ORIGINAL ARTICLE

Serum uromodulin concentrations correlate with glomerular filtration rate in patients with chronic kidney disease

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KEY WORDS

chronic kidney disease, diagnostic accuracy, glomerular filtration rate, serum uromodulin

ABSTRACT

INTRODUCTION Urinary uromodulin excretion has been associated with kidney diseases. However, serum uromodulin concentrations have not been extensively studied in patients with chronic kidney disease (CKD), and the results of published studies are inconsistent.

OBJECTIVES The aims of the study were to evaluate serum uromodulin concentrations in patients with CKD and to assess the utility of serum uromodulin measurements for diagnosing CKD stages.

PATIENTS AND METHODS This observational study included 170 patients with CKD stages 1 to 5, not treated by renal replacement therapy, and 30 healthy individuals. The serum levels of creatinine, cystatin C, and uromodulin were measured, and estimated glomerular filtration rate (eGFR) was calculated according to the 2012 CKD Epidemiology Collaboration cystatin-creatinine equation.

RESULTS Among patients with CKD, serum uromodulin concentrations were significantly lower than in controls, and were strongly negatively correlated with renal retention markers (ie, serum creatinine and cystatin C) and strongly positively correlated with eGFR. An inverse, hyperbolic relationship between serum creatinine and uromodulin levels was analogous to the well-known association between serum creatinine concentrations and eGFR. A receiver-operating characteristic curve analysis showed a high diagnostic accuracy of the measurement of serum uromodulin concentrations in the assessment of CKD stages.

CONCLUSIONS Serum uromodulin concentrations are closely correlated with eGFR, which is the recommended measure of renal function. As uromodulin is produced exclusively by renal tubular cells, the assessment of uromodulin levels in patients with CKD may be an alternative method for evaluating the number of functioning nephrons.

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INTRODUCTION Uromodulin, also known as Tamm-Horsfall protein, under normal conditions, is the most abundant protein in urine. It is produced exclusively by the epithelial cells lining the ascending limb of the loop of Henle.[1-3] Uromodulin is anchored in the cytoplasmic membrane of epithelial cells via glycosylphosphatidylinositol located in the apical part of epithelial cells of renal tubules, where it is proteolytically cleaved and released into the lumen of the renal tubules. In this way, it is excreted in urine in amounts of 100 to 200 mg/d.[4,5] It has been shown that uromodulin can also be released from tubular cells in the basolateral region of the plasma membrane of the loop of Henle cells, from where it reaches the interstitial space of the kidneys and blood, and is present in serum at very low concentrations (70–540 ng/ml).[6,7] The significance and mechanism of uromodulin release in the basolateral area of tubular cells has not yet been clarified.[8]

Several important biological functions are attributed to uromodulin. It maintains water and electrolyte balance in renal tubules and suppresses the crystallization of calcium in the kidneys.[4,9-11] Uromodulin also acts as a defense against bacterial infections of the urinary tract, especially bacteria that produce type 1 fimbriae,[10,12] and exhibits immunomodulatory effects through interaction with the cells of the immune system.[13-15] Identified mutations in the *UMOD* gene leading to premature intracellular polymerization, resulting in an abnormal accumulation of mutant protein inside the cells of the renal tubules, increase damage and apoptosis of renal tubular cells, and cause a group of rare diseases called uromodulin-associated kidney disease, or uromodulin storage diseases.[4,16,17] Recent genome-wide association studies have shown that modifications in the *UMOD* gene are associated with an increased risk of chronic kidney disease (CKD), nephrolithiasis, and hypertension, and uromodulin-associated single nucleotide polymorphisms may either predispose an individual to CKD or accelerate its progression.[2,18,19] The relationship between uromodulin and CKD has not been fully defined, although it seems that uromodulin may play a role in the development and progression of CKD. Nevertheless, it is believed that uromodulin may be a potential urinary biomarker which reflects renal function, CKD, and hypertension.[20-22]

Most studies conducted so far have focused on uromodulin levels in urine, while the occurrence of uromodulin in blood and its serum concentrations have not been extensively studied with respect to CKD.[23]

The aims of our study were to evaluate serum uromodulin concentrations in patients with stages 1 to 5 of CKD regardless of the cause of the disease, and to assess the relationship between serum uromodulin levels and kidney function, as reflected by the markers of renal retention (serum creatinine and cystatin C) as well as the estimated glomerular filtration rate (eGFR). Moreover, we assessed the diagnostic accuracy of the measurement of serum uromodulin levels to differentiate between healthy individuals and CKD patients and to diagnose CKD stages.

