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CARDIOVASCULAR-KIDNEY-METABOLIC (CKM) SYNDROME: NEW DEVELOPMENTS IN SYMPTOMS, DIAGNOSIS, AND TREATMENT

KARDİYOVASKÜLER-BÖBREK-METABOLİK (CKM) SENDROMU: SEMPTOMLAR, TANI VE TEDAVİDE YENİ GELİŞMELER

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ABSTRACT

The association between obesity, type 2 Diabetes Mellitus (DM), cardiovascular disease (CVD), and chronic kidney disease (CKD) is increasingly and widely recognized in developed countries. This condition has been collectively defined by the American Heart Association (AHA) as the Cardiovascular-Kidney-Metabolic (CKM) syndrome, which is characterized by hyperglycemia, insulin resistance, and increased activity of the renin-angiotensin-aldosterone system (RAAS), formation of advanced glycation end products, oxidative stress, lipotoxicity, endoplasmic reticulum stress, abnormal calcium handling, mitochondrial dysfunction and impaired energy production, and chronic inflammation. Addressing their prevention, management, and treatment is of paramount importance to improve patient health outcomes. The aim of this review is to provide a comprehensive overview of the status and new treatment modalities for the recently described CKM syndrome.

Keywords: Cardiovascular Disease, Chronic Kidney Disease, Cardiovascular Kidney Metabolic Syndrome, Diabetes Mellitus, Obesity.

ÖZET

Obezite, tip 2 Diabetes Mellitus (DM), kardiyovasküler hastalık (KVH) ve kronik böbrek hastalığı (KBH) arasındaki korelasyon, gelişmiş ülkelerde giderek artan ve yaygın olarak kabul gören bir hastalıktır. Bu hastalık Amerikan Kalp Derneği (AHA) tarafından toplu olarak Kardiyovasküler-Böbrek-Metabolik (CKM) sendromu olarak tanımlanmış, hiperglisemi, insülin direnci, renin-anjiyotensin-aldosteron sisteminin (RAAS) artan aktivitesi, ileri glikasyon son ürünlerinin oluşumu, oksidatif stres, lipotoksisite, endoplazmik retikulum stresi, kalsiyum kullanımında anormallikler, mitokondrinin hatalı çalışması ve bozulmuş enerji üretiminin yanı sıra kalıcı kronik enflamasyon dahil olmak üzere birbirine bağlantılı bir dizi semptomla ilişkilendirilmiştir. Hastaların sağlık sonuçlarının iyileştirilmesi için bunların önlenmesi, yönetimi ve tedavilerinin ele alınması büyük önem taşımaktadır. Bu derlemenin amacı, yakın zamanda tanımlanan KBY sendromuna ilişkin mevcut durumun ve yeni tedavi metotlarının kapsamlı bir incelemesini sunmaktır

Anahtar Kelimeler: Diabetes Mellitus, Kardiyovasküler Böbrek Metabolik Sendromu, Kardiyovasküler Hastalık, Kronik Böbrek Hastalığı, Obezite.

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INTRODUCTION

Cardiovascular-Kidney-Metabolic (CKM) syndrome is a condition affecting both the cardiovascular and kidney systems. CKM is haracterized by paranoia concerning the development of hypertension because of persistent carelessness with caffeine consumption and the use of stimulating foods rather than relaxation therapy. This term refers to the close relationship and concomitant development of cardiovascular disease (CVD), kidney disease, and metabolic syndrome (Bedo et al., 2024). Cardiovascular disease is inherently a health hazard, particularly for patients with aortic deficiency, as it may lead to sudden death. Metabolic syndrome is a conglomerate of risk factors augmenting the development of abdominal obesity, insulin resistance, type II diabetes, and high serum cholesterol. CKD is the loss of kidney function due to an elevation of blood pressure, proteinuria, or diabetes mellitus (Campos et al., 2021; Hu et al., 2024; Masenga et al., 2023; Tilg et al., 2024).

