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Novel Biomarkers for Early Detection and Risk Stratification in Chronic Kidney Disease

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Abstract
Background: Chronic kidney disease (CKD) is a progressive condition characterized by largely irreversible structural and functional kidney damage, representing a major global public health burden and affecting approximately 13% of the world's population. Its asymptomatic nature in early stages and close association with cardiovascular morbidity and mortality often lead to delayed diagnosis and poor clinical outcomes.
Methods: This narrative review summarizes current evidence on emerging biomarkers for early detection and risk stratification in CKD. Peer-reviewed studies were examined focusing on biomarkers of tubular injury, inflammation, fibrosis, metabolic dysregulation, multi-omics integration, and the application of artificial intelligence and machine learning in biomarker-based risk prediction.
Results: Novel biomarkers such as neutrophil gelatinase-associated lipocalin, liver-type fatty acid-binding protein, monocyte chemoattractant protein-1, soluble tumor necrosis factor receptors, fibroblast growth factor 23, and uromodulin can detect kidney damage earlier and predict disease progression more accurately than traditional tests. New proteomic and metabolomic techniques allow multiple biomarkers to be combined into panels, improving the prediction of kidney and cardiovascular outcomes. The use of artificial intelligence further supports ongoing risk assessment and personalized monitoring of disease progression.
Conclusions: Biomarker-driven approaches offer significant potential to improve early diagnosis, risk stratification, and individualized management of CKD. Addressing translational barriers through large-scale validation and global collaboration is essential to improve patient outcomes.

Keywords: Chronic kidney disease, Biomarkers, Early detection, Risk stratification, Proteomics, Precision nephrology

2. Introduction

Chronic Kidney Disease (CKD) is the inability of the kidney to function, which is progressive and irreversible with time, most commonly evaluated by gradual deterioration of glomerular filtration rate (GFR). It is known to be one of the most significant world-wide public health issues and it affects about 13 per cent of the global population. Five stages are determined by the GFR values where stage 1 is mild kidney damage with preserved filtration where stage 5 is end-stage renal disease (ESRD) in which kidney functioning is severely impaired and necessitate the replacement of kidney. Being chronic and progressive, CKD is a large burden on healthcare systems all over the world and seriously compromises the quality of life of the patients. In addition to the renal complications, CKD has a strong linkage with cardiovascular morbidity and mortality. The incidence of cardiovascular disease in patients with CKD is significantly elevated, and it is the primary cause of mortality in patients. Prompt diagnosis and

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proper risk stratification is thus not only very important in slowing the progression of renal diseases, but also in the prevention of cardiovascular complications. Nevertheless, the silent progression of CKD in the early stages is one of the most crucial problems of the disease management, as well as the patients tend to be asymptomatic at that stage. Consequently, CKD is often diagnosed at later stages, when the damage to the kidney is already significant and curative methods are restricted.

Conventional methods of diagnosis of CKD are mainly based on the serum creatinine and estimated glomerular filtration rate (eGFR). These markers are greatly used in clinical practice but have significant limitations. The age, gender, muscle mass and diet are some of the factors behind serum creatinine that can cause wrong identification of the kidney performance especially in the initial disease stage. Also, eGFR could not be able to identify a subtle or early renal damage and is in most cases insensitive to dynamic renal damage. KDIGO 2012 clinical practice guidelines highlighted the importance of a higher level of diagnostic accuracy and a more prognostic evaluation of CKD, and the limitations of standard biomarkers in the detection of subclinical kidney damage and disease progression [1].

To address such constraints, there has been an extensive research to determine new biomarkers capable of diagnosing injury to kidneys at an earlier stage and with more effective risk stratification. Soluble urokinase-type plasminogen activator receptor (suPAR) is another novel biomarker that is receiving more and more attention as a promising predictor of CKD development and progression. Even without renal dysfunction or incident CKD, higher levels of suPAR have been linked to deteriorated renal functioning, implying that suPAR could find persons who are at high risk even when GFR-based reductions in renal functioning remain unchanged [2]. These results emphasize the possibility of suPAR to be used as an early risk assessment and preventive intervention tool.

Recent developments in proteomic technologies have also increased the field of CKD biomarker discovery. Urinary peptide profiling, specifically, has become a potent method that can be used to detect molecular signatures related to kidney disease. The CKD273 urinary peptide-based classifier is a combination of several urinary peptides indicative of pathological alterations in the kidney, and has shown excellent diagnostic prognostic performance [3]. It has been demonstrated by validation studies that CKD273 can correctly classify patients with CKD compared to healthy patients and also can better predict disease progression and poor renal outcomes than conventional markers [4]. Recent studies have solidified the clinical importance of urinary proteomics and highlighted the fact that they are more effective than traditional biomarkers in the prediction of CKD progression and response to therapy [5].