PATIENTS AND METHODS The study cohort consisted of 170 patients (men and women) with CKD stage 1 to predialysis stage 5, treated in the Nephrology Outpatient Clinic at the Department of Nephrology of the University Hospital in Krakow, Poland: 90 patients were recruited in the years 2011 to 2012 and 80 patients in 2015. The inclusion criteria were CKD stage 1 to predialysis stage 5 and age above 18 years. CKD in all patients was diagnosed prior to the study, according to the current guidelines of the Kidney Disease: Improving Global Outcomes[24] (ie, when functional or structural markers of kidney damage were present for at least 3 months). Following diagnosis, all patients remained under regular control at the Nephrology Outpatient Clinic for at least 6 months before the study. The control visits included serum creatinine measurements and eGFR assessment repeated every 3 to 6 months. Patients with acute worsening of renal disease or exacerbation of glomerulonephritis were not included in the study. The exclusion criteria were as follows: lack of approval for participation in the study, pregnancy or lactation in women, treatment with immunosuppressive drugs, the diagnosis of systemic autoimmune disease, amyloidosis, cancer, hepatitis B or C, and acute inflammation (C-reactive protein levels ≥10 mg/l; white blood cell count $\geq 10 \times 10^3/\mu l$, or fever). The study did not include patients after renal transplantation. The control group consisted of 30 healthy individuals. Both patients and controls provided signed informed consent for participation. The research project was approved by the Bioethics Committee of the Jagiellonian University, Kraków, Poland (approval number, KBET/212/B/2010).

On enrollment, patients were interviewed and examined physically, including blood pressure measurements and the assessment of body mass index (BMI). Fasting blood samples were taken for routine tests and immunochemistry. Routine laboratory tests were performed on the day of blood collection. Blood for the determination of uromodulin and cystatin C was allowed to clot for 30 minutes followed by centrifugation for 10 minutes at 4000 RPM at 16°C. The serum was aliquoted and frozen at –80°C until analysis. Before measurements, serum was thawed at room temperature and vortexed 3 times for 1 second at the intervals of 1 second.

Serum creatinine levels were measured using the Jaffe kinetic method, IDMS-standardized (Roche Diagnostics GMBH, Mannheim, Germany). The measurement of uromodulin and cystatin C levels was performed by an enzyme-linked immunosorbent assay (ELISA) using commercial reagent kits (Biovendor, Brno, Czech Republic) and an ELx808 spectrophotometer (Bio Tek ® Instruments, Inc., Winooski, Vermont, United States), according to the manufacturers' instructions. Uromodulin Human ELISA Assay was a sandwich ELISA with a biotin-labelled antibody, a calibration range of 0.5 to 32 ng/ml, and a detection limit of 0.12 ng/ml (the standard was human urine-based). Intra- and interassay coefficients of variation were 2.8% or less and 7.6% or less, respectively. Human Cystatin C ELISA was a sandwich enzyme immunoassay with a polyclonal antihuman cystatin C antibody conjugated with horseradish peroxidase, a calibration range of 200 to 10 000 ng/ml, and a detection limit of 0.25 ng/ml (standards were calibrated against the European Reference Material ERM-DA471/IFCC). Intra- and interassay coefficients of variation were 1.9% or less and 10.4% or less, respectively.

