepatokines and proinflammatory mediators further exacerbates endothelial dysfunction, oxidative stress and microvascular injury [50].

These synergistic mechanisms produce a renal phenotype that is often more severe than the sum of its individual components. Patients with obesity and MASLD, for example, exhibit higher rates of

albuminuria and more pronounced declines in eGFR compared with individuals with either condition alone [62]. Similarly, the coexistence of prediabetes or early diabetes with hepatic steatosis and visceral fat accumulation results in more rapid structural changes – mesangial expansion, podocyte stress and tubulointerstitial fibrosis – even when glycaemic abnormalities remain modest [63].
Clinically, mixed MKD is frequently under-recognised. Traditional screening strategies tend to focus on single risk factors – most often diabetes – thereby missing individuals who harbour substantial renal risk due to the cumulative effect of multiple metabolic abnormalities. This oversight is particularly relevant in younger or non-diabetic individuals with obesity and MASLD, in whom early renal involvement may be subtle yet progressive.
Recognising mixed MKD as a distinct and increasingly prevalent phenotype underscores the importance of integrated metabolic assessment in the evaluation of CKD risk. A comprehensive approach – including assessment of adiposity, glycaemic status, hepatic steatosis, blood pressure and lipid profile – allows for earlier identification of individuals at high risk and supports targeted interventions aimed at modulating metabolic stress. Ultimately, the mixed MKD phenotype exemplifies the concept of Metabolic Kidney Disease: a continuum of renal injury shaped not by a single metabolic defect, but by the interplay of multiple overlapping disturbances acting across organ systems. Such multilayered interactions are increasingly documented across metabolic phenotypes, supporting the concept of mixed MKD as a clinically relevant and mechanistically distinct entity.

Screening and Clinical Implications

The recognition of Metabolic Kidney Disease (MKD) as a unified conceptual framework has important consequences for screening strategies, particularly in populations traditionally not considered at high risk for chronic kidney disease. Current screening algorithms [64] often prioritise individuals with established type 2 diabetes or long-standing hypertension, overlooking a substantial proportion of patients who exhibit renal involvement driven primarily by obesity, prediabetes, MASLD or combinations thereof. As a result, early stages of metabolic renal stress frequently remain undetected [12] until albuminuria or declines in eGFR become clinically evident.
Integrating MKD-oriented screening into routine nephrology workflows could meaningfully shift clinical practice toward earlier detection, streamlined risk stratification, and more timely initiation of preventive interventions, particularly in metabolically vulnerable individuals.

Who Should Be Screened?

Given the burden of metabolic dysfunction in modern populations, screening should extend beyond conventional high-risk groups. Individuals with the following characteristics merit evaluation for possible MKD (Figure 3):

- Obesity with increased visceral fat accumulation, even in the absence of diabetes or hypertension
- Prediabetes, particularly in those with impaired glucose tolerance or rising HbA1c
- MASLD, regardless of glycaemic status, as emphasised by recent international guidelines [56]
- Family history of type 2 diabetes, CKD or early cardiovascular disease [12]
- Coexistence of multiple metabolic abnormalities, including dyslipidaemia, hyperuricaemia or elevated liver enzymes

In these individuals, glomerular hyperfiltration and endothelial dysfunction – hallmarks of early MKD – may precede measurable reductions in kidney function, highlighting the importance of timely assessment.

It is important to acknowledge that current CKD guidelines still do not formally recommend routine kidney screening in individuals with prediabetes or MASLD. The evidence supporting such an approach is growing, yet prospective validation and consensus-driven recommendations are still needed to define optimal screening thresholds and intervals.

What Tests Should Be Performed?

A pragmatic and clinically accessible initial evaluation may include:

- Estimated glomerular filtration rate (eGFR) using creatinine or combined creatinine-cystatin C equations
- Urine albumin-to-creatinine ratio (ACR) to detect early glomerular injury
- Assessment of metabolic health, including fasting glucose, HbA1c, lipid profile, uric acid and markers of hepatic steatosis
- Imaging, where appropriate, to evaluate hepatic steatosis or adipose distribution

Importantly, mild elevations in ACR or upward drifts in eGFR (suggesting glomerular hyperfiltration) should not be dismissed as normal variants in individuals with metabolic abnormalities, but rather considered potential markers of MKD.