Inflammation has a primary role in the CKD pathophysiology, which leads to the persistent renal damage, fibrosis, and disease progression. Prolonged signs of inflammation have been much examined as biomarkers. The independent predictive capacity of soluble tumor necrosis factor receptors 1 and 2 (sTNFR1 and sTNFR2) in predicting renal outcomes and mortality in patients with advanced CKD demonstrates their prognostic significance [6]. The sTNFRs have become especially robust biomarkers in the context of diabetic kidney disease to identify patients who are highly susceptible to a rapid development of the disease [7].

Ratios of tubular damage are also very useful in the revealing of the damage on the kidney at the tender age. Urinary neutrophil gelatinase-associated lipocalin (NGAL) has been demonstrated to be associated with renal function deterioration in individuals with glomerular diseases and thus can be used as an early warning of tubular damage [8]. Moreover, multi-biomarker panels use are receiving growing interest, with the combination of multiple complementary biomarkers having been reported to be much more effective in risk stratification and prediction of CKD progression than individual procedures [9]. Mineral metabolism biomarkers have also helped to gain deeper insight into progression of CKD. The early sign of mineral metabolism disturbance has been established as fibroblast growth factor 23 (FGF23), and this protein has been determined to be elevated in CKD patients even before parathyroid hormone and phosphate levels rose [10]. The results of longitudinal studies as in the case of Mild to moderate kidney disease (MMKD) study further affirmed that high FGF23 is an independent predictor of progressing CKD [11]. Moreover, b-trace protein and b2-microglobulin, which are low-molecular-weight proteins, have been linked to ESRD, cardiovascular events, and mortality and have been noted to be prognostic factors, surpassing classical filtration biomarkers [12].

Uromodlin, a kidney-specific protein has also been recently of interest as a plasma and urinary biomarker. Changes in uromodulin have been linked to kidney disease development in hypertensive CKD cohorts, suggesting that it can be used to risk stratify the development [13]. Inflammatory and tissue repair biomarkers have also enhanced the evidence of CKD progression by showing close relations with the long-term renal outcomes [14]. The monocyte chemoattractant protein-1 (MCP-1) in particular has become a major inflammatory biomarker that has been involved in the renal injury and fibrosis and has been shown useful in the ability to track the activities and progression of the disease [15].

In general, late diagnosis of the disease caused by the absence of symptoms at the initial phases and the low sensitivity of traditional markers are significant issues in the management of CKD. New biomarkers have a great potential of earlier detection, better risk stratification, and timely intervention and can slow the course of the disease and enhance clinical outcomes.

Research Objectives

1. To identify novel biomarkers for early detection of chronic kidney disease
2. To assess the role of biomarkers in risk stratification and disease progression

3. To explore the clinical utility of multi-biomarker and advanced analytic approaches in CKD management

Methods

Study Design

The present research was carried out as a narrative review in an attempt to synthesize and critically assess the available literature on novel biomarkers to be used in the early detection and risk stratification of chronic kidney disease (CKD). A review was done to offer a detailed picture of biomarkers that indicated major pathophysiological events, such as tubular damage, inflammation, fibrosis, mineral metabolism, and metabolic imbalance. It focused on biomarkers with clinical relevance or emerging clinical relevance in human populations affected with CKD. Moreover, the selected mechanistic and translational studies such as preclinical and acute kidney injury associated biomarker studies were also incorporated when they gave information on biological understanding of the pathways that were involved in the progression of CKD or informed the translational capacity of biomarkers in CKD.

Literature Search

A thorough search of the literature was conducted in the key biomedical databases, such as PubMed, Scopus, and Web of Science, to find the literature on the topic published until December 2025. Combinations of preset keywords were used in search strategy, i.e., chronic kidney disease, CKD, biomarkers, early detection, risk stratification, proteomics, metabolomics, inflammation, fibrosis, tubular injury, and precision nephrology. Further specific searches were done to find studies of translational biomarker studies that were first designed in acute kidney injury or experimental models where the biomarkers had been found relevant to chronic kidney disease pathogenesis or pathogenesis. Besides doing database searches, reference lists of articles and recent reviews that were selected were also screened manually to determine any other publications of relevance that were not listed in the first search process.