The eGFR was calculated based on age, sex, race, and serum creatinine and cystatin C concentrations, according to the 2012 CKD Epidemiology

TABLE 1 Characteristics of the study group

Parameter	Total cohort (n = 170)	Women (n = 73)	Men (n = 97)	*P* value
age, y	55 ±19	58 ±19	53 ±19	0.08
BMI, kg/m^2	26.1 (22.9–29.4)	25.0 (22.0–29.2)	27.7 (23.8–29.8)	0.07
body surface area, m^2	1.92 (1.72–2.06)	1.71 (1.62–1.88)	2.00 (1.90–2.11)	<0.001
systolic blood pressure, mmHg	131 ±14	130 ±14	132 ±14	0.2
diastolic blood pressure, mmHg	81 ±9	79 ±9	82 ±9	0.04
serum creatinine, µmol/l	128 (86–205)	107 (72–166)	150 (101–237)	<0.001
serum cystatin C, ng/ml	1.48 (0.99–2.05)	1.43 (0.95–1.96)	1.50 (1.10–2.06)	0.4
serum uromodulin, ng/ml	68.8 (38.2–109.9)	72.6 (38.7–126.0)	68.8 (37.2–105.3)	0.4
eGFR (CKD-EPI $_{cr\text{-}cys}$) ml/min/1.73 m^2	43.3 (25.0–77.4)	46.9 (26.7–80.5)	42.8 (22.7–65.4)	0.3
uric acid, µmol/l	367 (308–417)	332 (276–415)	380 (345–440)	0.04
urea, mmol/l	8.0 (6.1–11.7)	9.0 (6.4–11.8)	7.9 (6.1–10.4)	0.7
total cholesterol, mmol/l	5.15 (4.50–5.70)	5.40 (4.80–6.10)	5.00 (4.40–5.60)	0.4
CRP, mg/l	1.26 (ND–3.47)	1.62 (ND–3.66)	1.23 (ND–2.79)	0.2

Data are shown as mean ± SD or median (lower–upper quartile).

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; CKD-EPI $_{cys\text{-}cr}$, 2012 Chronic Kidney Disease Epidemiology Collaboration cystatin-creatinine equation; CRP, C-reactive protein; ND, not detected (below the limit of detection)

Collaboration cystatin-creatinine (CKD-EPI$_{cr\text{-}cys}$) equation.[24]

Statistical analysis The number of patients (percentage of the group) was reported for categories, and mean ± SD or median (lower–upper quartile) for quantitative variables, according to distribution. The Shapiro-Wilk test was used to check for normality. Differences between groups were studied using the *t* test or the Mann–Whitney test for 2 groups, and the Kruskal–Wallis analysis of variance with the Conovan post-hoc test for more than 2 groups. Contingency tables were analyzed with the Pearson χ^2 test. Pearson correlation coefficients and multiple linear regression were used to study associations between serum uromodulin levels and other variables; right skewed variables (including serum uromodulin) were log-transformed with natural logarithm before the analysis. A receiver-operating characteristic (ROC) curve analysis was used to assess the diagnostic accuracy of serum uromodulin levels in diagnosing CKD (ie, differentiating between healthy volunteers and CKD patients) and determining CKD stages. The values of the area under the ROC curves were reported with 95% confidence intervals. The tests were 2-tailed and the results were considered significant at a *P* value of less than 0.05. The STATISTICA 10 package (StatSoft, Tulsa, Oklahoma, United States) was used for all computations.

RESULTS The study cohort consisted of 170 patients with CKD (73 women, 97 men) at a mean age of 55 ±19 years. The causes of CKD were glomerulonephritis in 45% of the patients, pyelonephritis in 23%, diabetic kidney disease in 12%, polycystic kidney disease in 1%, and other causes in 19%. The baseline characteristics of the participants are shown in **TABLE 1**. Women had lower systolic blood pressure, body surface area, and serum concentrations of creatinine and uric acid. The other analyzed parameters did not differ between women and men. The stages of CKD were classified based on the eGFR calculated using the CKD-EPI $_{cr\text{-}cys}$ equation. Stage 1 was diagnosed in 28 patients (16%); stage 2, in 30 (18%); stage 3a, in 26 (15%); stage 3b, in 26 (15%); stage 4, in 44 (26%); and predialysis stage 5, in 16 (9%).