Clinical Integration

Incorporating MKD into routine practice involves adopting a more comprehensive view of metabolic health, recognising that renal involvement can occur long before diagnostic thresholds for diabetes or CKD are reached. Early identification enables timely implementation of therapeutic strategies – such as weight optimisation, dietary interventions, metabolic modulation and blood pressure control – that mitigate renal stress and may alter longterm trajectories.

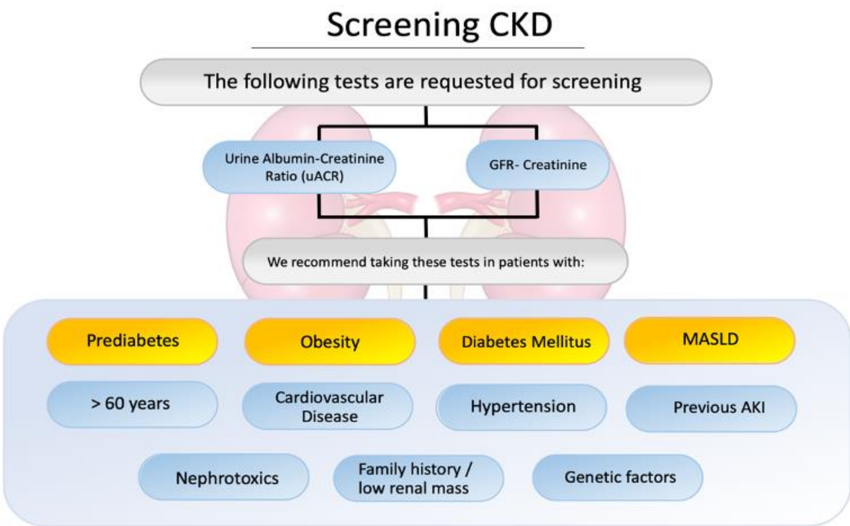

Figure 3. Recommended screening tests for chronic kidney disease (CKD). Screening includes estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (ACR). These tests are recommended for individuals with obesity, prediabetes, hypertension, T2DM, cardiovascular disease, prior AKI, or age >60 years.

Conclusions

Metabolic Kidney Disease represents an important conceptual and clinical evolution in our understanding of the interplay between metabolic dysfunction and renal health. This framework offers clinicians a more actionable understanding of metabolic renal risk, promoting earlier recognition of kidney involvement and more timely implementation of prevention strategies. By integrating obesity, prediabetes, type 2 diabetes, MASLD and mixed phenotypes within a single conceptual framework, MKD offers a more coherent representation of the pathophysiological processes driving early kidney injury in contemporary populations. This approach emphasises the central role of adipose tissue dysfunction, insulin resistance, chronic low-grade inflammation and lipid dysregulation as shared mechanisms across the metabolic spectrum.

Recognising MKD broadens opportunities for earlier diagnosis, particularly in individuals who would not be captured by traditional CKD screening criteria. It also underscores the need for multidimensional management strategies that address metabolic dysfunction across organ systems, rather than focusing solely on glycaemic control or blood pressure.

As the prevalence of metabolic disorders continues to rise globally, incorporating the MKD framework into clinical practice may offer a path toward more effective prevention and improved longterm renal and cardiovascular outcomes. This review highlights the importance of a unified, metabolically informed approach to kidney health – an approach that aligns with modern evidence and reflects the complex, interconnected nature of metabolic disease.