Eligibility Criteria

Studies were included if they were peer-reviewed publications reporting on biomarkers relevant to the diagnosis, progression, or prognostic assessment of chronic kidney disease in human populations. Eligible study designs included original research articles, prospective and retrospective cohort studies, clinical trials, systematic reviews, and meta-analyses. Only articles published in English were considered. Key mechanistic studies, including selected experimental and acute kidney injury-focused investigations, were also included when they provided foundational biological insight into biomarker pathways, renal injury mechanisms, or fibrosis processes relevant to CKD progression. Studies focusing exclusively on dialysis modalities, kidney transplantation, pediatric populations without relevance to adult CKD, or experimental animal models lacking translational applicability were excluded to maintain focus on clinically meaningful biomarkers for chronic kidney disease.

Study Selection

The selection of the study was done in a step-by-step manner. To start with, the titles and abstracts obtained in the database search were filtered by their relevance to the review objectives. At this stage, articles that were evidently not meeting the inclusion criteria were filtered out. The potentially eligible studies were then evaluated in the form of full-texts to ensure relevance and eligibility using predetermined criteria. The selection of the studies was done so as to have a balanced representation of clinical, translational, and mechanistic evidence of the role of biomarkers in CKD detection, progression, and risk stratification. This selection process had the benefit of consistency, reduction in irrelevant literature, and enhancement of scientific consistency and clinical relevance of the narrative synthesis.

Pathophysiology of CKD

The condition of chronic kidney disease occurs as a result of enduring damage to renal epithelial, vascular, and interstitial cells, which causes a gradual loss of nephrons and deterioration of renal functions. Unremitting epithelial damage is at the center of the progression of diseases because injured tubular cells acquire maladaptive phenotypes that support inflammatory and fibrotic responses. It has been shown experimentally that sustained upregulation of kidney injury molecule-1 in tubular epithelial cells is a direct cause of interstitial fibrosis and structural remodeling, thus indicating the significance of epithelial-derived signaling in CKD progression [16]. These destructive repair mechanisms stimulate fibroblasts and stimulate extracellular matrix deposition with permanent tissue scarring. When combined, constant cell damage, ineffective repair processes, and fibrotic remodeling are some of the major factors that trigger chronic kidney disease to end-stage renal failure [17].

Overview of CKD Progression

Chronic kidney disease develops by accruing damage to glomerular, tubular and interstitial structures which eventually leads to progressive nephron destruction and degrading renal function. Maladaptive cellular responses that interrupt normal healing processes are triggered by early pathological injuries like ischemia, metabolic stress, hypertension, and immune-mediated injury. Injury of tubular epithelial cells, dysfunction of the endothelium and a change in microvascular integrity contribute even more to the rapid development of the disease. Chronic cell stress stimulates inflammatory, fibrotic, and accretional extra cellular matrix, which results in permanent structural remodeling of kidney tissue. These pathological processes lead to a progressive reduction in the rate of glomerular filtration rate, which ultimately results in the development of chronic kidney disease with severe persistent conditions and subsequent end-stage renal disease necessitating renal replacement therapy [18,19]. Table 1 shows the key pathophysiological processes that take place in the development of chronic kidney disease. It synthesizes the interaction of glomerular, tubular, inflammatory and fibrotic processes in promoting progressive nephron loss. The table identifies the shift between the initial cellular damage and the irreversible structural remodeling.

Table 1. Key Pathophysiological Mechanisms in CKD Progression

Pathological Process	**Cellular/Molecular Features**	**Impact on CKD Progression**
Glomerular injury	Podocyte loss, capillary damage	Reduced filtration
Tubular injury	Epithelial stress, apoptosis	Nephron loss
Inflammation	Cytokines, macrophage infiltration	Fibrosis promotion
Fibrosis	ECM accumulation	Irreversible damage

Source: Synthesized by the authors from the literature

Role of Inflammation and Fibrosis

The major role of chronic inflammation in maintaining kidney damage is the persistent recruitment of immune cells to the renal interstitium and enhancement of the local inflammatory response. This process centers around chemokines like monocyte chemoattractant protein-1, which helps to mediate leukocyte infiltration, activation of macrophages and the release of pro-fibrotic cytokines later. Unremitting inflammatory signaling enhances the growth of fibroblasts and overproduction of extracellular matrix. This compensatory repair process in the long run leads to progressive interstitial fibrosis, the end common pathway of chronic kidney disease. Fibrotic remodeling causes permanent loss of nephrons, renal architecture derangement and functional impairment that would eventually progress the disease to end-stage renal failure [20].

