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Review

Advances in the Pathogenesis and Mechanisms of Comorbidity Between Chronic Kidney Disease and Metabolic Syndrome Based on Multi-Omics Technologies

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Abstract: Chronic kidney disease (CKD) is a clinical condition that involves the progressive deterioration of renal function and represents an important medical, social, and economic burden with high morbidity and mortality rates. Metabolic syndrome (MS) is a group of conditions characterized by hypertension (HTN), hyperglycaemia or insulin resistance (IR), hyperlipidaemia, and abdominal obesity. MetS is associated with a high incidence of cardiovascular events and mortality and is an independent risk factor for CKD. MetS can cause CKD or accelerate the progression of kidney disease. Recent studies have found that MetS and kidney disease have a cause-and-effect relationship. With the innovation of new technologies such as large sample population cohort and precision medicine, a large number of multi-omics studies have revealed the intricate molecular networks and genetic maps in organisms through high-throughput sequencing and in-depth mining of bioinformatics, thus laying the foundation for the accurate diagnosis of diseases and the formulation of new therapeutic strategies. Therefore, it is becoming increasingly important to elucidate the relevant mechanisms of research based on multi-omics techniques for chronic kidney disease associated with metabolic syndrome in order to develop new strategies to prevent and slow the progression of kidney disease. To further advance the treatment of chronic kidney disease with metabolic syndrome, future work should focus on a deeper understanding of nephro-metabolic comorbidity, the development of more advanced metabolomics techniques, and the design of highly effective interventions.

Keywords: muti-omics; chronic kidney diseases (CKD); metabolic syndrome (MS); therapeutics; precision medicine

1. Introduction

Chronic Kidney Disease (CKD) is a group of chronic conditions characterized by kidney damage resulting from various primary kidney diseases as well as multiple causes such as diabetes and hypertension. CKD carries high morbidity and mortality rates, imposing a significant medical, social and economic burden on society [1]. CKD is a long-term disease, typically progressing over several years from mild reductions in glomerular filtration rate to end-stage renal failure, which may ultimately require renal replacement therapy [2]. Symptoms such as fatigue, nausea, loss of appetite, itching, cramps, muscle spasms and oedema often only appear in the late stages of the disease [3]. CKD is also closely associated with cardiovascular disease, diabetes and hypertension, and the prevalence of these conditions increases significantly as CKD progresses [3–5].

Metabolic syndrome (MS) is a clinical syndrome centered on insulin resistance, encompassing central obesity, hypertension, insulin resistance, and dyslipidaemia [6]. MS represents a cluster of metabolically interrelated risk factors that increase the likelihood of developing conditions such as diabetes and hyperglycaemia, as well as raising

the risk of cardiovascular diseases like atherosclerosis and chronic kidney disease [7]. The mechanisms by which MS exacerbates renal impairment are multifactorial and primarily involve haemodynamic alterations, neuroendocrine dysregulation and metabolic abnormalities, collectively worsening renal function [8–11].

In recent years, research has confirmed that MS is an independent risk factor for CKD [12–14]. The prevalence of CKD in individuals with MS is 1.8 to 2.5 times higher than in the general population. Furthermore, the MS-CKD comorbidity may result in higher rates of all-cause mortality and cardiovascular events [15–18]. This study reviews the epidemiological characteristics, genetic research, multi-omics technology-supported treatment studies, and future application feasibility of metabolic syndrome combined with chronic kidney disease. The aim is to provide references for the prevention and treatment of chronic kidney disease in patients with metabolic syndrome and high-risk populations.

2. Epidemiological Characteristics and Correlations of Chronic Kidney Disease Combined with Metabolic Syndrome

The latest global survey, conducted in 2024, indicates that individuals with impaired kidney function or chronic kidney disease (CKD) account for around 10% of the global population [19]. In 2019, there were 18.99 million new CKD cases worldwide, bringing the total prevalence to 697 million. Furthermore, 1.43 million deaths were attributed to CKD in 2019. From 1990 to 2019, the average annual incidence rate of CKD increased by 0.69%. With mortality and incidence rates rising annually, CKD is projected to become the fifth leading cause of death globally [3,20,21]. In 2019, elevated systolic blood pressure accounted for 61.6% of CKD-related deaths, while elevated fasting blood glucose contributed to 34.2% of mortality. Furthermore, obesity (excessive BMI) accounted for 27.8% of deaths [22,23]. CKD is typically asymptomatic in its early stages, a characteristic that has led to its designation as a “silent disease” [24]. This lack of symptoms, combined with the absence of routine screening in standard health examinations, frequently results in these early stages being underdiagnosed. This poses a major barrier to constructing sufficiently large cohorts of individuals confirmed to be free of CKD at baseline and prospectively following them over time to identify incident cases of early-stage disease [25–28]. The 2023 survey conducted in China revealed that only 10% of the population is aware of the risks associated with CKD [29]. This indicates that a significant number of individuals in China remain oblivious to their elevated risk for CKD. Such unawareness complicates the early prediction and diagnosis of CKD progression, imposing substantial medical and economic burdens on both the healthcare system and society at large. Consequently, this situation may adversely affect China’s sustainable economic development and hinder efforts toward building a harmonious society [30].