BIBLIOGRAPHY

1. NCD Countdown 2030 collaborators. NCD Countdown 2030: worldwide trends in non-communicable disease mortality and progress towards Sustainable Development Goal target 3.4. Lancet Lond Engl. 22 settembre 2018;392(10152):1072–88. https://doi.org/10.1016/s0140-6736(18)31992-5.
2. Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. Kidney Int Suppl. aprile 2022;12(1):7–11. https://doi.org/10.1016/j.kisu.2021.11.003.
3. Lucas B, Taal MW. Epidemiology and causes of chronic kidney disease. Medicine (Baltimore). 1 marzo 2023;51(3):165–9. https://doi.org/10.1016/j.mpmed.2022.12.003.
4. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants. Lancet Lond Engl. novembre 2024;404(10467):2077–93. https://doi.org/10.1016/s0140-6736(24)02317-1.
5. Día mundial de la diabetes 2024 [Internet]. Cuenta de Alto Costo. [citato 1 dicembre 2025]. Disponibile su: https://cuentadealtocosto.org/noticias/dia-mundial-de-la-diabetes-2024/
6. Said S, Hernandez GT. The link between chronic kidney disease and cardiovascular disease. J Nephropathol. luglio 2014;3(3):99–104. https://doi.org/10.12860/jnp.2014.19.
7. Dunlay SM, Givertz MM, Aguilar D, Allen LA, Chan M, Desai AS, et al. Type 2 Diabetes Mellitus and Heart Failure: A Scientific Statement From the American Heart Association and the Heart Failure Society of America: This statement does not represent an update of the 2017 ACC/AHA/HFSA heart failure guideline update. Circulation. 13 agosto 2019;140(7):e294–324. https://doi.org/10.1161/cir.0000000000000691.
8. González-Robledo G, Jaramillo Jaramillo M, Comín-Colet J. Diabetes mellitus, insuficiencia cardiaca y enfermedad renal crónica. Rev Colomb Cardiol. marzo 2020;27:3–6. https://doi.org/10.1016/j.rccar.2019.12.009.
9. Cobo Marcos M, de la Espriella R, Gayán Ordás J, Llàcer P, Pomares A, Fort A, et al. Prevalence and clinical profile of kidney disease in patients with chronic heart failure. Insights from the Spanish cardiorenal registry. Rev Espanola Cardiol Engl Ed. gennaio 2024;77(1):50–9. https://doi.org/10.1016/j.rec.2023.05.003.
10. Laffin LJ, Bakris GL. Intersection Between Chronic Kidney Disease and Cardiovascular Disease. Curr Cardiol Rep. 16 luglio 2021;23(9):117. https://doi.org/10.1007/s11886-021-01546-8.
11. Moreno-Pérez O, Reyes-García R, Modrego-Pardo I, López-Martínez M, Soler MJ. Are we ready for an adipocentric approach in people living with type 2 diabetes and chronic kidney disease? Clin Kidney J. aprile 2024;17(4):sfae039. https://doi.org/10.1093/ckj/sfae039.
12. Ndumele CE, Neeland IJ, Tuttle KR, Chow SL, Mathew RO, Khan SS, et al. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association. Circulation. 14 novembre 2023;148(20):1636–64. https://doi.org/10.1161/CIR.0000000000001186.
13. García-Carrasco A, Izquierdo-Lahuerta A, Medina-Gómez G. The Kidney-Heart Connection in Obesity. Nephron. 2021;145(6):604–8. https://doi.org/10.1159/000515419.
14. Zoccali C, Mallamaci F. The cardiovascular-renal link and the health burden of kidney failure. Eur Heart J. 1 aprile 2023;44(13):1167–9. https://doi.org/10.1093/eurheartj/ehad039.
15. Rangaswami J, Bhalla V, Blair JEA, Chang TI, Costa S, Lentine KL, et al. Cardiorenal Syndrome: Classification, Pathophysiology, Diagnosis, and Treatment Strategies: A Scientific Statement From the American Heart Association. Circulation. 16 aprile 2019;139(16):e840–78. https://doi.org/10.1161/cir.0000000000000664.
16. Lawson CA, Seidu S, Zaccardi F, McCann G, Kadam UT, Davies MJ, et al. Outcome trends in people with heart failure, type 2 diabetes mellitus and chronic kidney disease in the UK over twenty years. EClinicalMedicine. Febbraio 2021;32:100739. https://doi.org/10.1016/j.eclinm.2021.100739.
17. Cases A, Broseta JJ, Marqués M, Cigarrán S, Julián JC, Alcázar R, et al. Cardiovascular-kidney-metabolic syndrome definition and its role in the prevention, risk staging, and treatment. An opportunity for the Nephrology. Nefrologia. 2024;44(6):771–83. https://doi.org/10.1016/j.nefroe.2024.11.011.
18. Ndumele CE, Rangaswami J, Chow SL, Neeland IJ, Tuttle KR, Khan SS, et al. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. Circulation. 14 novembre 2023;148(20):1606–35. https://doi.org/10.1161/CIR.0000000000001184.
19. Clark B, Mulrooney M, Miao B, Kataria D, Kulkarni A, Skaar JR. Defining Cardio-renal-metabolic (CRM) Syndrome: A Targeted Literature Review. Metab – Clin Exp [Internet]. 1 giugno 2024 [citato 1 dicembre 2025];153. https://doi.org/10.1016/j.metabol.2024.155856.
20. Garofalo C, Borrelli S, Minutolo R, Chiodini P, De Nicola L, Conte G. A systematic review and