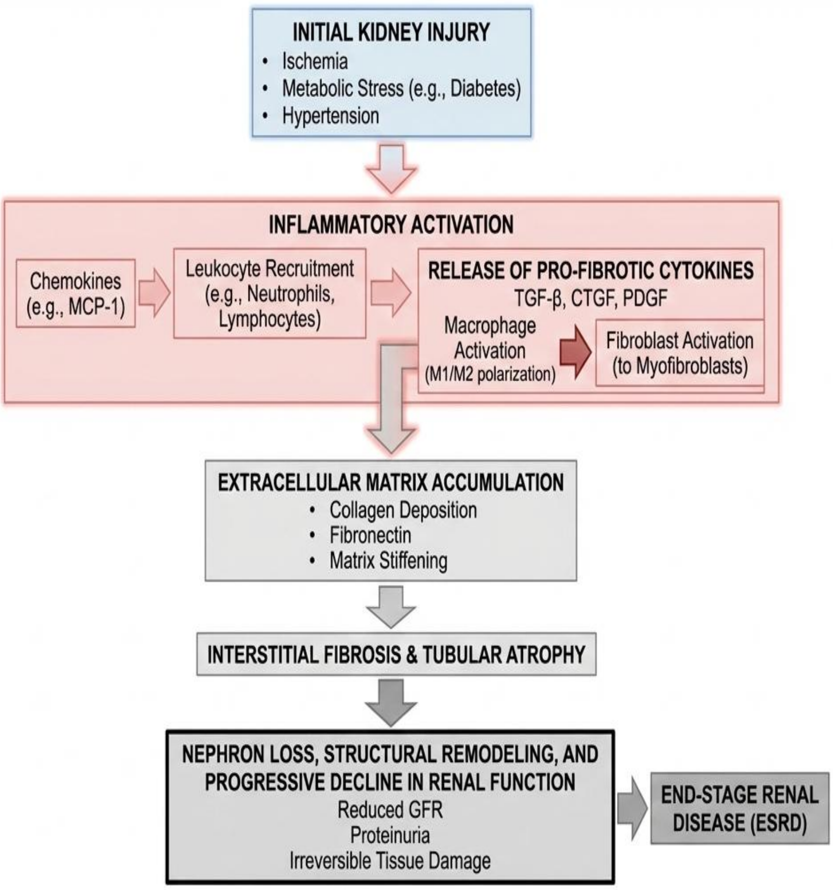

Figure 1. Inflammatory and fibrotic pathways driving chronic kidney disease progression

Source: Author-generated schematic based on published literature

Figure 1 gives a schematic view of the inflammatory and fibrotic pathways that lead to the chronic kidney disease progression. Continuous production of pro-fibrotic cytokines enhances fibroblast stimulation and over-expression of extracellular matrix. The result of this maladaptive response of repair is interstitial fibrosis, tubular atrophy, and progressive loss of nephrons. Eventually, these mechanisms lead to an irreversible structural remodelling, deterioration of renal functioning and the development of end-stage renal disease.

Criteria for an Ideal Biomarker

A perfect biomarker must have a reliable expression of underlying disease biology and exhibit high sensitivity and specificity in the detection of disease at early stages.

The development of biomarkers should have a staged process, starting with the discovery and validation, before its application in clinical practice, which must be reliable and reproducible across populations [21]. The biomarkers that are clinically useful must be measured by means of the standardized, non-invasive, and inexpensive assays, allowing the use in practice on a routine basis. Also, biomarkers are supposed to offer prognostic or predictive to current clinical measures and aid clinical decision-making. Biological relevance, analytical validity, and clinical utility are the primary merits that define effective biomarkers and not an exploratory indicator; they can be easily translated into valuable disease diagnosis, monitoring, and risk stratification tools [22].

Specificity and Sensitivity

A perfect example of the biomarker that can be used to detect chronic kidney disease must be highly specific to renal pathology and sensitive enough to identify early kidney damage before the patient has experienced functional impairment that is detectable. The diagnosis of subclinical disease can be made early enough hence therapeutic intervention, closer follow-up and better prognosis in the long term. Biomarkers that are indicative of ongoing pathological events like inflammation, tubular damage, or fibrosis are more clinically useful than traditional ones, which tend to reflect end stage functional dysfunction. Risk stratification of otherwise clinically stable patients using sensitive biomarkers enables an individual approach to handling the patients. Unlike conventional biomarkers, biomarkers based on pathophysiology have a high level of diagnostic accuracy, prognostic accuracy, and predictability of disease progression at an earlier stage of CKD [23,24].