The proportion of patients with specified causes of CKD was not uniform throughout the CKD stages. In particular, patients with glomerulonephritis accounted for 79% of those with stage 1, 63% of those with stage 2, 42% of those with stage 3a, 27% of those with stage 3b, 25% of those with stage 4, and 37% of those with stage 5 of CKD. No significant stage-independent differences in serum uromodulin levels were detected between patients with different CKD causes.

Uromodulin concentrations in the serum of patients with CKD were significantly lower than those in the control group: 68.8 ng/ml (38.2–109.9 ng/ml) vs 191.2 ng/ml (89.1–299.1 ng/ml), respectively (*P* <0.001). There were significant differences between controls and patients with CKD stages 2 to 5. Among patients with CKD, we observed a gradual decline in the concentrations of serum uromodulin levels with progression of kidney disease, as shown in **FIGURE 1**. The median serum uromodulin concentrations were 149.5 ng/ml in stage 1, 97.8 ng/ml in stage 2, 97.4 ng/ml in stage 3a, 65.3 ng/ml in stage 3b, 34.6 ng/ml in stage 4, and 25.1 ng/ml in stage 5 of CKD. The differences between patients with different CKD stages were significant, except for the difference between stages 2 and 3a,

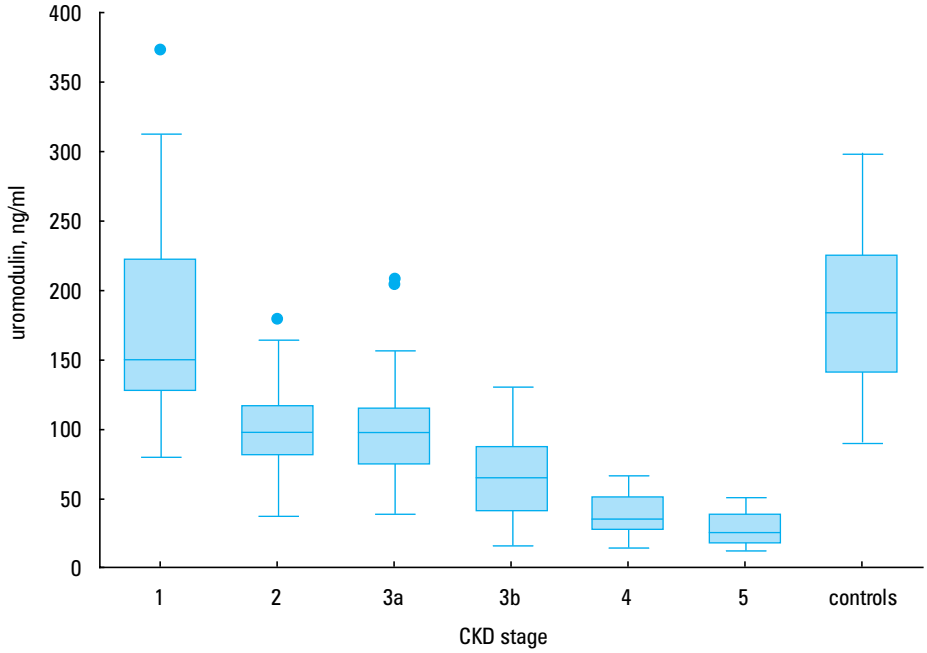

FIGURE 1 Serum uromodulin concentrations in patients with chronic kidney (CKD) disease stages 1 to 5 and in healthy controls. Data are shown as median, interquartile range (box), nonoutlier range (whiskers), and outliers (points).

and stages 4 and 5. There were no significant differences in serum uromodulin levels between patients recruited between the years 2011 and 2012 and those recruited in 2015, when eGFR was used as a covariate ($P = 0.2$).