Multiple clinical cohort studies have shown that in the early stages of hypertension and diabetes, damage to vascular endothelial cells can lead to microalbuminuria, and the degree of increase in urinary albumin excretion rate (UAER) is significantly associated with the subsequent risk of developing chronic kidney disease (CKD). As the progression of CKD deepens, the risk of cardiovascular disease (CVD) significantly increases. More than 40% of CKD patients die from cardiovascular disease, and CVD has become the “number one killer” of CKD patients [31].

The National Health and Nutrition Examination Survey (NHANES) in the United States has demonstrated that diabetes, hypertension, cardiovascular disease, and obesity are independent risk factors for CKD [32]. These conditions not only contribute significantly to the pathogenesis of MS but also serve as its core components and associated risk factors. A systematic analysis [33] revealed a significant association between the presence of MS and the development of CKD, with the risk increasing progressively as the number of MS components rises. A study of individuals undergoing health check-ups in China demonstrated that those with metabolic syndrome (MS) face a 1.99-fold higher risk of developing CKD compared to those without MS. Furthermore, the risk escalated with the accumulation of metabolic abnormalities, with individuals exhibiting 3, 4, or 5 metabolic components showing 1.82-, 2.92-, and 3.07-fold increased risks of CKD, respectively [34]. Similar results were also found in a five-year cohort study in Japan [15]. MS can aggravate the occurrence and development of CKD, mainly manifested in its influence on proteinuria and glomerular filtration rate. Compared with the non-MS group, the MS group exhibited significantly elevated proteinuria levels, with a 2.57-fold higher risk of developing proteinuria (≥0.4 g/day) [35]. Another prospective study [36] demonstrated that CKD patients with MS were at increased risk of all-cause mortality and cardiovascular events during a 6.5-year follow-up period, with the strength of this association rising in parallel with the number of MS components present. Extensive clinical and basic research findings indicate that hypertension, diabetes, dyslipidemia, and overweight/obesity are common risk factors for both CVD and CKD. While the cardiovascular disease cascade typically progresses from hypertension/diabetes to atherosclerosis, myocardial ischemia/infarction, and ultimately heart failure, a similar renal disease pathway extending from hypertension and diabetes to microalbuminuria, CKD, and end-stage renal disease may

concurrently accelerate. This bidirectional cardio-renal interaction substantially increases the risks of HF, renal failure, and mortality.

Despite extensive research on the association between MS and CKD, the causal relationship between the two remains unproven. The precise sequence of their onset is equally difficult to define. Due to the susceptibility of individual metabolic syndrome components to fluctuating values and sensitivity to unmeasured lifestyle changes, drug effects, or acute illnesses, some subjects may experience shifts in their overall metabolic syndrome status during follow-up. Similarly, estimated glomerular filtration rate (eGFR) values based on arbitrary eGFR thresholds and CKD diagnoses exhibit variability. Furthermore, simplified diagnostic criteria for metabolic syndrome further limit the ability to draw definitive conclusions about this association. Rising prevalence rates of obesity and CKD may confound the observed link between these two common disease entities. To elucidate the mechanisms underlying the association between metabolic syndrome and CKD, future studies should integrate longitudinal data at the individual level and employ multilevel analysis methods.

3. Research on Genetic Susceptibility to Chronic Kidney Disease and Metabolic Syndrome

With advances in technologies such as large-scale population cohorts and precision medicine, numerous studies have employed high-throughput sequencing and bioinformatics analyses to reveal intricate molecular networks and genetic landscapes. This progress facilitates the characterization of disease-associated genetic variants at the population level, laying the groundwork for precise diagnosis and novel therapeutic strategies.