Predictive Value and Clinical Feasibility

Clinically useful biomarkers must consistently forecast disease progression, cardiovascular complications and mortality yet be non-invasive, reproducible as well as analytically robust. Biomarkers in successful translation to routine clinical practice should be measurable with standardized and validated assays that are similar across laboratories. Affordability and convenience of availability are also significant to facilitate rampant use in various health care institutions. Patient compliance and clinical utility are improved using biomarkers that are included in a regular blood or urine test. Finally, practically feasible with high levels of predictive performance is what can define whether or not a biomarker can be effectively applied to daily nephrology practice and make a significant contribution to improved patient management and outcome [25,26]. Table 2 shows the key features that an ideal biomarker in chronic kidney disease should possess. It assigns a high value to sensitivity, specificity, predictive ability and clinical feasibility. The table shows that the performance of biomarkers may determine the performance of early detection, risk stratification, and disease monitoring. It also brings out the shortcomings of basing only on the traditional functional markers. On the whole, the table gives an outline on how to determine the clinical usefulness of existing and emerging biomarkers.

Table 2. Characteristics of an Ideal Biomarker for CKD

Criterion	Description	Clinical Relevance
Sensitivity	Detects early injury	Early intervention
Specificity	Kidney-specific	Diagnostic accuracy
Predictive value	Forecasts progression	Risk stratification
Feasibility	Easy, low-cost testing	Clinical adoption

Source: Synthesized by the authors from the literature.

Current Biomarkers in CKD

The present clinical evaluation of chronic kidney disease is mainly based on serum creatinine-based estimated glomerular filtration rate and albuminuria as the fundamental diagnostic and prognostic biomarkers. Estimated glomerular filtration rate offers a standardized kidney performance assessment and is the key to CKD staging and management in a variety of clinical practices. Albuminuria is an indicator of glomerular damage and is highly predictive of renal and cardiovascular outcomes. The clinical relevance of eGFR and albuminuria has been supported by large population-based studies that have shown that these two variables are independent but synergistic predictors of mortality and deleterious cardiovascular events. Although these biomarkers are sensitive to limited conditions in early disease diagnosis, they still form the basis of CKD diagnosis, the ability to risk stratify, and to guide care [27,28].

Conventional Biomarkers

The estimation of glomerular filtration rate, albuminuria, and serum creatinine are still the classic diagnostic and staging tools in the clinical practice of chronic kidney disease. The use of these markers is common due to their simplicity, low cost as well as established clinical thresholds. They give vital data that are necessary in classifying the disease, kidney function monitoring, and predicting the renal and cardiovascular outcomes among different patient groups. In specific, albuminuria is a valuable predictor of glomerular damage and vascular exposure. These conventional biomarkers are still at the center of practice in normal CKD evaluation and have been the foundation of the modern-day clinical guidelines and management approaches in spite of their limitations [29,30].

Limitations of Conventional Markers

Although widely used, traditional biomarkers are highly affected by non-renal factors that include age, muscle mass, sex, diet and comorbidity conditions. Such influences may cause inaccurate determination of kidney functioning, especially at the early disease stages. Also, conventional markers only indicate late functional damage as opposed to active tissue damage, and cannot be used to measure early pathological alterations or accurately predict disease process. Consequently, they do not give much information on the current disease activity and personal risk stratification. Such limitations highlight the high level of urgency of complementary biomarkers that can better reflect both early renal disease injury and dynamic disease pathways in chronic kidney disease [31].

