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Innovative technologies for the identifying risks of chronic kidney disease

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Abstract

Chronic kidney disease (CKD) represents a growing global health burden, affecting more than 10% of the adult population worldwide and significantly increasing morbidity, mortality, and healthcare costs. Early identification of individuals at risk of CKD progression remains a major clinical challenge, as traditional diagnostic approaches based on serum creatinine and estimated glomerular filtration rate (eGFR) often detect disease only at advanced stages. Recent advances in innovative technologies—including novel biomarkers, artificial intelligence (AI), omics sciences, digital health tools, and advanced imaging—have transformed risk stratification and early detection of CKD. This review summarizes current and emerging technologies for identifying CKD risk, highlighting their clinical relevance, limitations, and future perspectives. Integration of these innovative tools into routine clinical practice holds promise for improving early diagnosis, personalized risk prediction, and prevention of CKD progression.

Keywords: Chronic kidney disease; Risk stratification; Biomarkers; Artificial intelligence; Omics; Digital health; Precision nephrology

1. Introduction

Chronic kidney disease (CKD) is a major global public health problem, defined by persistent abnormalities in kidney structure or function lasting longer than three months and associated with adverse clinical outcomes [1]. According to epidemiological data, CKD affects more than 850 million people worldwide and is projected to become one of the leading causes of years of life lost in the coming decades [2]. The disease is strongly interconnected with non-communicable conditions such as cardiovascular disease, diabetes mellitus, arterial hypertension, obesity, and aging, forming a complex cardio–renal–metabolic continuum. Importantly, CKD not only leads to end-stage kidney disease (ESKD) but also markedly increases the risk of cardiovascular morbidity and mortality, even in its early stages [3].

Despite substantial progress in nephrology, CKD remains underdiagnosed and undertreated, particularly in its initial phases. Early-stage CKD is often clinically silent, with patients remaining asymptomatic until significant nephron loss has occurred [4]. This diagnostic delay represents a critical missed opportunity for prevention, as early intervention has been shown to slow disease progression, reduce cardiovascular complications, and improve long-term outcomes [5]. The challenge of early detection is further compounded by the heterogeneity of CKD etiologies, which include diabetic kidney disease, hypertensive nephrosclerosis, ischemic nephropathy, glomerulopathies, and tubulointerstitial disorders.

Traditional CKD risk assessment relies predominantly on serum creatinine–based estimated glomerular filtration rate (eGFR) and the presence of albuminuria. While these markers are widely available, inexpensive, and incorporated into international guidelines, they have well-recognized limitations. Serum creatinine is influenced by age, sex, ethnicity, muscle mass, diet, and medications, which can result in substantial inter-individual variability and misclassification of kidney function [6]. Albuminuria, although a powerful prognostic marker, may be absent in a significant proportion of

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patients with progressive CKD, particularly in non-diabetic, ischemic, or tubulointerstitial forms of the disease. As a result, reliance on these conventional parameters often leads to late diagnosis, when structural damage and fibrosis are already advanced and largely irreversible.

Moreover, conventional markers primarily reflect established functional impairment rather than early molecular, inflammatory, or structural kidney injury. CKD progression is driven by a complex interplay of hemodynamic stress, endothelial dysfunction, inflammation, oxidative stress, metabolic disturbances, genetic susceptibility, and maladaptive repair processes [7]. These pathophysiological mechanisms precede detectable changes in eGFR by months or even years, highlighting the urgent need for more sensitive and mechanistically informative tools for risk identification.

In response to these challenges, recent years have witnessed rapid development of innovative technologies aimed at transforming CKD risk assessment from a reactive to a proactive and personalized approach. Novel biomarkers reflecting tubular injury, inflammation, fibrosis, and mineral metabolism provide earlier and more specific signals of kidney damage. Omics-based technologies—including genomics, proteomics, metabolomics, and transcriptomics—enable comprehensive characterization of molecular pathways underlying CKD susceptibility and progression, paving the way for precision nephrology [8]. In parallel, advances in artificial intelligence (AI) and machine learning have facilitated the integration of large-scale clinical, laboratory, and imaging datasets to generate highly accurate predictive models of CKD onset and progression.