3.1. Large-Scale Cohorts and Genetic Studies of Chronic Kidney Disease

Large-scale genome-wide association studies (GWAS) have substantially advanced our understanding of the genetic basis of kidney function. A notable German study, for example, integrated 42 longitudinal cohorts encompassing over 300,000 individuals of European ancestry with up to 15 years of follow-up, identifying six novel genetic loci associated with renal function decline. However, as most GWAS, including this one, are based predominantly on European populations [37], the generalizability of these findings to East Asian, particularly Chinese, cohorts remains to be further verified.

With the advancement of precision medicine, disease research has moved beyond phenotypic characterization. Large-scale population studies are evolving from a focus on genetics and transcriptomics to explanations at the proteomic and metabolomic levels. There is a growing trend toward employing integrated multi-omics approaches—spanning genomics, proteomics, and metabolomics—to elucidate complex disease mechanisms and advance predictive disease modeling. For instance, a large-scale study of 35,559 Icelanders uncovered associations between plasma protein levels and 373 diseases and other traits [38]. Another integrated plasma and urine metabolomics-genomics cohort study of 5217 Germans identified 1299 significant genetic associations with plasma and urine metabolites [39], enhancing understanding of distinct metabolomic signatures of renal function. By examining 7073 metabolite-disease combinations, it uncovered links between kidney health and other diseases. For example, the association between dipeptidase 1 and circulating digestive enzymes and hypertension aids in better predicting CKD. These investigations highlight the promise of metabolites as biomarkers for predicting the progression from kidney damage to failure and introduce a novel multi-metabolite model that more accurately predicts the trajectory of renal function decline than traditional approaches. Furthermore, new evidence establishes that metabolic alterations are not only a feature but also a contributor to the pathogenesis of renal fibrosis [40,41]. The integration of omics technologies in cell-tracing animal models, supported by subsequent functional studies, demonstrates that cell type–specific metabolic shifts play a specialized role in driving the fibrotic response [42].

These studies provide valuable insights into the molecular mechanisms of complex diseases. While genetic factors undoubtedly provide a crucial blueprint for disease predisposition, this static view alone cannot capture the dynamic complexity of biological systems. Metabolites, as the functional readouts of cellular processes, offer a real-time snapshot of the physiological state and the organism's dynamic response to environmental and genetic perturbations.

3.2. Genetic Susceptibility to Metabolic Syndrome

Metabolic syndrome arises from a complex interplay of genetic predisposition, environmental exposures, and their interactions. As a polygenic trait, its susceptibility is influenced by the collective effect of numerous genes. Twin studies estimate its narrow-sense heritability to be approximately 13–30%, which can reach up to 50% for certain metabolic components [43–47]. Existing studies have utilized single nucleotide polymorphisms (SNPs) as genetic markers, employing either candidate gene strategies or genome-wide association studies (GWAS) to identify genetic susceptibility loci associated with quantitative metabolic traits [48–54]. These efforts have

revealed multiple susceptibility loci, including the notable tag SNPs rs9939609 F7O, rs629301 SORTI, S12678919 LPL, S1532085 LIPC, S651821 APOA5, IS7412 APOE, rs1532624 CETP, rS671 ALDH2, rS4607517 GCK, and others. Among these representative tag SNPs, some have been localized to causal variants. These include the lipid-associated rs2266788 located in the 3′ UTR of APOA5 and the missense mutation rs671 within an ALDH2 exon, which have been mechanistically linked to alterations in metabolic pathways [55,56].

Beyond using quantitative metabolic indicators as phenotypes, some studies treat metabolic syndrome as a disease entity, seeking core genetic variants that concurrently influence multiple metabolic abnormalities [57–61]. Although the concept of metabolic syndrome is widely adopted in clinical and public health contexts, its utility in genetic research remains controversial. Critics argue that metabolic syndrome represents an aggregate of correlated traits rather than a distinct biological or phenotypic entity. Conversely, other researchers maintain that the metabolic syndrome phenotype holds research value for reflecting shared pathophysiological mechanisms. Genetic investigations into metabolic syndrome susceptibility aim to identify genes and susceptibility loci associated with multiple metabolic phenotypes—specifically those consistent with the pleiotropy hypothesis. Pleiotropy, where in a single genetic variant affects several distinct phenotypes, represents a widespread and efficient biological mechanism. Several pleiotropic phenomena have been documented, such as genetic variants associated with lipid metabolism indicators including high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) [62]. A systematic review suggests that a substantial number of genes and genetic variants exhibit polygenic polyphenicity for complex phenotypes [63]. This evidence supports the notion that genetic pleiotropy is a prevalent feature underlying metabolic abnormalities. Therefore, investigating metabolic syndrome as an integrated phenotype to identify susceptibility loci that coordinately influence multiple metabolic traits is a scientifically justified approach, serving as a vital complement to analyses of individual metabolic components.