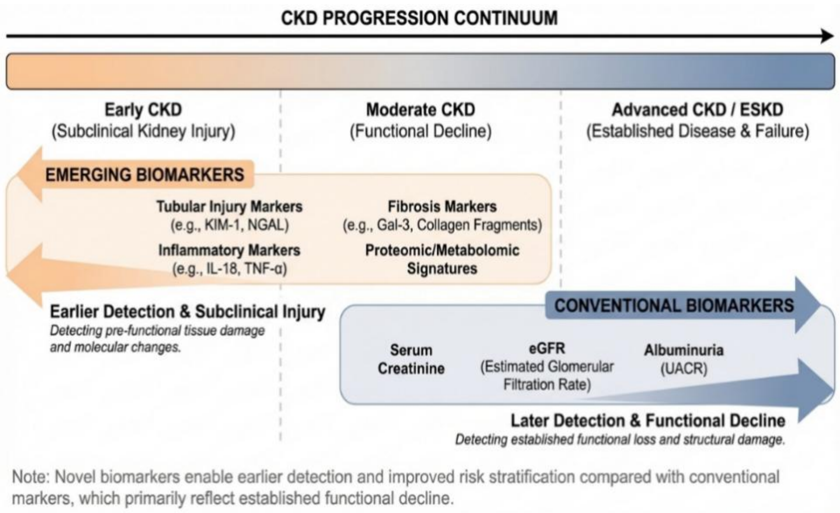

Figure 2: Biomarker–Disease Continuum in CKD

Source: Author-generated schematic based on published literature

The progression of chronic kidney disease and the approximate time at which biomarkers can be detected at any given stage of the disease are shown in Figure 2. It shows that new biomarkers such as tubular injury, inflammation, fibrosis, and omics-based biomarkers can be observed at early and preclinical stages of CKD. Conversely, the traditional biomarkers of serum creatinine, estimated glomerular filtration rate, and albuminuria predominantly indicate the manifested functional loss in the late stages of the disease. This graphic analogy shows the weakness of the conventional signs in detecting at an early stage. In general, the figure highlights how the new biomarkers can be used to facilitate early diagnosis, better risk stratification, and prevention of chronic kidney disease.

Emerging Novel Biomarkers for Early Detection

The new biomarkers have a better sensitivity to identify kidney injury before it becomes impossible to restore normal functioning. Circulating inflammatory biomarkers tourism, especially soluble tumor necrosis factor receptors 1 and 2, have been shown to be strong predictors of the development of end-stage renal disease, notably in patients at high risk like patients with diabetes [32]. Such indicators indicate systemic and renal inflammatory processes that are antecedents of quantifiable decreases of glomerular filtration rate. Secondly, biomarkers of injury have also become relevant clinically as a measure of early renal injury following toxic, ischemic, or metabolic injury. In the clinical use of these biomarkers, early diagnosis, timely intervention, and risk stratification of patients with progressive chronic kidney disease are improved [33].

Urinary and Serum Biomarkers

Biomarkers that indicate tubular damage, inflammation and fibrosis provide better sensitivity in order to detect chronic kidney disease early. Neutrophil gelatinase-associated lipocalin and liver-type fatty acid-binding protein are urinary markers that directly reveal tubular stress and ischemic damage, thus allowing one to detect renal damage prior to the onset of functional deterioration. Inflammatory mediators also trap active pathological processes leading to disease progression and being linked to adverse renal outcomes and mortality. Serum biomarkers are useful as they are complementary to urinary biomarkers because they reflect both systemic inflammation and organ-specific injury, which can offer a more detailed understanding of the disease activity and the risk of progression in chronic kidney disease patients [34,35].

Proteomics and Metabolomics

Multi-marker signatures that indicate the complexity and multifactorial pathophysiology of chronic kidney disease can be identified using high-throughput proteomic and metabolomic technologies. These methods can simultaneously detect dynamic biological changes in relation to inflammation, fibrosis, metabolic dysregulation, and tubular injury by measuring a large number of proteins and metabolites. This type of extensive profiling is more efficient than individual biomarkers in terms of diagnostic accuracy and gives the opportunity to detect disease activity earlier. Further, proteomic and metabolomic research offers beneficial mechanistic information on disease heterogeneity, allowing to distinguish between different CKD phenotypes and disease processes, contributing to better risk stratification and design of specific therapeutic strategies [36]. Table 3 shows a comparison of traditional and novel biomarkers applied in assessing chronic kidney disease. It provides an example of how novel biomarkers are more sensitive reflecting indications of biological pathological processes, including inflammation and fibrosis. The table compares the functional markers with injury-based and multi-marker methods. It emphasizes the promise of proteomic and metabolomic biomarkers to be used in the early diagnosis and precision medicine. The above comparison highlights how biomarkers are increasingly playing a role in enhancing the management of CKD.

Table 3. Conventional vs Emerging Biomarkers in CKD

Biomarker Type	Examples	Reflects	Limitations
Conventional	Creatinine, Egfr	Function	Late detection
Urinary novel	NGAL, L-FABP	Tubular injury	Validation needed
Serum novel	Inflammatory markers	Disease activity	Cost
Omics-based	Proteomic panels	Multi-pathway	Complexity

Source: Synthesized by the authors from the literature.

Biomarkers in Risk Stratification

Biomarkers are important in ranking patients with chronic kidney disease based on their susceptibility to renal and cardiovascular events. Proteinuria, especially, can be considered an effective prognostic biomarker indicating both damage to the glomeruli and the dysfunction of the vascular system in general. High-volume meta-analytic data have also indicated that the degree of proteinuria is independently related to a greater risk of coronary occurrences and mortality regardless of the initial extent of kidney capability. This underscores that proteinuria is not only a useful indicator of the severity of renal diseases but also a predictor of cardiovascular disease. Proteinuria should be included in the risk assessment models to enhance the efficacy of prognostic accuracy and assist in establishing the more personalized clinical management plans in chronic kidney disease patients [37].