In patients with CKD, an inverse, hyperbolic relationship between serum creatinine and uromodulin levels closely reflected the well-known association between serum creatinine concentrations and eGFR (FIGURE 2). Strong negative correlations were observed between log-transformed serum uromodulin and serum creatinine and cystatin C levels, and a strong positive correlation was revealed between log-transformed serum uromodulin levels and eGFR calculated using the CKD-EPI $_{cr\text{-}cys}$ equation (FIGURE 3). Serum uromodulin levels did not correlate with BMI or body surface area ($P = 0.6$). Inverse correlations were observed between log-transformed serum uromodulin levels and age ($r = -0.39$; $P < 0.001$) as well as systolic blood pressure ($r = -0.18$; $P = 0.02$). The association between log-transformed serum uromodulin levels and log-transformed eGFR was independent of sex, age, BMI, and body surface area (TABLE 2).

We attempted to evaluate the diagnostic accuracy of serum uromodulin concentrations in the differentiation between CKD patients and healthy subjects and in diagnosing CKD stages. The results of the ROC curve analysis are shown in FIGURE 4. The values of area under the ROC curve were in each case well above 0.8. For the selected cut-off points, the diagnostic sensitivity was above 80% and the diagnostic specificity above 60% in all cases.

DISCUSSION In the present study, we showed that serum uromodulin concentrations in patients with CKD were significantly lower than in healthy subjects, and that the lower concentrations were associated with more advanced stages of CKD. This correlation was contrary to those observed for other widely used markers, such as serum creatinine and cystatin C, the concentrations of which increase due to renal retention along with the progressive loss of active nephrons. Instead, uromodulin levels correlated positively with eGFR calculated using the CKD-EPI $_{cr\text{-}cys}$ equation. The relationship between serum creatinine and uromodulin levels was inversely proportional and hyperbolic, and largely reflected a similar relationship between serum creatinine and eGFR. A positive linear correlation between log-transformed uromodulin and log-transformed eGFR was highly significant. Moreover, serum uromodulin measurements enabled a diagnosis of CKD and its stages with high diagnostic accuracy.

The filtration process is necessary to eliminate byproducts of ongoing metabolism (uremic toxins) and GFR is widely considered the single most important and useful indicator of overall kidney function. Uromodulin is produced exclusively in the renal tubules, and the high correlation between serum uromodulin levels and eGFR suggests that serum uromodulin may be an alternative accurate marker of kidney function.

We observed a strong negative correlation between blood uromodulin concentrations and age, which is consistent with the well-known deterioration of kidney function in elderly patients, reflected by increasing serum creatinine and cystatin C levels and by decreasing GFR. However, serum uromodulin did not correlate with BMI or body surface area. The relationship between serum uromodulin concentrations and eGFR (CKD-EPI $_{cr\text{-}cys}$) was independent of age, sex, BMI, and body surface area. Therefore, it may be a potential indicator of kidney function with a diagnostic value similar to that of eGFR, independently of standard demographic parameters.