Although some genome-wide association studies (GWAS) targeting metabolic syndrome and its components exist, currently identified genetic susceptibility loci explain less than 10% of genetic variation—far below estimates from twin studies, indicating missing heritability. The remaining heritability requires further investigation [64,65]. Additionally, large-scale genome-wide studies of metabolic abnormalities have primarily focused on European populations, with very limited research on East Asian populations, particularly the Han Chinese. Given the genetic background differences between ethnic groups, it is necessary to explore genetic susceptibility loci suited to the genomic characteristics of the Chinese population.

Although genome-wide association studies have identified several loci associated with metabolic syndrome and its components, these collectively explain less than 10% of the estimated heritability—far below estimates from twin studies, indicating missing heritability. The remaining heritability requires further investigation [64,65]. Additionally, large-scale genome-wide studies of metabolic abnormalities have primarily focused on European populations, with very limited research on East Asian populations, particularly the Han Chinese. Given the impact of ethnic-specific genetic architecture, there is a clear imperative to identify susceptibility loci relevant to the unique genomic characteristics of these populations.

Compared to genetic studies, there remains a lack of large-scale research data validated in Chinese populations. This limitation hinders our comprehensive understanding of biological systems, particularly in applications such as early disease diagnosis, pathological process tracking, and discovery of novel therapeutic targets in Chinese populations. Therefore, large-scale metabolomics data are needed to provide new perspectives and tools for elucidating the mechanisms underlying the interaction between chronic kidney disease and metabolic syndrome.

4. The Role of Multi-Omics Technologies in Chronic Kidney Disease Combined with Metabolic Syndrome

4.1. The Imperative for Multi-Omics Research

As a vital branch of modern life sciences, multi-omics research aims to systematically decode the complexity of biological systems and the fundamental nature of disease through the integrated analysis of genomic, transcriptomic, proteomic, and metabolomic data. Central to this approach is the elucidation of biological mechanisms operating across multiple interconnected levels. At the genomic level, variations and alterations in DNA sequences directly influence an individual's genetic characteristics and disease susceptibility [66]. Transcriptomics, the analysis of RNA expression, reveals how genes are activated or suppressed under specific conditions, reflecting the complexity of gene expression regulation [67]. Proteomics focuses on protein expression, modifications, and interactions, offering crucial insights into cellular function and signaling networks [68]. Metabolomics tracks changes in metabolite profiles, serving as a functional readout of the organism's response to internal and external perturbations [69]. These omics layers are not isolated entities but form an intricately connected network of molecular pathways that collectively regulate physiological processes and drive disease pathogenesis.

The necessity of multi-omics approaches lies in their ability to provide an integrative perspective that reveals synergistic interactions across molecular layers. Gene mutations (genomics) may lead to functional alterations in specific proteins (proteomics), which in turn affect metabolic pathways (metabolomics), with these changes ultimately manifesting as phenotypic traits. By integrating these data, researchers can construct complete pathways from genes to phenotypes, uncovering core molecular mechanisms of disease. Furthermore, multi-omics studies can reveal redundancy and robustness within biological systems—how organisms maintain homeostasis when specific pathways are disrupted.

Multi-omics technologies—including genomics, transcriptomics, proteomics, and metabolomics—provide a systems-level view of molecular alterations in CKD by integrating data across different levels. For instance, systems biology approaches have been leveraged to incorporate metabolomic profiles into dynamic models of CKD, helping to pinpoint key pathogenic drivers and candidate therapeutic targets [70]. This integrated multi-omics strategy advances not only the discovery of novel biomarkers but also provides a scientific basis for personalized treatment. Research in cardiorenal syndrome (CRS) has demonstrated that its pathogenesis stems from a synergistic interplay of endothelial damage, immune dysregulation, inflammatory cascades, and oxidative stress [71]. In parallel, diabetic kidney disease (DKD) progression is governed by concurrent shifts in DNA methylation, transcriptional programs, and metabolic pathway dynamics [72].

Multi-omics studies hold promise for identifying new therapeutic targets, as evidenced by SGLT2 inhibitors that effectively retard the progression of diabetic kidney disease. Beyond treatment, metabolomics combined with clinical variables enables more accurate profiling of individuals at high risk for developing CKD.