Cardio-Kidney-Metabolic Syndrome is a precursor to Cardiovascular-Kidney-Metabolic Syndrome. CKM Syndrome expounds the butterfly heart lesions' progression from the abdominal aorta up through the heart to the head, leading to a slow, progressive disaster with the potential to generate simultaneous kidney disease, metabolic syndrome, and cardiovascular disease. CKM manifests solely in cardiovascular and kidney diseases, which share analogous symptomatology, such as sudden death, and whose onset is imperceptible until multiple organs are involved (Sebastian et al., 2024). CKD is the most researched field in CKM. CKM syndrome is only recently gaining global awareness, so limited treatment options or protocols exist, complicating treatment efforts. CKM is forecast to exacerbate the burden of healthcare expenditure. CKM raises public health concerns; therefore, this study endeavors to examine CKM from an etiological perspective to raise awareness and urge crafting prevention strategies. Given multifaceted symptomatology, this effort combines traditional analysis methods, machine learning, and epidemiological methods (Ndumele et al. 2023; Tetteh et al., 2021; Ndumele et al. 2023).

Background and Significance

In this article, we examine the Cardiovascular-Renal-Metabolic syndrome and review newly developed methods. Owing to its early state, restrictive criteria are employed to mirror the recent critical investigations. Acknowledging whether an individual is in a chronic state that leads to hypertension, type 2 diabetes mellitus, metabolic dysfunction-associated fatty liver disease, and atherosclerosis (coronary and carotid) is key to understanding a propensity for cardiovascular diseases and chronic kidney disorders. These interconnected states form the foundation for the Cardiovascular-Kidney-Metabolic (CKM) syndrome, which was recently included in the American Heart Association's scientific statement. This represents the most recent expansion of the encyclopedic disease list, introduced with detailed criteria in the context of the 2022 epidemic year, as discussed by (Bedo et al., 2024). However, it is acknowledged that while cardiorenal syndrome, cardiovascular disorders as a group, and chronic kidney disorders as a separate category share similar risk attributes and some pathways, metabolic syndrome taken alone does not suffice to explain the complex and intricate face of the syndromes; CKM is a conceptually vast rubric Topics and clinical actions does provide a fruitful dystopic portrayal of the wider pathway aspects emerging from metabolic syndrome (Zoccali, 2025). The sentence is not coherent or meaningful in its current form. It needs to be rewritten for clarity, ensuring appropriate scientific terminology and logical structure are utilized. Nevertheless, it reminds most of the gentlefolx of the far-reaching nature of the CKM syndrome, and that emphasis on a rather small part represents only the small piece of the ritualistic issues. Further details can be obtained in the currently released material, including newly initiated examinations of specific grey areas (Lei et al., 2024; Chen et al., 2024; Li et al., 2024).

EPIDEMIOLOGY OF CKM SYNDROME

The main objective of this section is to provide a comprehensive overview of the emerging Cardiovascular-Kidney-Metabolic (CKM) Syndrome, which represents a set of disorders associated with the kidneys, heart, and metabolic abnormalities. This article aims to describe new developments in the understanding of pathophysiology, clinical manifestations, screening methods, and treatment strategies of the CKM syndrome, as there is currently no evidence in biomedicine reference and research publications. Cardiovascular-Kidney-Metabolic Syndrome, which was named for the metabolic abnormalities of the patients included in this study and the pathological anxiety seen in the heart and kidneys, is defined as the presence of chronic kidney disease (CKD), metabolic syndrome (MS), and

hypertension (HT) in the same patient (Yim et al., 2025). Multiple epidemiological aspects, variations in the incidence of CKM syndrome in different population groups, as well as changing trends and risk factors that have been expanding the public health significance of CKM syndrome. These will be addressed in this study by summarizing previous biomedicine reference studies published in current journals. The increasing prevalence of the CKM syndrome has provided impressive evidence of the rapid shift from chronic non-communicable diseases to diseases related to metabolism and aging in developed and developing countries. It has also been concluded that the prevalence of CKM syndrome will increase in the future in the general population (Xiao et al., 2022). The middle-class population is frequently affected by chronic diseases such as hypertension, diabetes cardiovascular events, as well as CKD. Family history of hypertension, obesity, diabetes, smoking, and malnutrition, i.e., environmental causes, raise the prevalence and risk groups of CKM syndrome (Agarwal et al., 2012). Lastly, it was underlined that the measure, taken independently of any cause and numerous social factors that are considered later, can change the distribution of socioeconomic categories, education, and ethnicity, thereby influencing the incidence and access to health services in the population. Recognizing these changes from all perspectives is valuable in terms of presenting a solution (Claudel et al., 2024; Minhas et al., 2024; Zhang et al., 2025).