Prediction of Disease Progression

Biomarkers that describe major pathophysiological events including inflammation, fibrosis, and metabolic dysregulation allow better patient stratification of chronic kidney disease based on their risk of progression. These biomarkers are able to measure persistent disease activity that cannot be measured by conventional clinical measures. They are by far more effective in predicting the adverse renal and cardiovascular outcomes by incorporating the biological signals of renal injury and systemic complications. The improved risk stratification enables the identification of high-risk individuals earlier, which in turn enables the timely therapeutic intervention, closer observation and personalized management approach that slows down the progression of the disease and lowers the morbidity and mortality [38,39].

Personalized Treatment Strategies

Personalized management of chronic kidney disease based on risk stratification with a set of validated biomarkers assists in determining the intensity of treatment, the frequency, and the choice of nephroprotective interventions. The biomarker-based measurement can help clinicians to design the treatment plans based on an individual risk profile of a patient, not depending only on the population-based thresholds. This personalized care promotes a more timely intervention of the high-risk patients and prevents the unnecessary testing and treatment in the low-risk patients. The biomarker-driven strategies enhance clinical outcomes, reduce disease progression, and improve patient care by better aligning clinical decision-making with underlying disease activity and improving utilization of healthcare resources and reducing overall disease burden [40].

Integrating Biomarkers with Clinical Practice

The use of biomarkers in clinical practice improves the early identification of kidney injury and assists in making clinical decisions in a timely manner. The benefits of urinary biomarkers are the absence of invasiveness and the direct measure of the damage to the renal tubules. It has been shown in clinical trials that urinary biomarkers are more sensitive and specific in detecting kidney damage than traditional functional markers, enabling one to identify kidney injury before substantial drops in glomerular filtration rate have taken place. The use of these biomarkers in the general evaluation can help to intervene earlier, monitor better and assess prognostic patterns. Such advances aid in the shift toward proactive rather than reactive kidney care, reinforcing the use of biomarkers as the complementary tool in the practice of nephrology, along with the traditional diagnostic measures [41].

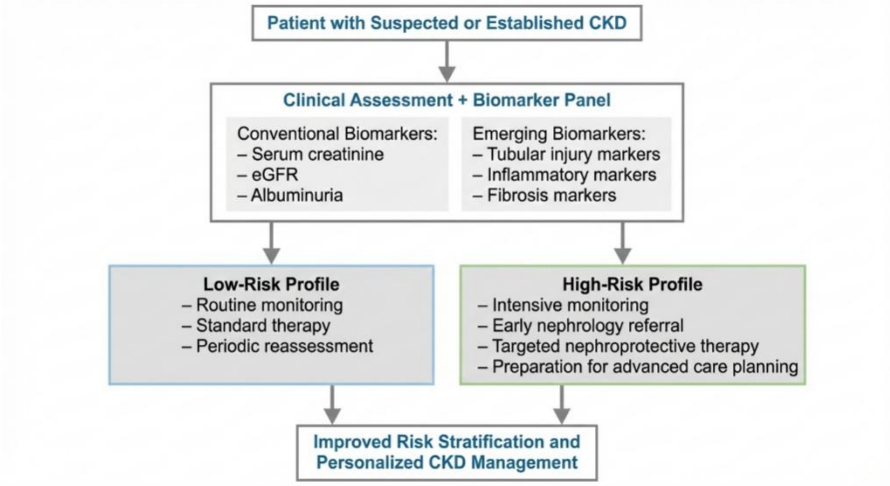

Figure 3: Biomarker-Guided Risk Stratification and Clinical Decision Pathway

Source: Author-generated schematic based on published literature

Figure 3 shows a clinical decision pathway with biomarkers that should be used in the management of chronic kidney disease. The figure shows that the combination of traditional biomarkers with newer biomarkers improves risk stratification in the case of patients with suspected and known CKD. According to a combined clinical and biomarker profile, patients will be divided into low-risk and high-risk profiles. This stratification directs the intensity of monitoring, the decision-making of therapeutics and the period of nephrology referral. On the whole, the figure indicates that biomarker-informed assessment can help to facilitate individual CKD management and proactive clinical care.

Biomarker Panels and Clinical Decision-Making

Integrating biomarkers into composite panels improves the accuracy of prognosis because these biomarkers complement one another in terms of biological processes mediating chronic kidney disease. Multi-biomarker strategies capture the different mechanisms which include inflammation, tubular injury, fibrosis and metabolic dysregulation giving a more in-depth evaluation of the disease activity process compared to the single markers. Clinical decisions based on biomarkers could help to refer patients to nephrology care earlier, escalate therapy on time, and plan renal replacement therapy better. Biomarker panels can help clinicians to meet their monitoring plans and intensities of treatment by enhancing a more accurate risk stratification, to ensure better patient outcomes as well as allowing them to proactively manage chronic kidney disease at its different stages[42, 43].