4.2. Application of Metabolomics in Renal Impairment

Metabolomics, a non-invasive, high-throughput analytical technique capable of quantifying metabolite abundance and mapping metabolic pathways, has been extensively applied to CKD research, providing crucial insights into its pathophysiology.As renal function declines, the metabolomic profiles of CKD patients undergo substantial remodeling, with numerous metabolites demonstrating strong associations with disease progression, cardiovascular events, and all-cause mortality [73]. Furthermore, metabolomic studies of both acute kidney injury and CKD progression have highlighted the critical involvement of lactate metabolism and the tricarboxylic acid cycle in renal pathology [74].

Metabolomics demonstrates potential in early prediction and risk assessment for CKD, particularly in disease diagnosis, risk forecasting, and mechanism research. By employing high-throughput, highly sensitive analytical techniques to systematically profile metabolites in biological samples, metabolomics enables the screening and identification of novel biomarkers for early diagnosis and prediction of CKD progression [66]. Lipidomics, as a specialized branch of metabolomics, has emerged as particularly valuable in early CKD diagnosis and monitoring. While conventional renal biomarkers exhibit limited sensitivity in early disease stages, lipidomics offers a more sensitive and specific approach. For instance, liquid chromatography–mass spectrometry (LC-MS)-based metabolomic studies have revealed significant alterations in plasma and urine metabolites in CKD patients, including glucaric acid, 5-hydroxyindole-3-acetic acid, and asymmetric dimethylarginine, which are closely associated with disease progression [67]. Furthermore, metabolomics has revealed abnormalities in arginine and proline metabolism, tryptophan metabolism, and the pentose phosphate pathway in CKD patients. For instance, metabolomic analysis has identified certain metabolites (such as citrulline and choline) as significantly associated with CKD onset, potentially reflecting non-GFR-dependent renal function. The application of urine metabolomics also shows promise for early disease detection [75].

Clinically, metabolomics technologies have been applied to enhance assessment of glomerular filtration rate and identify risk biomarkers for CKD and its complications [68]. Future research should further explore the specific mechanisms linking metabolic syndrome to CKD and develop metabolomics-based early diagnostic and therapeutic strategies. Additionally, prospective studies and multicenter collaborations represent key directions for advancing this field.

Metabolomics plays a vital role in identifying and quantifying small-molecule metabolites whose alterations are closely associated with kidney disease progression. For instance, studies reveal that 193 metabolites exhibit significant changes in end-stage renal disease (ESRD) patients compared to CKD patients, and these alterations can predict CKD progression to ESRD [69]. Amino acids and their metabolites are associated with multiple aspects of CKD, including its onset, progression, cardiovascular events, and immune responses [76–78]. Alterations in these metabolites offer novel insights and targets for CKD prevention, diagnosis, and treatment.

In terms of mechanism research, Metabolomic studies have revealed significant gut microbiota dysbiosis in CKD patients, underscoring the impact of microbial ecological imbalance and dysregulated microbiota-derived

metabolites. For instance, functional interactions between the gut microbiota and host metabolism play a crucial role in CKD progression [79]. Research has also identified the tryptophan metabolic pathway has been implicated in CKD pathogenesis, suggesting that inhibiting this pathway may be a promising target for slowing disease progression [80].

4.3. Application of Metabolomics-Based Personalized Therapeutic Strategies in Chronic Kidney Disease Management

Metabolomic profiling provides a powerful approach for personalizing CKD management by identifying high-risk patients and optimizing therapeutic strategies. For instance, metabolomics can pinpoint specific metabolic pathway abnormalities in patients, enabling selection of the most suitable drugs and treatment plans [81]. Furthermore, metabolomics can help identify novel therapeutic targets, such as the role of DNA-PKcs in chronic kidney disease [82], opening possibilities for developing new treatment strategies.

Regarding disease heterogeneity and subtype identification, metabolomics demonstrates significant potential in characterizing chronic kidney disease subtypes. A prominent example is the Kidney Precision Medicine Project (KPMP), a decade-long initiative sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases, which employs multi-omics approaches—including metabolomics—to redefine the molecular taxonomy of CKD and acute kidney injury, while simultaneously identifying novel therapeutic targets [83,84]. This multicenter collaborative research holds promise for achieving personalized and revolutionary care by defining disease heterogeneity and validating precise pathways for specific drug targets.

