

Albuminuria as a Predictor of Kidney Failure Progression: A Systematic Review and Meta-Analysis of Clinical Evidence

Daniel Corina*

Center for Atherosclerosis, Polyclinic of Tor Vergata, Rome, Italy

***Corresponding author:**

Daniel Corina, Center for Atherosclerosis, Polyclinic of Tor Vergata, Rome, Italy. E-mail: dany_corina@gmail.com

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Abstract

Albuminuria is widely recognized as an important indicator of kidney damage and is routinely used to evaluate disease severity and progression in individuals with chronic kidney disease (CKD). Because alterations in urinary albumin excretion often occur before irreversible loss of kidney function, changes in albuminuria have been proposed as an early surrogate endpoint in clinical trials investigating CKD therapies. However, confirmation of its predictive value across different patient populations and treatment strategies remains essential.

Keywords: Albuminuria; Chronic Kidney Disease; Kidney Failure; Urinary Albumin-to-Creatinine Ratio (UACR); Surrogate Endpoint; Renal Disease Progression; Systematic Review; Meta-Analysis; Randomised Controlled Trials; Biomarkers.

Introduction

Albuminuria, defined as the abnormal excretion of albumin in the urine, has long been recognized as a hallmark of glomerular injury and a key clinical indicator of kidney damage. Beyond its diagnostic utility, albuminuria—commonly quantified using the urinary albumin-to-creatinine ratio (UACR)—has emerged as an important prognostic marker, with higher levels consistently associated with faster rates of kidney function decline, increased cardiovascular risk, and elevated mortality. Given that changes in albuminuria often precede measurable declines in glomerular filtration rate (GFR), it has been proposed as an early and responsive marker of treatment efficacy in CKD (1).

Chronic kidney disease (CKD) is a progressive condition affecting a substantial proportion of the global population and is associated with significant morbidity, mortality, and healthcare burden. As CKD advances, the risk of kidney failure—requiring dialysis or transplantation—rises considerably, making early identification of patients at risk and timely therapeutic intervention critical priorities in nephrology care (2).

Traditional clinical trials assessing kidney-protective therapies have relied on hard outcomes such as kidney failure or a doubling of serum creatinine concentration. While clinically meaningful, these endpoints typically require long follow-up periods and large sample sizes, since they occur relatively late in the disease course (3). This creates practical and financial challenges for evaluating new therapeutic agents, particularly as it may delay patient access to potentially beneficial treatments. Consequently, there has been growing interest in identifying valid surrogate endpoints that can reliably predict long-term kidney outcomes over a shorter time frame, thereby accelerating the pace of clinical research and drug development (4).

Given its close biological relationship with kidney damage and its responsiveness to therapeutic intervention, albuminuria has been proposed as a candidate surrogate endpoint for CKD progression (5). Several individual trials evaluating renin-angiotensin system inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors, and other nephroprotective agents have demonstrated that reductions in albuminuria are frequently accompanied by improved long-term renal outcomes. However, the consistency,

magnitude, and generalizability of this relationship across diverse patient populations, underlying CKD etiologies, and treatment classes have not been fully established through pooled analysis (6).

To address this gap, we conducted a systematic review and individual participant data (IPD) meta-analysis of randomized controlled trials to evaluate the relationship between early treatment-induced changes in UACR and subsequent risk of major kidney outcomes, including kidney failure and doubling of serum creatinine. By synthesizing data across a large number of trials and participants, this analysis aims to strengthen the evidence base supporting the use of albuminuria as a valid and clinically meaningful surrogate endpoint, with the goal of informing future trial design and regulatory decision-making in nephrology (7).

This systematic review and meta-analysis integrated individual participant data from 48 randomized controlled trials comprising 85,681 participants with varying causes of CKD. The analysis examined the relationship between treatment-induced changes in the urinary albumin-to-creatinine ratio (UACR) after six months and subsequent major renal outcomes, including kidney failure or a doubling of serum creatinine concentration. Statistical models were applied to quantify the association between early reductions in albuminuria and long-term renal risk (8) (Figure 1).

Discussion

The pooled findings demonstrated a consistent association between early decreases in UACR and improved renal outcomes. On average, every 30% reduction in geometric mean UACR in the intervention group, relative to the control group, corresponded to an approximately 19% lower risk of reaching the composite

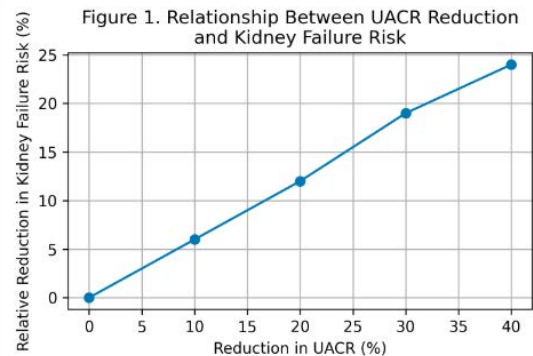


Figure 1: Relationship between reduction in urinary albumin-to-creatinine ratio (UACR) and the relative reduction in kidney failure risk.

kidney outcome. The strength of the association remained moderate to high across the included studies, with a median coefficient of determination (R^2) of 0.66. Subgroup analyses indicated that the predictive relationship was generally consistent irrespective of the underlying cause of CKD, suggesting broad clinical applicability (9, 10).

Conclusion

The evidence indicates that reductions in albuminuria are closely linked with a lower likelihood of progressive kidney dysfunction and kidney failure. These findings reinforce the value of albuminuria as a reliable surrogate endpoint for evaluating therapeutic efficacy in CKD clinical trials and support its incorporation into future nephrology research and drug development.

Characteristic	Description
Study design	Randomized controlled trials (RCTs)
Number of studies	48
Total participants	85,681
Study population	Adults with chronic kidney disease (CKD) of various etiologies
Intervention types	Renin–angiotensin system inhibitors, SGLT2 inhibitors, immunosuppressive agents, antihypertensive therapies, and other nephroprotective interventions
Comparator	Placebo, standard care, or active comparator
Surrogate endpoint	Six-month change in urinary albumin-to-creatinine ratio (UACR)
Primary clinical outcome	Kidney failure or doubling of serum creatinine concentration
Mean follow-up	Variable across studies (typically 2–5 years)
Statistical approach	Individual participant data meta-analysis with Bayesian regression modeling
Main finding	A 30% reduction in UACR was associated with an approximately 19% lower risk of kidney failure or doubling of serum creatinine
Overall conclusion	Early reduction in albuminuria is a meaningful surrogate marker for long-term renal outcomes

Table 1. Characteristics of Studies Included in the Meta-Analysis

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