PATHOPHYSIOLOGY OF CKM SYNDROME

On a whole-body scale, functions are provided by six different systems: cardiovascular, immune, metabolic, neurologic, hormonal, and renal. Interactions between these systems ensure the regulation of physiological function under variable circumstances. However, when one is disturbed, the others may become adversely affected (Bedo et al., 2024). Dysfunctions in the cardiovascular system may represent well-established actors specific to the genesis or exacerbation of diseases in the immune, renal, or metabolic system, involving a cyclonic development of disability, and vice versa. Chronic inflammation, oxidative stress, or endothelial dysfunction could act as intermediary mechanisms for different interactions among the six systems (Rotariu et al., 2022). For example, oxidative stress is implicated in the development of various dermatological, degenerative, and vascular diseases, and it is a relevant mechanism for interactions among the cardiovascular, immune, metabolic, and renal systems (Ciccarelli et al., 2021; Silveira et al., 2022; Cenko et al., 2021). Taking initial research into account and the detection of CKM syndrome, earlier interventions can be made to prevent its progression to an irreversible state. Initial preventive strategies could be proposed for relatively healthy people regarding the identified mechanisms most likely associated with the interrelations among cardiovascular, immune, metabolic, neurologic, hormonal, and renal dysregulation (Tecce et al., 2024). For example, events from documented epidemiological studies that can be endorsed for the prevention of neurologic disease do include bowel, strenuous physical activity, a Mediterranean dietary pattern, and adequate intake of antioxidant micro- and macro-nutrients. There is a noteworthy concordance among these events and the interconnectedness of pathogenetic mechanisms for different outcomes in dermatological disease, epilepsy, metabolic syndrome, nephropathy, Parkinson's disease, and sleep apnea (Garba et al., 2024; Khan et al., 2023; Zhang et al., 2025).

Interplay between Cardiovascular, Kidney, and Metabolic Systems

Increased life expectancy has led to a growing incidence of chronic conditions, often in concert rather than isolation (Bedo et al., 2024). One striking representation of interactions among simultaneous diseases is the development of the interconnected cardiovascular, kidney, and metabolic (CKM) syndrome. It has been recognized by authoritative organizations and specialized scientific research, but there is still much to understand about this complex and systemic interplay. This subsection critically considers CKM Syndrome, aiming to broaden the current comprehension of its onset, progression, and treatment by drawing an analogy to a simple daily choice (Li et al., 2024). A holistic view of this interconnected pathology can impact different levels, from understanding symptoms via diagnosis to improving treatment and refining the evaluation of outcomes. While the text addresses a broad audience, it primarily focuses on medical students, junior doctors, and all healthcare professionals, emphasizing the need for interdisciplinary collaboration in the future identification and management of CKM Syndrome. A comprehensive summary of the most recent developments in CKM Syndrome is also provided, focusing on aspects most pertinent to the biomedical community (Al et al., 2022; Wu et al., 2023).

At first glance, three separate domains can be identified: cardiovascular medicine, nephrology, and internal medicine, considering the metabolic component. In a simplified view, it is known that dysfunction in one system causes a series of linked pathologies that directly affect others and reciprocally amplify the failure of the first system (Sarma et al., 2021). Instead, these feedback loops usually involve several signaling mechanisms, such as neurohormonal pathways and newly discovered metabolic signals from target organs. There is much more to the interplay than that seen in a regular clinical visit, involving individual behaviors and changes in lifestyle, with a special focus on diet and physical activity. On a macro scale, the pursuit of a healthy diet and regular exercise modifies the metabolic framework, leading to a healthier patient. By promoting the reduction of high-energy food and the improvement of kidney and cardiovascular function, pathological network might have been slowed, preventing the onset of myocardial infarction and the need for hemodialysis. Two different patient cases, labeled "A" and "B," are analyzed in four check-ups. As an educational exercise, the patients and symptoms are representative, while the results of check-ups provided are strictly hypothetical. However, it is hoped that this contemplation on crossed effects will highlight to authors the great benefit of a complete itinerary for routine check-ups (Calabresi et al. 2023).

CLINICAL MANIFESTATIONS OF CKM SYNDROME

The Cardiovascular-Kidney-Metabolic (CKM) Syndrome is associated with several clinical manifestations varying greatly among patients (Bedo et al., 2024). While the interconnection between e.g., hypertension, chronic heart failure and renal impairment is obvious somehow, a vast spectrum of symptoms must be considered before taking an effective and individualized therapeutic decision (Sebastian et al., 2024). Hypertension, for instance, may be either intermittent or resistant hypertension, or even an over-treated normotensive condition. Intermittent aldosterone hyper-secretion may also develop; a potassium side effect from renin-angiotensin-aldosterone drugs contributes to such malfunction. Diabetic or non-diabetic CKD development is favored by an increase in the efferent arteriole resistance, and inappropriate vasoconstriction resulting from renin under-expression affects kidneys that are already impaired (Batko et al., 2024; Kanbay et al., 2024).