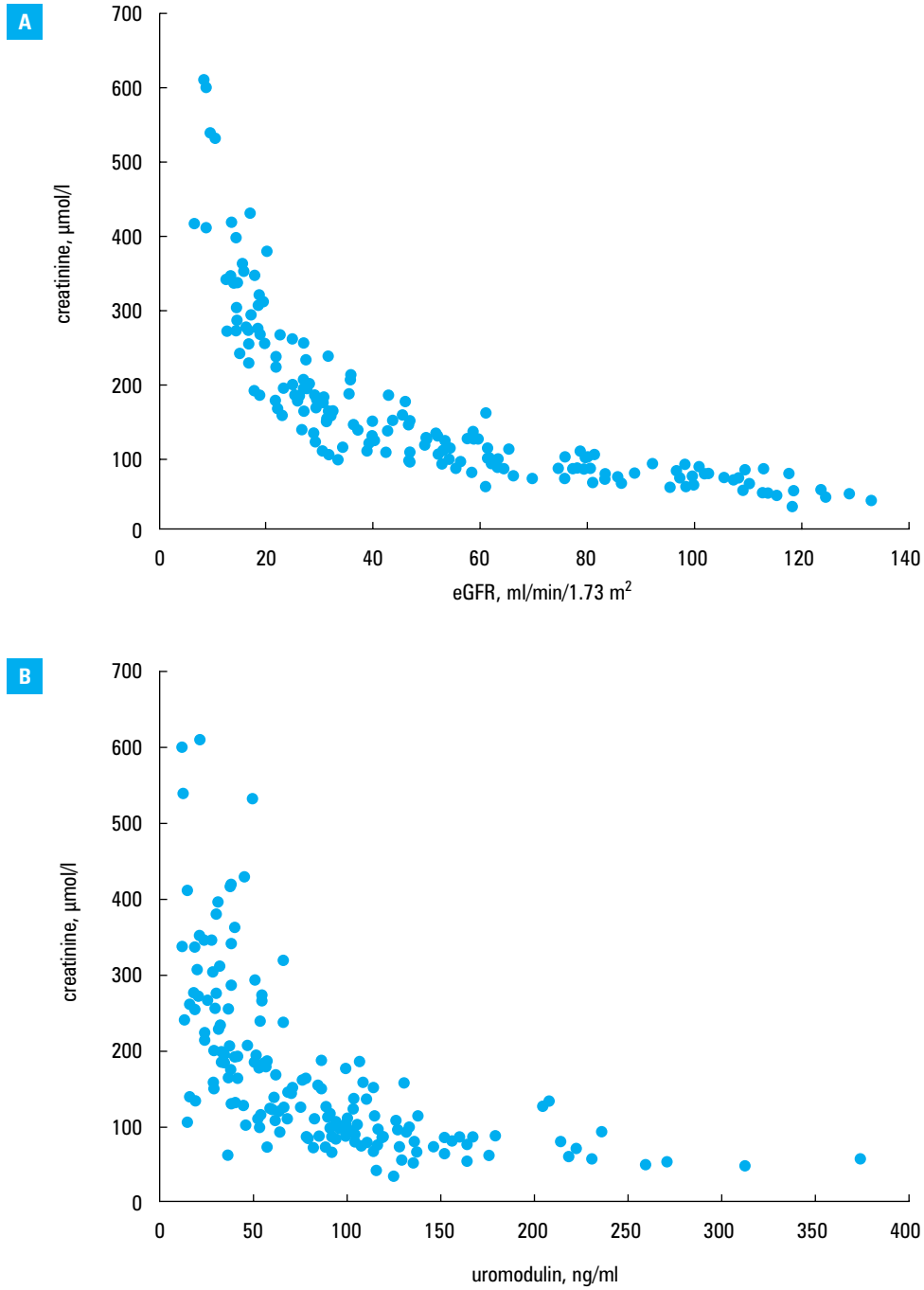

FIGURE 2 Correlations between estimated glomerular filtration rate (eGFR) calculated using the 2012 Chronic Kidney Disease Epidemiology Collaboration cystatin--creatinine equation, and serum creatinine levels (**A**) and relationship between serum uromodulin and serum creatinine levels (**B**)

To date, most published studies exploring the association between uromodulin and kidney function concentrated on urinary uromodulin levels.[7,8,25-27] The most recent study by Garimella et al[25] examined the predictive value of uromodulin excretion in urine to assess the progress of kidney disease and all-cause mortality in a large elderly population, including 2948 participants of the Framingham Heart Study. The higher levels of urinary uromodulin were associated with a reduced risk of progression of kidney disease and mortality. The authors concluded that the amount of uromodulin excreted in urine may indicate renal tubular function and may serve as a prognostic marker independent of eGFR and albumin-to--creatinine ratio.