meta-analysis suggests obesity predicts onset of chronic kidney disease in the general population. Kidney Int. maggio 2017;91(5):1224–35. https://doi.org/10.1016/j.kint.2016.12.013.
21. Tuttle KR, Alicic RZ, Duru OK, Jones CR, Daratha KB, Nicholas SB, et al. Clinical Characteristics of and Risk Factors for Chronic Kidney Disease Among Adults and Children: An Analysis of the CURE-CKD Registry. JAMA Netw Open. 2 dicembre 2019;2(12):e1918169. https://doi.org/10.1001/jamanetworkopen.2019.18169.
22. Rico-Fontalvo J, Daza-Arnedo R, Rodríguez-Yanez T, Osorio W, Suarez-Romero B, Soto O, et al. Obesidad y enfermedad renal crónica. Una mirada desde los mecanismos fisiopatológicos. Revisión narrativa. Rev Soc Ecuat Nefrol Diálisis Traspl. 30 settembre 2022;10(2):97–107. http://doi.org/10.56867/32.
23. Wada J, Makino H. Inflammation and the pathogenesis of diabetic nephropathy. Clin Sci Lond Engl 1979. febbraio 2013;124(3):139–52. https://doi.org/10.1042/cs20120198.
24. Vallon V, Thomson SC. Targeting renal glucose reabsorption to treat hyperglycaemia: the pleiotropic effects of SGLT2 inhibition. Diabetologia. febbraio 2017;60(2):215–25. https://doi.org/10.1007/s00125-016-4157-3.
25. Brambilla Pisoni M, Catania M, Rivera RF, De Rosa LI, Kola K, Paolisi M, et al. The Hidden Iceberg of ADPKD: Early Organomegaly-Driven Malnutrition and Sarcopenia Beyond Preserved eGFR. Int J Mol Sci. 2026;27(4):1667. https://doi.org/10.3390/ijms27041667
26. Alibrandi MTS, Pisoni MB, Rivera RF, Catania M, Vespa M, De Rosa LI, et al. Body water distribution, early malnutrition and sarcopenia in ADPKD: insights from a cross sectional study. J Nephrol. 2025;38(7):1917–25. https://doi.org/10.1007/s40620-025-02327-0.
27. Catania M, Vezzoli G, Sciarrone Alibrandi MT. Highlighting the impact of hormonal factors on hepatic cystogenesis: Implications for pathophysiology and clinical practice. J Hepatol. 2025;82(4):e180–1. https://doi.org/10.1016/j.jhep.2024.09.041.
28. Petrone M, Catania M, De Rosa LI, Degliuomini RS, Kola K, Lupi C, et al. Role of Female Sex Hormones in ADPKD Progression and a Personalized Approach to Contraception and Hormonal Therapy. J Clin Med. 2024;13(5):1257. https://doi.org/10.3390/jcm13051257.
29. Delli Zotti GB, Sangiovanni E, Brioni E, Ratti MM, Sciarrone Aliprandi MT, Spotti D, et al. [Psychological Assessment of a sample of women with ADPKD: quality of life, body image, anxiety and depression]. G Ital Nefrol Organo Uff Della Soc Ital Nefrol. 2019;36(2):2019-vol2. PubMed PMID: 30983181.
30. Rivera RF, Alibrandi MTS, Di Lullo L, Fioccari F. Clinical management of anemia in patients with CKD. G Ital Nefrol. 2017;34(Suppl 69):20–35. PubMed PMID: 28682026.
31. Rivera RF, Guido D, Del Vecchio L, Corghi E, D'Amico M, Camerini C, et al. Impact of European medicines agency recommendations for hypersensitivity reactions on intravenous iron prescription in haemodialysis centres of the Lombardy region. J Nephrol. 2016;29(5):673–81. https://doi.org/10.1007/s40620-015-0254-5. PubMed PMID: 26715394
32. Rivera RF, Sciarrone Alibrandi MT, Foligno NE, Magagnoli L, Ciceri P, Cozzolino M. Uremic Toxin-Driven Vascular Calcification in Chronic Kidney Disease: Molecular Pathways and Integrated Phenotypes. Toxins. 2026;18(2):112. https://doi.org/10.3390/toxins18020112. PubMed PMID: 41745778; PubMed Central PMCID: PMC12944978.
33. Vijay K, Neuen BL, Lerma EV. Heart Failure in Patients with Diabetes and Chronic Kidney Disease: Challenges and Opportunities. Cardiorenal Med. 2022;12(1):1–10. https://doi.org/10.1159/000520909.
34. Svačina Š. [Obesity and cardiovascular disease]. Vnitr Lek. 2020 Spring;66(2):89-91. Czech. PMID: 32942882.
35. Hall JE, Mouton AJ, da Silva AA, Omoto ACM, Wang Z, Li X, et al. Obesity, kidney dysfunction, and inflammation: interactions in hypertension. Cardiovasc Res. 7 luglio 2021;117(8):1859–76. https://doi.org/10.1093/cvr/cvaa336.
36. Yim HE, Yoo KH. Obesity and chronic kidney disease: prevalence, mechanism, and management. Clin Exp Pediatr. ottobre 2021;64(10):511–8. https://doi.org/10.3345/cep.2021.00108.
37. Stasi A, Cosola C, Caggiano G, Cimmarusti MT, Palieri R, Acquaviva PM, et al. Obesity-Related Chronic Kidney Disease: Principal Mechanisms and New Approaches in Nutritional Management. Front Nutr. 2022;9:925619. https://doi.org/10.3389/fnut.2022.925619.
38. Tsuboi N, Okabayashi Y. The Renal Pathology of Obesity: Structure-Function Correlations. Semin Nephrol. luglio 2021;41(4):296–306. https://doi.org/10.1016/j.semnephrol.2021.06.002.
39. Tsuboi N, Okabayashi Y, Shimizu A, Yokoo T. The Renal Pathology of Obesity. Kidney Int Rep. marzo 2017;2(2):251–60. https://doi.org/10.1016/j.ekir.2017.01.007.
40. Herman-Edelstein M, Weinstein T, Chagnac A. Obesity-Related Glomerulopathy: Clinical Management. Semin Nephrol. luglio 2021;41(4):358–70. https://doi.org/10.1016/j.semnephrol.2021.06.007.
41. Choung HYG, Bomback AS, Stokes MB, Santoriello D, Campenot ES, Batal I, et al. The spectrum of kidney biopsy findings in patients