Hypertensive ISH patients, older age females especially, are most likely to develop cardiac remodeling because of the "afterload mismatch". The loss of arterial elasticity with age renders perfusion pressure more dependent on the flow rate, but coronary vaso-reactivity decreases as well, under older age. A reduction in the diastolic phase of the valve when HR and stroke volume drop may reduce the myocardial perfusion pressure below required levels and thereby provide an ideal substrate for the Chronic Heart Failure epidemic (Shaftoe & Gillis, 2024). Such unhealthy effects cause a further loss in physical activity and related effects on the glycemic and lipidic profiles. The latter are, however, compromised by the CKD itself, with all these factors contributing to a worse degenerative evolution of vascular walls. Dyslipidemia and insulin resistance, however, vary among patients and various populations. Drug treatments may then require fine-tuning, possibly strengthening lipid lowering through absorption inhibitors, or by choosing anti-diabetic drugs that preferentially act on human kidney tissue, such as agonists. Variability within etiopathogenic mechanisms implies differences in age, gender, and co-morbidity, including childhood abuse as a factor significantly influencing therapeutic response (Lange et al., 2023). Other factors include shortness of breath when lying down, that worsens during the night or with exertion; weight gain, reflecting fluid retention and thus high blood pressure; slowness and deterioration of physical activity; fatigue; and poor diuresis. Polyuria and worrisome developments such as chronic urinary tract infections require a prompt specialist evaluation to distinguish aggression by multi-resistant gram-negative bacteria from "simple" over-growth. Along with the proper identification and multidisciplinary approach of the physical clinical history, profound psychological clinical considerations must be reported (Tanacli et al., 2025; Karmazyn & Gan, 2023).

DIAGNOSTIC APPROACHES

Cardiovascular-Kidney-Metabolic (CKM) Syndrome, which is regarded as an integration of metabolic syndrome (MetS), chronic kidney disease (CKD), and cardiovascular disease (CVD), is an emerging topic in medicine. Cardiovascular-Kidney-Metabolic (CKM) Syndrome is a relatively recent term. Poorly controlled metabolic syndrome, leading to type II diabetes and its complications, can cause vasoconstriction and reduce kidney function. Their occurrence or coexistence facilitates the development of other associated disorders, degradation, and co-morbid conditions — is essential to

discriminate against the nature of the pathological condition. Early symptoms can be misinterpreted as symptoms of less serious diseases. Also, when the disease manifests with the combination of the symptoms from the three disorders, these symptoms can be mistaken for other conditions, preventing the correct choice of treatment (Sheen & Huey-Herng Sheu, 2011). Early and accurate diagnosis is of great importance for treatment strategies; thus, novel approaches employing high-performance and multidisciplinary strategies must be exploited. Diagnostic approaches for CKM were derived from traditional methods such as patient examination, laboratory tests, and imaging. Diagnosis might be more accurate when symptoms from three aspects are considered. As the symptoms of CKM might be confusing, because they overlap in the three diseases, doctors in the three divisions need to work together. Fatality can be reduced by diagnosis even when the condition is considered untreatable. However, these three divisions can still overlook the severity of the condition if the patient has a traumatic history, and, at the same time, serious diseases can arise from minor symptoms, which demand precise examinations and high-performance multidisciplinary strategies (Piko et al., 2021). Various diagnostic methods, ranging from traditional methods such as patient examination, laboratory tests, and imaging studies to emerging technologies for biomarker investigation, have been introduced. Abdominal obesity, assessed by waist circumference or waist-to-hip ratio, is the most common feature of MetS patients. CKD patients might have occult moderate hypertension without subjective symptoms. Therefore, SBP, DBP, and pulse rate should also be measured in the medical examination (Matsushita et al., 2022). Urine dipstick, BUN, and eGFR are often measured in kidney function tests. Urinary albumin usually remains negative but can be positive in CKD patients. In addition to the typical test, there are tests such as non-invasive tests of arterial stiffness. Among the various non-invasive tests available to evaluate cardiovascular risk in the current guidelines, testing of carotid intima-media thickness (IMT) and stiffness indices is strongly recommended. CKD is clearly associated with an increased risk of CVD, which is the most common cause of death in patients affected by renal disease. It has been recognized that CV mortality in patients with CKD is at least ten times higher than in the general population. In addition to the traditional markers of cardiovascular risk, such as lipid profile or glucose metabolism, other markers (uric acid, endothelin-1, fibronectin, fibrinogen, C-reactive protein, etc.) have recently been considered as useful tools to improve the assessment of cardiovascular risk and mortality. This is also particularly important for patients with DM. In patients with CKD, the measurement of the CRP significantly correlates with carotid IMT, whereas, in patients with CKD and DM, the measurement of apolipoprotein is significantly correlated with carotid-femoral Pulse Wave Velocity. Nevertheless, major limitations prevent widespread use of these non-invasive tools. Given the widely known increased CV risk, further studies are warranted to improve the understanding of the mechanisms underlying this increased risk. Potential new markers may be explored, or non-invasive tools may be further investigated to refine the assessment of CV risk (Hannan et al., 2021; Figuer et al., 2023; Zocalli et al., 2023).