The relationship between renal function and serum or plasma uromodulin concentrations has been less extensively studied than that between renal function and urinary uromodulin levels, and the results of these studies are inconsistent.[6,23,28-30] In 1985, Thornley et al[30] showed increased plasma concentrations of uromodulin in 65 patients with CKD and observed a positive correlation between the measured clearance of endogenous creatinine and concentration of uromodulin in plasma; however, they did not observe such a correlation in 26 healthy subjects. More recently, Prajczer et al[29] studied uromodulin concentrations in serum and urine in 14 healthy persons and 77 patients with CKD. In this study, decreased eGFR was accompanied by reduced excretion of uromodulin in urine. The relationship

FIGURE 3 Correlations between log-transformed (natural logarithm [ln]) serum uromodulin and ln serum creatinine (**A**), ln serum cystatin C (**B**); and ln estimated glomerular filtration rate (eGFR) calculated using the 2012 Chronic Kidney Disease Epidemiology Collaboration cystatin-creatinine equation (**C**)

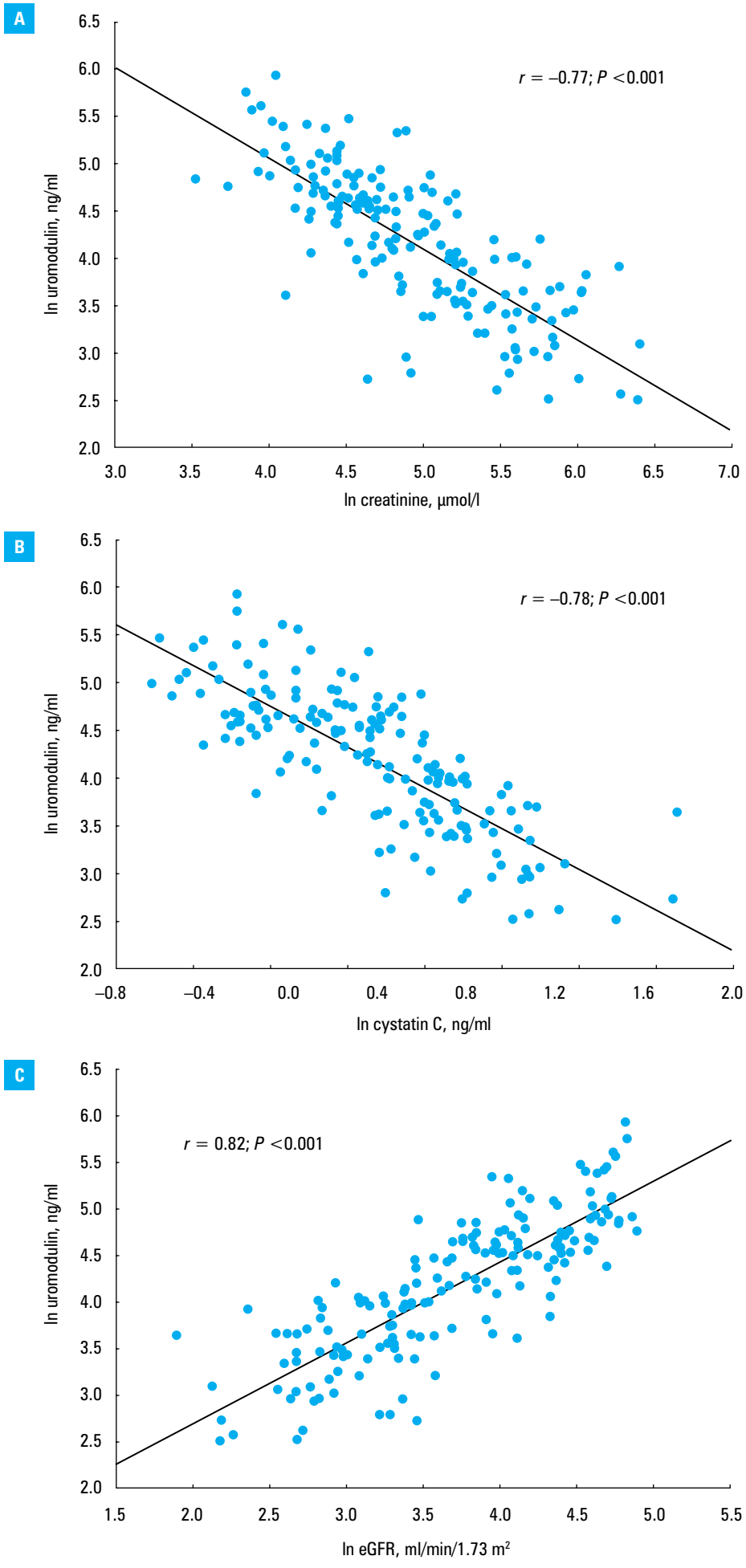

TABLE 2 Multiple regression to predict log-transformed estimated glomerular filtration rate calculated using the 2012 Chronic Kidney Disease Epidemiology Collaboration cystatin-creatinine equation