Advanced imaging techniques, such as functional magnetic resonance imaging, elastography, and contrast-enhanced ultrasound, offer non-invasive assessment of renal perfusion, oxygenation, and fibrosis, complementing biochemical and computational approaches [9]. Additionally, digital health solutions—including wearable devices, mobile health applications, and remote monitoring platforms—allow continuous tracking of physiological parameters and lifestyle factors that influence kidney health, particularly in high-risk populations.

Against this background, the present review explores recent and emerging technological advances for identifying the risk of chronic kidney disease [10]. Emphasis is placed on biomarker innovation, artificial intelligence–based prediction models, omics approaches, advanced imaging modalities, and digital health tools. By synthesizing current evidence, this review aims to highlight how these technologies can improve early detection, refine risk stratification, and support personalized prevention strategies, ultimately contributing to a reduction in the global burden of CKD.

2. Limitations of Conventional CKD Risk Assessment

Serum creatinine-based eGFR remains the cornerstone of CKD diagnosis; however, it reflects functional decline rather than early structural or molecular kidney injury. Albuminuria, although a strong prognostic marker, may be absent in certain CKD phenotypes, such as tubulointerstitial disease or ischemic nephropathy.

Furthermore, conventional risk prediction models inadequately capture the complexity of CKD progression, which involves hemodynamic, inflammatory, metabolic, genetic, and environmental factors [11]. These limitations have driven the development of innovative tools designed to detect subclinical kidney injury and predict future decline before irreversible damage occurs.

3. Novel Biomarkers for Early CKD Risk Identification

The development of functional and structural biomarkers has significantly advanced the early identification of kidney injury, addressing major limitations of serum creatinine and creatinine-based estimated glomerular filtration rate (eGFR) [12]. Unlike creatinine, which reflects global renal function and rises only after substantial nephron loss, emerging biomarkers provide insight into early, subclinical kidney damage, particularly at the tubular and interstitial levels.

Cystatin C has emerged as a robust alternative marker of glomerular filtration. It is produced at a constant rate by all nucleated cells and freely filtered by the glomerulus, with minimal influence from muscle mass, age, or sex. Numerous studies have demonstrated that cystatin C–based eGFR more accurately predicts CKD progression, cardiovascular events, and mortality compared with creatinine-based estimates, particularly in elderly patients and those with diabetes or sarcopenia. Importantly, elevated cystatin C levels may detect early renal dysfunction even when creatinine remains within normal limits.

Markers of tubular injury play a crucial role in identifying early kidney damage before measurable declines in eGFR occur. Neutrophil gelatinase-associated lipocalin (NGAL) is rapidly upregulated in renal tubular epithelial cells in response to ischemic, toxic, or inflammatory injury [13]. While initially studied in acute kidney injury, persistent elevations of NGAL have been associated with chronic tubular damage, accelerated CKD progression, and adverse cardiovascular outcomes. Both plasma and urinary NGAL provide valuable prognostic information, particularly in high-risk populations.

Kidney injury molecule-1 (KIM-1) is a transmembrane glycoprotein expressed in proximal tubular cells following injury. Urinary KIM-1 levels correlate strongly with tubular inflammation, fibrosis, and histopathological damage [14]. Elevated KIM-1 has been shown to predict CKD progression independently of albuminuria and eGFR, highlighting its utility in detecting ongoing tubular pathology that may otherwise remain clinically silent.

Low-molecular-weight proteins such as β2-microglobulin and α1-microglobulin are freely filtered by the glomerulus and almost completely reabsorbed by proximal tubules. Increased urinary excretion of these proteins reflects impaired tubular reabsorption and serves as an early indicator of tubulointerstitial dysfunction. Their measurement is particularly valuable in non-albuminuric CKD phenotypes, drug-induced nephrotoxicity, and ischemic nephropathy.

Collectively, functional and structural biomarkers enable earlier detection of kidney injury, improved phenotyping of CKD, and enhanced risk stratification beyond traditional measures.

3.1. Inflammatory and Fibrotic Biomarkers

Chronic inflammation and progressive fibrosis are central mechanisms driving CKD initiation and progression, linking renal dysfunction with systemic cardiovascular complications. Biomarkers reflecting these processes provide critical prognostic information and offer insights into disease activity and progression risk.

Interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) are key pro-inflammatory cytokines implicated in endothelial dysfunction, oxidative stress, and tubular injury [15]. Elevated circulating levels of these cytokines have been consistently associated with faster eGFR decline, increased albuminuria, and higher rates of cardiovascular events in CKD patients. TNF receptor levels, in particular, have demonstrated strong predictive value for CKD progression in diabetic and non-diabetic populations.

Fibrosis represents the final common pathway of CKD, characterized by excessive extracellular matrix deposition and irreversible nephron loss. Transforming growth factor-β (TGF-β) is a master regulator of renal fibrosis, promoting fibroblast activation and epithelial-to-mesenchymal transition [16]. Elevated TGF-β signaling is closely linked to progressive renal scarring and poor long-term outcomes.

Fibroblast growth factor-23 (FGF-23), a hormone involved in phosphate metabolism, has emerged as a powerful biomarker of early CKD and adverse prognosis. Elevated FGF-23 levels occur early in CKD, even before hyperphosphatemia, and are strongly associated with left ventricular hypertrophy, cardiovascular mortality, and CKD progression.

Incorporating inflammatory and fibrotic biomarkers into predictive models significantly improves CKD risk stratification by capturing active disease mechanisms rather than solely functional impairment. This approach supports a pathophysiology-driven framework for early intervention and personalized management of chronic kidney disease.

4. Omics Technologies and Precision Nephrology

4.1. Genomics and Polygenic Risk Scores

Genomic studies have identified multiple genetic variants associated with CKD susceptibility, including APOL1 risk alleles in individuals of African ancestry. Polygenic risk scores (PRS) aggregate these variants to estimate an individual's inherited risk of CKD.

Genomic risk stratification allows early identification of high-risk individuals long before clinical manifestations appear, supporting targeted prevention strategies.

4.2. Proteomics and Metabolomics

Proteomic profiling enables detection of disease-specific protein signatures associated with early kidney damage and fibrosis. Urinary proteomic classifiers, such as CKD273, have demonstrated predictive value for CKD progression.

Metabolomic analyses identify alterations in amino acids, lipids, and uremic toxins that precede declines in eGFR. These approaches provide insights into disease mechanisms and uncover novel therapeutic targets.

4.3. Transcriptomics and Epigenetics

Transcriptomic and epigenetic modifications reflect dynamic changes in kidney tissue in response to injury. MicroRNAs and DNA methylation patterns have emerged as promising biomarkers for CKD risk and progression.

5. Artificial Intelligence and Machine Learning in CKD Risk Prediction

AI and machine learning (ML) have revolutionized CKD risk identification by analyzing large, complex datasets beyond human analytical capacity.

5.1. Predictive Modeling Using Electronic Health Records

ML algorithms applied to electronic health records (EHRs) integrate demographic data, laboratory values, comorbidities, medications, and longitudinal trends to predict CKD onset and progression. These models outperform traditional risk scores in predicting rapid eGFR decline and progression to end-stage kidney disease [17].

5.2. Deep Learning and Imaging Integration

Deep learning techniques analyze renal imaging, pathology slides, and ultrasound data to detect subtle structural changes associated with CKD. Automated image analysis enhances diagnostic accuracy and reduces inter-observer variability.

5.3. Clinical Decision Support Systems

AI-powered decision support tools provide real-time risk alerts, individualized prognostic estimates, and therapeutic recommendations, facilitating earlier interventions and improved clinical outcomes.

6. Advanced Imaging Technologies

Innovative imaging modalities offer non-invasive assessment of renal structure and function:

- **Functional MRI (fMRI)** techniques, including diffusion-weighted imaging and blood oxygen level–dependent MRI, assess renal perfusion and fibrosis [18].
- **Contrast-enhanced ultrasound** evaluates microvascular perfusion without nephrotoxic contrast agents.
- **Elastography** measures renal tissue stiffness, correlating with fibrosis severity.

These technologies enhance early detection of CKD-related structural changes and improve risk stratification.

7. Digital Health and Wearable Technologies

Digital health solutions play an increasing role in CKD risk identification and monitoring:

- **Wearable devices** track blood pressure, physical activity, and heart rate variability—key determinants of kidney health.
- **Mobile health applications** support patient engagement, medication adherence, and lifestyle modification.
- **Remote monitoring platforms** enable continuous assessment of high-risk patients, facilitating early detection of deterioration [19].

Integration of digital tools with AI-driven analytics enables personalized, real-time CKD risk assessment.