Challenges in Clinical Implementation

Although biomarkers have potential clinical uses, a number of issues have been associated with the application of biomarkers in everyday nephrology. These are absence of standardization of assay, discrepancy in the analytical performance, necessity of regulatory approval and cost limitation of conducting tests. Familiarity with limited clinician familiarity and uncertainty with the interpretation also contribute to lack of adoption. Also, most biomarkers would need to be validated in large populations before being clinically adopted. To provide a definition of clinical thresholds, utility validation, and reproducibility, it is necessary to establish consensus guidelines and perform strong prospective studies. It will be essential to tackle these obstacles so that the research on biomarkers can be applied to practice and optimize their use as a part of controlling chronic kidney disease [44].

Future Directions

To change the current status of CKD in the world, equal access to proven biomarkers and predictive instruments will be needed, especially in the low- and middle-income nations where the disease burden is disproportionately large. Major multinational partnerships are necessary to guarantee the validation of biomarkers in different populations and health care systems. Even smaller projects such as the Global Kidney Health Atlas show that there is a necessity to organize research methods, data repositories, and policy-level engagement in improving kidney care infrastructures at a global scale [45]. The combination of these interventions will contribute to transforming CKD management into an inclusive, predictive, and preventative, and globally precision medicine system. One of the notable future directions of precision nephrology is incorporation of multi-omics information like genomic, transcriptomic, proteomic and metabolomic layers. High-frequency and pathway-based techniques add strength to prognostic gene signatures, which can be applied in the personalized risk prediction and target therapeutic platforms in CKD populations [46]. Optimal computation models also result in the practical examination of heterogeneous omics information, that is, the recognition of molecular pathways involving the development of diseases [47]. AI and machine learning are highly likely to become even more central to the process of biomarker discovery and clinical risk stratification of chronic kidney disease. Big-data analytics can be used to work with the analysis of complex, high-dimensional clinical data, enhancing the modeling of disease and facilitating data-driven decision-making in nephrology care [48]. AI systems that can predict risk continuously and whose clinical applications can be used to identify patients with a risk of kidney damage sooner than traditional methods have shown this potential to revolutionize longitudinal CKD monitoring and prognosis determination [49]. Such emerging technologies are added to well-known clinical biomarkers, e.g. estimated glomerular filtration rate and albuminuria, to give a more detailed biological understanding of disease heterogeneity and disease progression. The combination of classic risk indicators with modern computational and molecular solutions enhances the accuracy of prognostics and contributes to the more individual approach to the management of CKD [50].

Conclusion

Chronic kidney disease (CKD) is one of the major health challenges in the world due to its insidious progression, lack of symptoms during the early stages, and close presence with cardiovascular morbidity and mortality. Although the standard diagnostic markers of serum creatinine, estimated glomerular filtration rate, and albuminuria have widespread clinical application, they lack sensitivity to diagnose early kidney damage and do not sufficiently reflect patient differences in the disease progression. Consequently, most of the patients are diagnosed at a later stage, when treatment is not as effective and permanent damage has already been done. Emerging biomarkers of tubular damage, inflammation, fibrosis, and metabolic dysfunction have important benefits compared to conventional measures that can help understand ongoing processes of disease activity. These biomarkers contribute to better prognostic outcome because they increase the earlier detection, and permit more accurate risk stratification. The recent advancements in the area of proteomics, metabolomics, and other multi-omics instruments expanded the scope of biomarkers even further, as they can be utilized to characterize the changes in molecules that are associated with CKD in greater detail and explain the heterogeneity of the disease. These measures will help to increase the level of knowledge in the field of pathophysiology and identify patients who are at high risk of the rapid development. Integration of biomarker panels based on artificial intelligence and machine learning can be referred to as an important step towards precision nephrology. These technologies make it possible to make the predictions of risks 24/7, track them in real-time, and develop the management plans, which are specific to the particular patients. To translate these developments into the clinical setting it is however required to possess a standardized assay, large scale validation in heterogeneous populations, cost effective testing, and improved understanding of biomarker interpretation by clinicians. It is of essence that these barriers are overcome through the involvement of collaborative research, multinational research, and international health programs to ensure that biomarker-based care is delivered in a fair manner. Overall, the implementation of novel biomarkers has great potential to transform the CKD care system by allowing earlier intervention, increasing the risk stratification, slowing down the disease progression, and ultimately improving patient outcomes. Future validation studies are required and regular clinical practice cannot be developed.

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