Although the application of metabolomics in chronic kidney disease (CKD) management remains at a nascent stage, its potential is increasingly evident. For instance, metabolomic analysis has been employed to elucidate the therapeutic mechanisms of Fushengong Decoction (FSGD) in chronic renal failure (CRF), revealing its efficacy and demonstrating the utility of metabolomics in studying traditional Chinese medicine interventions. Furthermore, the introduction of metabolomics technologies offers a more comprehensive and in-depth perspective for the clinical diagnosis of chronic kidney disease.

5. Multi-omics Technologies for Treating Chronic Kidney Disease Combined with Metabolic Syndrome in Future Research

Multi-omics anticipated to most significantly advance the diagnosis and management of chronic kidney disease (CKD) encompass the convergence of proteomic and transcriptomic profiling, multiplexed ion beam imaging (MIBI), urinary proteomics, artificial intelligence (AI), and magnetic resonance imaging (MRI). Together, these approaches leverage complementary strengths to provide multidimensional insights into disease mechanisms, progression, and therapeutic opportunities.

5.1. Integrative Proteomics and Transcriptomics

Research indicates that integrating proteome and transcriptome data can identify multiple novel therapeutic targets for chronic kidney disease [85]. This approach employs various statistical genetic analysis methods, such as Mendelian randomization analysis and colocalization analysis, to screen for targets with potential impact on chronic kidney disease from multi-omics data, providing crucial reference for CKD treatment and new drug development.

5.2. Multiplexed Ion Beam Imaging Technology

Multiplexed Ion Beam Imaging (MIBI), combined with spatial transcriptomic platforms, enables the simultaneous identification of key renal cell populations and infiltrating immune cells at single-cell resolution [86]. This technique enables the acquisition of multiple markers at single-cell resolution, providing deeper insights into the mechanisms underlying kidney disease progression to improve diagnosis and treatment.

5.3. Urinary Proteomics

Urinary proteomics has garnered increasing attention for its potential in early diagnosis and monitoring of chronic kidney disease. Rapid advances in mass spectrometry have propelled urine proteomics research, including techniques such as two-dimensional gel electrophoresis-mass spectrometry (2DE-MS), liquid chromatography-mass spectrometry (LC-MS), surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF-MS), and capillary electrophoresis-mass spectrometry (CE-MS) [87].These techniques facilitate the identification of urinary biomarkers, thereby playing a crucial role in diagnosing kidney diseases, monitoring disease progression, and developing drug targets.

5.4. Artificial Intelligence Technology

Artificial intelligence (AI) is creating new opportunities for predicting and treating chronic kidney disease (CKD) through enhanced diagnostic tools. AI technologies can identify patient risks earlier, enabling more effective prevention and treatment. For example, an AI prediction model using the XGBoost algorithm achieved a C-statistic of 0.84 for predicting end-stage kidney disease, while demonstrating the ability to handle missing patient variables and generate an interpretable scoring system [88].

5.5. Magnetic Resonance Imaging (MRI) Technology

Advanced MRI technology has enabled the development of detailed structural and functional "maps" of the human kidney, enhancing our understanding of renal function and ultimately improving the monitoring and treatment of chronic kidney disease [89,90]. This non-invasive assessment, which evaluates renal blood flow and oxygen delivery within a single one-hour scanning session, demonstrates significant potential for clinical translation and broader implementation in routine patient care.

6. Conclusions and Future Perspective

Metabolism has garnered considerable attention in nephrology research, leading to deeper mechanistic understanding of its role in renal pathophysiology. The availability of high-throughput metabolomic and transcriptomic platforms, combined with functional analyses, has enabled comprehensive characterization of the metabolic landscape in chronic kidney disease (CKD) [91,92]. Furthermore, circulating metabolite profiling is emerging as an innovative non-invasive approach for diagnosing and monitoring CKD, assessing prognosis, and evaluating therapeutic responses, although definitive data translation to clinical practice remains pending. Understanding the cellular specificity of renal metabolite production is crucial for comprehending whole-organ metabolic changes, validating therapeutic targets, and improving the rational selection of biomarkers [93]. Building on current insights, forthcoming studies ought to prioritize the development of innovative treatment modalities by leveraging integrated proteomic and metabolomic frameworks to refine patient stratification in acute kidney injury. Such approaches will help delineate genetic determinants of disease susceptibility and therapeutic response, validate clinically relevant biomarkers, and establish functional stress assays—collectively accelerating the translation of mechanistic discoveries into targeted clinical interventions.

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The authors declare no conflict of interest.

Reference

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