8. Integration of Multimodal Technologies

The future of CKD risk identification lies in the integration of multimodal data—clinical, biochemical, genetic, imaging, and digital health information—into unified predictive platforms. Such systems support precision nephrology, enabling individualized prevention and treatment strategies [20].

Multidisciplinary collaboration between nephrologists, cardiologists, data scientists, and engineers is essential for successful implementation and clinical translation.

9. Challenges and Ethical Considerations

Despite their promise, innovative technologies face several challenges:

- Limited accessibility and high costs
- Data standardization and interoperability issues
- Need for external validation and clinical trials
- Ethical concerns related to data privacy, algorithm transparency, and bias
- Addressing these challenges is critical for equitable and effective implementation.

10. Future Perspectives

Ongoing advancements in artificial intelligence, omics sciences, and digital health technologies are expected to further refine the identification and prediction of chronic kidney disease risk, shifting clinical practice toward a truly preventive and personalized nephrology model. Future research should prioritize longitudinal, multicenter validation of emerging biomarkers and AI-driven prediction models across diverse populations, including patients with diabetes, cardiovascular disease, advanced age, and varying ethnic and genetic backgrounds. Such validation is essential to ensure robustness, generalizability, and clinical reliability [21].

A key future direction lies in the seamless integration of innovative technologies into routine clinical workflows. AI-based risk stratification tools must be embedded within electronic health record systems, enabling real-time risk alerts, automated interpretation of multimodal data, and decision support without increasing clinician workload. User-centered design and clinician training will be crucial to promote adoption and trust in these systems.

From a health system perspective, future studies must also demonstrate the cost-effectiveness and scalability of advanced CKD risk identification strategies. Economic evaluations should assess whether early detection through biomarker panels, omics profiling, or AI-based screening translates into reduced progression to end-stage kidney disease, lower hospitalization rates, and decreased cardiovascular complications. These data are essential for policy-makers and payers to support widespread implementation [22].

Finally, future innovations should emphasize patient-centered outcomes, including quality of life, self-management, and engagement. Integration of wearable devices, remote monitoring platforms, and mobile health applications with predictive analytics can empower patients to participate actively in disease prevention. Collectively, these developments will enable a shift from reactive CKD management to proactive risk mitigation, ultimately reducing the global burden of chronic kidney disease.

11. Conclusion

Innovative technologies have fundamentally transformed the identification and stratification of chronic kidney disease risk, marking a decisive shift from conventional, late-stage diagnostic paradigms toward an integrated precision medicine approach. Traditional reliance on serum creatinine, eGFR, and albuminuria—while still clinically valuable—is increasingly recognized as insufficient for early detection and individualized prognostication. In contrast, emerging tools now allow clinicians and researchers to capture subclinical kidney injury, molecular alterations, and dynamic risk trajectories long before irreversible functional decline becomes evident.

The integration of novel biomarkers reflecting tubular injury, inflammation, fibrosis, and metabolic dysregulation provides deeper insight into the heterogeneous pathophysiology of CKD. Omics-based technologies—genomics, proteomics, metabolomics, and transcriptomics—further expand this understanding by identifying inherited susceptibility, molecular signatures of progression, and potential therapeutic targets. When combined with artificial

intelligence and machine learning, these data sources enable the development of highly accurate predictive models that surpass traditional risk scores and support proactive, individualized clinical decision-making.

Advanced imaging modalities and digital health technologies complement biochemical and computational approaches by offering non-invasive, real-time assessment of renal structure, function, and patient behavior. Wearable devices, remote monitoring platforms, and mobile health applications enhance longitudinal surveillance and patient engagement, which are essential for effective prevention strategies in high-risk populations such as individuals with diabetes, cardiovascular disease, or chronic hypertension.

Despite these advances, successful translation into routine clinical practice requires overcoming challenges related to accessibility, cost, data interoperability, validation, and ethical governance. Multidisciplinary collaboration, robust clinical trials, and health system-level integration are critical to ensure equitable implementation. Ultimately, the strategic adoption of innovative technologies holds substantial promise to reduce CKD incidence, slow disease progression, mitigate cardio-renal complications, and alleviate the growing global burden of chronic kidney disease through earlier, smarter, and more personalized care.

Compliance with ethical standards

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No conflict of interest o be disclosed.

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