with morbid obesity. Kidney Int. marzo 2019;95(3):647–54. https://doi.org/10.1016/j.kint.2018.11.026.
42. D'Agati VD, Chagnac A, de Vries APJ, Levi M, Porrini E, Herman-Edelstein M, et al. Obesity-related glomerulopathy: clinical and pathologic characteristics and pathogenesis. Nat Rev Nephrol. agosto 2016;12(8):453–71. https://doi.org/10.1038/nrneph.2016.75.
43. American Diabetes Association Professional Practice Committee. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2025. Diabetes Care. 1 gennaio 2025;48(1 Suppl 1):S27–49.
44. Kim GS, Oh HH, Kim SH, Kim BO, Byun YS. Association between prediabetes (defined by HbA1C, fasting plasma glucose, and impaired glucose tolerance) and the development of chronic kidney disease: a 9-year prospective cohort study. BMC Nephrol. 16 aprile 2019;20(1):130.
45. Rico Fontalvo J, Soler MJ, Daza Arnedo R, Navarro-Blackaller G, Medina-González R, Rodríguez Yánez T, et al. Prediabetes and CKD: Does a causal relationship exist. Nefrologia. 2024;44(5):628–38. https://doi.org/10.1016/j.nefro.2024.06.008.
46. Echouffo-Tcheugui JB, Narayan KM, Weisman D, Golden SH, Jaar BG. Association between prediabetes and risk of chronic kidney disease: a systematic review and meta-analysis. Diabet Med J Br Diabet Assoc. dicembre 2016;33(12):1615–24. https://doi.org/10.1111/dme.13113.
47. Lin L, Lu J, Chen L, Mu Y, Ye Z, Liu C, et al. Glycemic status and chronic kidney disease in Chinese adults: Findings from the REACTION study. J Diabetes. Settembre 2017;9(9):837–45. https://doi.org/10.1111/1753-0407.12490.
48. García-Carro C, Vergara A, Bermejo S, Azancot MA, Sellarés J, Soler MJ. A Nephrologist Perspective on Obesity: From Kidney Injury to Clinical Management. Front Med. 2021;8:655871. https://doi.org/10.3389/fmed.2021.655871.
49. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. aprile 2024;105(4S):S117–314. https://doi.org/10.1016/j.kint.2023.10.018.
50. Mosquera EY, Montejo Hernández JD, Chacón Acevedo KR, Daza R, De La Espriella-Badel V, Machacón Miranda E, et al. Update of the Colombian clinical practice guideline on diabetic renal disease. Rev Colomb Nefrol [Internet]. 20 novembre 2024. https://doi.org/10.22265/acnef.11.3.912.
51. Rico Fontalvo JE, Daza Anedo R, Raad Sarabia M, Pájaro Galvis N, Bello Espinosa A, Uparella Gulfo I, et al. Proteoma urinario en la enfermedad renal diabética. Estado del arte: Urinary proteome in diabetic kidney disease: state of the art. Rev Colomb Nefrol. 18 agosto 2021;8(3):e546. https://doi.org/10.22265/acnef.8.3.546.
52. Rico-Fontalvo J, Aroca-Martinez G, Daza-Arnedo R, Raad-Sarabia M, Torres J, Pajaro-Galvis N, et al. Artículo de Revisión Enfermedad renal diabética no proteinúrica: Estado del arte Non-proteinuric diabetic kidney disease: State of art. Rev Nefrol Dial Traspl 2022424330-339 [Internet]. [citato 1 dicembre 2025]; Disponibile su: https://www.researchgate.net/publication/366812175_Articulo_de_Revision_Enfermedad_renal_diabetica_no_proteinurica_Estado_del_arte_Non-proteinuric_diabetic_kidney_disease_State_of_art.