Biomarkers And Imaging Techniques

The Cardiovascular-Kidney-Metabolic (CKM) Syndrome – which encompasses chronic kidney disease (CKD), metabolic disorder (MD), hypertension (HTN) and cardiovascular abnormality (CA), – has emerged as a severe public health problem. It is crucial to strengthen the understanding and detection of CKM syndrome to design, implement, and evaluate suitable therapies for all components simultaneously (Sebastian et al., 2024). In addition to promoting this new concept, this review further reveals the symptoms, diagnostic methods, and treatments for each component of CKM syndrome, with particular emphasis on recent findings towards an integrated and more efficient approach to CKM syndrome (Zoccali, 2023).

The syndrome resulting from the complex association of CKD, MD, HTN, and CA has gained the attention of clinicians and basic science researchers. Standardized strategies and creative therapies for CKD, HTN, and CA have been reviewed and explored, with a wide focus on the individual components but often neglecting the systematic view of symptoms, diagnosis, and treatment of these three components. It is worth noting that improvements in metabolic disorders and kidney function generally lower blood pressure (BP) and improve coronary endothelial function. The development of effective methods to identify and manage the CKM syndrome will significantly improve comprehensive patient care (Ndumele et al. 2023).

TREATMENT STRATEGIES

Staging and diagnosis represent common approaches in all diseases and shall not be repeated here. Cardiovascular-Kidney-Metabolic (CKM) syndrome treatment plans will typically combine various elements of services known to be effective in broader therapeutic contexts, ideally in a coordinated and harmonized manner. Patient-centered management focuses on the most pressing issues related to the individual rather than the disease process in isolation (Kanbay et al., 2024). A holistic approach is of essential importance because disease states are connected, multifactorial, and have a significant impact on the patient's overall wellbeing. Often, CKM syndrome treatment will include lifestyle-based interventions such as diet, physical activity, and strength training. In this manner, the concept of treatment and lifestyle interventions will be foundational. There may also be pharmacotherapy focused on blood pressure or cholesterol control. Kidney function loss often requires regular follow-up with a nephrologist. Patient counseling and behavior changes can have a dramatic impact on disease progression over time. Given viable treatment options, compliance and desired outcomes can depend on patient preferences and circumstances (Zoccali et al., 2023).

Since some treatments can target multiple disease outcomes, there may be therapeutic agents and interventions that fall outside classification under commonly understood treatment modalities. Finally, some treatments may be experimental, controversial, contraindicated, or not well recognized. These differences are especially important to consider given the relative novelty of CKM syndrome as a unifying term for diseases that have been recognized as interrelated, but have previously been the domain of organized, specific treatment fields (Logeshwaran et al., 2022). It is well known that there is no one-size-fits-all approach to treatment planning, especially given how wide-ranging the potential treatment landscape within CKM syndrome can be. Frequently, treatment plans are tailored to individual patients, based on disease severity, progression, comorbidities, risk factors, patient cooperation, attitudes, or expectations. As such, a detailed overview of therapeutic interventions and treatment approaches can only be of ancillary guidance to healthcare providers, potentially confronting these issues for the first time or considering how to acquire academic knowledge or otherwise assist these patient populations. With this, a broader overview is provided in the hope of giving some guidance, context, and bearings on how to proceed further (Dixon & Isaac, 2023; Davare et al., 2024).

