Πανεπιστημιακο
Γενικο Νοσοκομειο Ιωαννινων

Challenging the Albuminuria Paradigm: Why Total Protein Remains Essential in High-Grade GN

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UACR (ACR) in Screening and Risk Stratification

American Diabetes Association®

KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES® KDIGO

ESH European Society of Hypertension

Screening

Monitoring

Risk Stratification

Treatment Guidelines

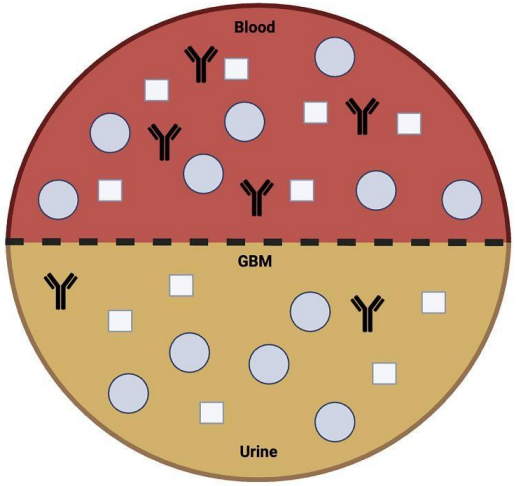
ACR, albumin-creatinine ratio; UACR, urinary albumin-creatinine ratio.

1. KDIGO CKD Work Group. *Kidney Int*. 2024;105(4S):S117-S314; 2. American Diabetes Association Professional Practice Committee. *Diabetes Care*. 2025;48(1 Suppl 1):S59-S85; 3. Mancia G, et al. *J Hypertens*. 2023;41(12):1874-2071.

Pros and cons of albuminuria in diagnosis and prognosis of kidney diseases

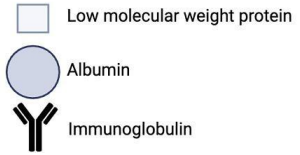
Pros

- Reflects damage to glomerular capillaries
- More highly standardized
- Higher specificity and sensitivity to changes in glomerular permeability
- Higher sensitivity to detect some glomerular diseases, such as diabetic nephropathy
- UACR is more costly than UPCR, but increases in diagnostic accuracy justify the higher cost
- Better and more reliable marker in CKD



Cons

- Does not capture other urinary proteins associated with kidney disease, e.g. light chains, myoglobin
- Limited evidence for outcome prediction in GN



1. **Better standardization**
2. **Higher precision**
3. **Pathophysiological relevance of albumin as a marker of glomerular injury**

Nephrol Dial Transplant, gfag020, https://doi.org/10.1093/ndt/gfag020

Study Aims

Background

- Albuminuria (UACR) is the primary biomarker for CKD detection, risk stratification, and monitoring — endorsed by KDIGO, ADA, and ESH guidelines
- In glomerulonephritis (GN), the relative contribution of albumin vs. non-albumin proteinuria (NAP) varies substantially by disease type and severity

Study Aims

- Evaluate whether UACR can replace UPCR or 24h total protein (24h-UTPR) as a monitoring tool in patients with biopsy-proven GN
- Assess longitudinal reliability of each proteinuria metric using intraclass correlation coefficients (ICC)
- Quantify clinical agreement between UACR and total protein measurements across varying levels of protein excretion using Bland-Altman analysis

Methods

Study design

- Retrospective cohort study — 84 patients with biopsy-proven glomerular disease, followed for up to 24 months
- 3 Greek nephrology centres (University of Ioannina, Hippokration Athens, University of Patras)

Inclusion criteria

- Biopsy-proven GN with concurrent availability of UACR and UPCR and/or 24h-UTPR and/or 24h-Ualb

Statistical analysis

- Pearson/Spearman correlation coefficients for cross-sectional associations
- Intraclass correlation coefficients (ICC) for longitudinal reliability of each metric
- Bland-Altman analysis for clinical agreement between UACR and total protein measurements
- Proportional bias assessed by regression analysis

Patient Characteristics

Baseline Characteristics (n= 84)	
Demographics	
Mean age	61 ±1 4 years
Sex	66% male
Etiology	
IgA Nephropathy	36%
Membranous Nephropathy	28%
FSGS	14%
Baseline laboratory values	
eGFR (ml/min/1.73m^2)	63 ± 30
UPCR (g/g Crea)	3.5 ± 4.3
UACR (g/g Crea)	2.6 ± 3.2
24h-UTPR (g/day)	3.6 ± 4.8
24h-Ualb (g/day)	2.5 ± 3.1

Baseline Characteristics (n= 84)	
Treatment at baseline	
ACEi/ARB	95%
SGLT2i	64%

Follow-up events (24 months):

- 1 death
- 1 started KRT
- 5 with >40% eGFR decline
- 6 MACE

Results: Longitudinal Reliability and Correlation

Longitudinal reliability — intraclass correlation coefficients (ICC)

- All four metrics showed high longitudinal stability (all $p < 0.001$)

Measurement	ICC- Average Measures	Sig
UPCR	0.86	<0.001
UACR	0.91	<0.001
UTPR 24h	0.87	<0.001
UAlb 24h	0.93	<0.001