53. Sugahara M, Pak WLW, Tanaka T, Tang SCW, Nangaku M. Update on diagnosis, pathophysiology, and management of diabetic kidney disease. Nephrol Carlton Vic. giugno 2021;26(6):491–500. https://doi.org/10.1111/nep.13860.
54. Toth-Manikowski S, Atta MG. Diabetic Kidney Disease: Pathophysiology and Therapeutic Targets. J Diabetes Res. 2015;2015:697010. https://doi.org/10.1155/2015/697010.
55. Jorge RF, Rodrigo DA, Tomas RY, Maria Cristina MA, Jose C, Maria Ximena CB, et al. Inflammation and Diabetic Kidney Disease: New Perspectives. J Biomed Res Environ Sci. luglio 2022;3(7):779–86. https://doi.org/10.37871/jbres1513.
56. European Association for the Study of the Liver, European Association for the Study of Diabetes, European Association for the Study of Obesity. EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD): Executive Summary. Diabetologia. novembre 2024;67(11):2375–92. https://doi.org/10.1007/s00125-024-06196-3.
57. Bilson J, Mantovani A, Byrne CD, Targher G. Steatotic liver disease, MASLD and risk of chronic kidney diseaseFegato steatotico, MASLD e rischio di malattia renale cronica. Diabetes Metab. 1 gennaio 2024;50(1):101506. https://doi.org/10.1016/j.diabet.2023.101506.
58. Lonardo A. Association of NAFLD/NASH, and MAFLD/MASLD with chronic kidney disease: an updated narrative review. Metab Target Organ Damage. 7 aprile 2024;4(2):N/A-N/A. https://doi.org/10.20517/mtod.2024.07.
59. Musso G, Gambino R, Tabibian JH, Ekstedt M, Kechagias S, Hamaguchi M, et al. Association of non-alcoholic fatty liver disease with chronic kidney disease: a systematic review and meta-analysis. PLoS Med. luglio 2014;11(7):e1001680. https://doi.org/10.1371/journal.pmed.1001680.

60. European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines on the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). Obes Facts. 2024;17(4):374–444.
61. European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. settembre 2024;81(3):492–542. https://doi.org/10.1016/j.jhep.2024.04.031.
62. Mahmoodnia L, Aghadavod E, Beigrezaei S, Rafieian-Kopaei M. An update on diabetic kidney disease, oxidative stress and antioxidant agents. J Ren Inj Prev. 2017;6(2):153–7. https://doi.org/10.15171/jrip.2017.30.
63. Benlloch S, Moncho F, Górriz JL. Esteatosis hepática metabólica y nefropatía diabética: una llamada a la acción. Nefrología. marzo 2024;44(2):129–38. https://doi.org/10.1016/j.nefroe.2024.03.009.
64. Khan SS, Coresh J, Pencina MJ, Ndumele CE, Rangaswami J, Chow SL, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association. Circulation. 12 dicembre 2023;148(24):1982–2004. https://doi.org/10.1161/cir.0000000000001191.