Pharmacological Interventions

Cardiovascular-Kidney-Metabolic (CKM) Syndrome is a very high mortality syndrome that has been recently recognized, high mortality syndrome in which organ crosstalk results in clinical amplification of cardiovascular disease, chronic kidney disease, diabetes mellitus, obesity, and related risk factors comprising a deadly spiral. Undiagnosed, the CKM syndrome advances to premature death with the first manifesting fatal event. Recognizing symptoms is paramount. A 90-minute consultation workshop for health care professionals to fill this knowledge gap was created and will be conducted two to three times a year (Vanholder et al., 2018). However, some may wish to know what pharmacological treatment is appropriate. Whereas some are concerned this does not fit in with the treatment-by-consultation visionary concept, it is acknowledged that such a guideline is missing for health care professionals caring for some of the victims, however futuristic the conservative care visionary approach is (Aggarwal et al., 2024). Pharmacodynamics and pharmacokinetics need to be understood, however, to consider medications that are metabolized through non-oral routes, and to adjust for alterations in V, CL, t1/2, and accumulation over time. To maximize efficacy, optimized pharmacotherapy comprises renin-angiotensin system (RAS) blockade individualized to circadian and individual drug-to-drug variability of BP, cardiotonic drugs, and vitamin K antagonists or DOACs for anticoagulation, the regimens and considerations of which will be discussed. However, pharmacological therapeutic effects have a narrow therapeutic window, which may be the reason for their exclusion from long-term planning, and the interplay with personal and internal environmental factors may bring about side effects (Ndumele et al., 2023). A combined treatment blocking the proposed pathways may offer the most potent clinical benefit. The competitive heavy weight of metabolic, kidney, and cardiovascular failure components and related risk factors, which amass in complex organ crosstalk, resulting in the CKM syndrome, accounts for the observed 6-month progression, giving credit to the hypothesis. Recently discovered RAS-independent alternative pathways contribute additional evidence to the hypothesis that epoxyeicosatrienoic acids compromise the kidney and emphasize the potential to maintain or partially restore kidney function by blocking EET biosynthesis. Pharmacologically, this may be accomplished by a combination of

treatments involving soluble epoxide hydrolase inhibition and drugs counteracting platelet-activating factor or its receptor overexpressed in renal proximal tubule epithelial cells. Newly identified concealment mechanisms are expected to ensure long-term efficacy. In this manner, conservative care offers potential to maintain or improve worsening kidney function up to 1-year follow-up after its implementation (Sebastian et al., 2024). This cautiously opens a novel treatment option for the patients with CKM syndrome, largely neglected in prior art, providing an inventive step in the synthesis of the interleaving parts. These insights may pave the way towards follow-up studies or similar ideas for more effective and novel innovative treatment strategies. Summarily, in contrast to the dearth of guidelines presently available for the CKM syndrome, developed combination regimens are thought to offer the most potent clinical benefit possible. However, the narrow therapeutic window for some pharmacotherapy and the interplay with so many external environmental and personal factors may cause side effects (Cases et al., 2024; Li et al., 2024; Lei et al., 2024).

EMERGING THERAPIES AND FUTURE DIRECTIONS

Traditionally, classifications related to kidney health have been divided into categories such as : 1) acute kidney injury, 2) urine abnormalities, 3) structural kidney disease, 4) variations in glomerular filtration rate, and 5) kidney damage with normal or increased GFR. The latter two divisions are commonly associated with cardiovascular risk factors and damage. CKM progresses as certain stages evolve, gradually leading to multiorgan damage and morbidity. Several controlled studies that followed participants from relatively healthy states to CKM-induced cardiovascular and kidney failures provide a clearer understanding of this process. Novel research illustrates how both individual and multiple components of CKM syndrome diagnosis significantly increase long-term risk (Bedo et al., 2024). Consequently, routine determination of multiple risk factors would greatly facilitate timely recognition of the disease process, thereby increasing the life expectancy of many individuals. On the other hand, the ongoing debate about the most appropriate way to apply these findings in clinical practice acknowledges serious gaps in our knowledge, which constitutes an argument to limit the use of emerging statistical models (Vanholder et al., 2018). Ongoing intensive research efforts continue to unravel the CKM syndrome, eventually leading to a new type of medical intervention that will be much more effective. At this point, the development of simple statistical models or AI that would accurately predict the progression of CKM might be accelerated by sharing ongoing research (Choi et al., 2022; Peng et al., 2024; Murton et al., 2021).

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