Correlation analysis

- **UACR vs. UPCR: r = 0.91 (p < 0.01)**
- **UACR vs. 24h-UTPR: r = 0.88 (p = 0.02)**

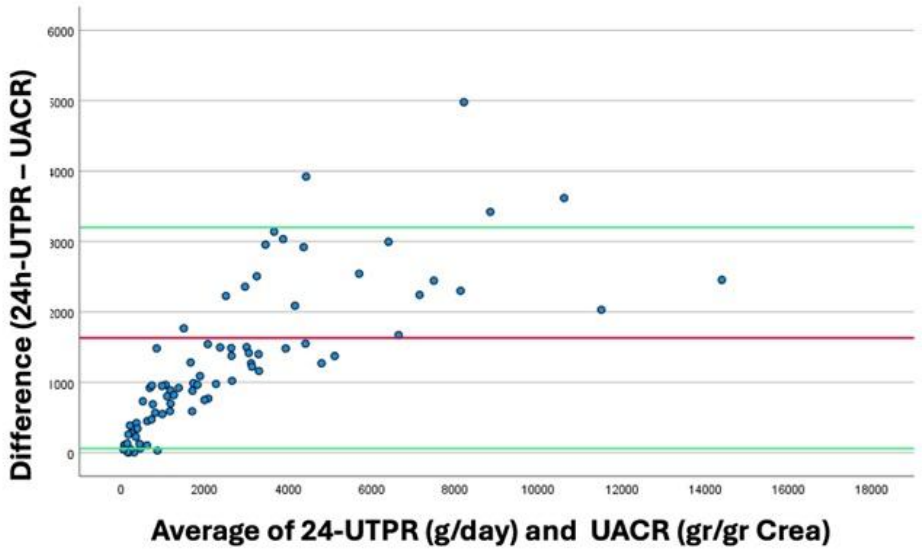
- Albumin-specific metrics (UACR, 24h-UAlb) showed the highest internal measurement consistency
- Strong correlations suggest UACR and total proteinuria track similarly in mild-moderate disease

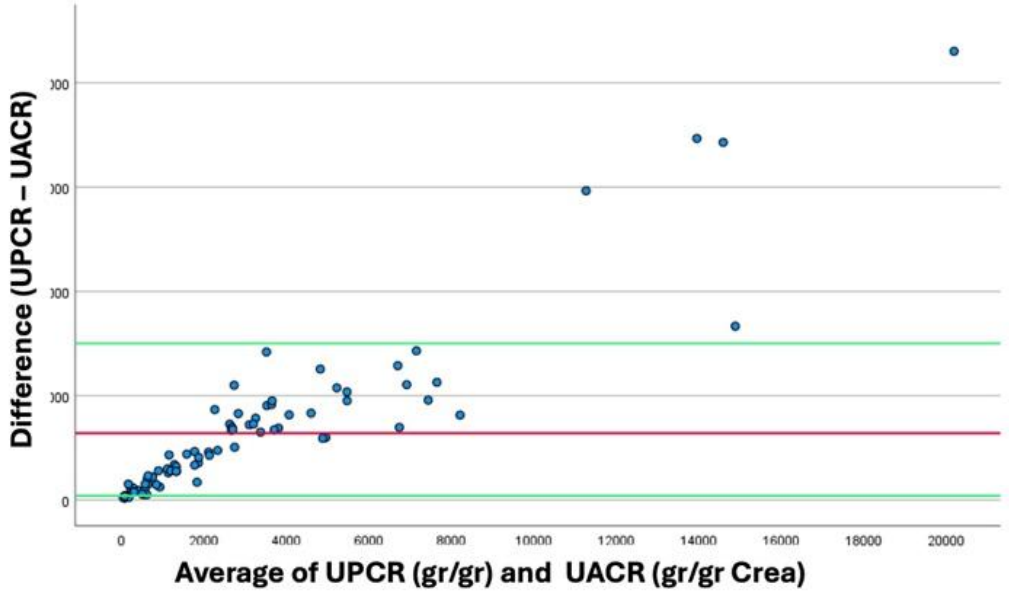
Results: Bland-Altman Analysis

Bland-Altman analysis: UACR vs. total protein measurements

- **Agreement was maintained at proteinuria levels below 3 g/day**

- **At levels above 3 g/day (nephrotic range):**
  - Trumpet-shaped divergence pattern indicating increasing variance
  - Significant proportional bias ($p < 0.01$) — UACR systematically underestimates total proteinuria
  - Growing contribution of non-albumin proteinuria (NAP) not captured by UACR





Conclusions

- UACR and UPCR are highly correlated in mild-to-moderate GN — both track similarly when total protein excretion is below 3 g/day
- **They are NOT interchangeable in patients with high-grade (nephrotic) proteinuria — significant proportional bias emerges above 3 g/day**
- UACR likely underestimates total protein burden in nephrotic-range GN, potentially leading to inaccurate risk stratification
- **Total proteinuria (UPCR or 24h-UTPR) remains the more reliable monitoring metric for patients with highly proteinuric glomerular disease**