Independent variable	β ± standard error	*P* value
ln (serum uromodulin)	0.70 ±0.05	<0.001
age	−0.30 ±0.05	<0.001
BMI	−0.03 ±0.07	0.6
body surface area	0.12 ±0.09	0.2
female sex	0.14 ±0.06	0.03
whole model	R^2 =0.75; *P* <0.001	

Abbreviations: ln, natural logarithm; others, see **TABLE 1**

between eGFR and serum uromodulin concentrations was nonsignificant, but the authors insisted on a trend toward higher serum uromodulin concentrations in patients with lower eGFR, which is contrary to our results as well as those of 2 other studies.[23,31] In 2014, Risch et al[23] examined 289 elderly, subjectively healthy individuals and showed that serum uromodulin concentrations were lower among those with decreased eGFR. The positive relationship between eGFR and serum uromodulin levels was independent of sex, age, smoking status, and BMI. The authors also showed negative correlations between serum uromodulin levels and conventional markers of renal retention (creatinine, urea, cystatin C).[23] Our results are in agreement with these findings. The strength of the positive correlation between serum uromodulin levels and eGFR observed in our group of CKD patients (r = 0.82) was much higher than that observed by Risch et al (r = 0.38); however, the severity of renal impairment in our group was also higher (median eGFR, 43 ml/min/1.73 m^2 vs 85 ml/min/1.73 m^2).

In 2016, Steubl et al[31] published the results of a study in which plasma uromodulin concentrations were measured in 355 patients with CKD and 71 patients without kidney disease. The authors demonstrated that plasma uromodulin levels were significantly lower in patients with CKD compared with those without kidney disease and gradually decreased with the progression of renal disease. They reported a strong negative correlation between plasma uromodulin levels and markers of renal retention (serum creatinine, cystatin C, and blood urea nitrogen) and a strong positive correlation between plasma uromodulin levels and eGFR, which is in line with our results. These correlations remained significant after adjustment for age, sex, BMI, disease causes, and pharmacological treatment. Moreover, Steubl et al[31] emphasized that plasma uromodulin levels enabled a differentiation between patients with stage 1 CKD and individuals without kidney disease. In our study, median serum uromodulin levels in healthy individuals were slightly higher than those in patients with stage 1 of CKD, but the ranges were similar and no significant difference was found between the groups. We hypothesize that this discrepancy may be due to a higher proportion of patients with glomerulonephritis in the group of patients with stage 1 of CKD, as compared with the cohort studied by Steubl et al[31] (79% vs. 47%). Assuming that serum or plasma uromodulin levels reflect the number of remaining functional tubular cells, as suggested by Steubl et al,[31] early glomerulonephritis does not have to be associated with decreased serum uromodulin levels. Indeed, an average concentration of serum uromodulin levels in our patients with stage 1 of CKD was higher than plasma uromodulin levels in patients with stage 1 of CKD studied by Steubl et al,[31] while the concentrations were comparable in patients with more advanced CKD.

Although the majority of studies discussed above reported positive correlations between serum or plasma uromodulin levels and eGFR, there are significant discrepancies between the results that deserve explanation. Undoubtedly, the discrepancies may be caused by population heterogeneity (the presence or absence of CKD), or differences between the methods used for the determination of uromodulin. However, one of the most important sources of the discrepancy may be the lack of standardization in preparation, freezing, and thawing of clinical material before measuring uromodulin levels. Uromodulin shows a high tendency to form aggregates and potentially unstable protein complexes, which has been reported to cause discrepancies between the results of the methods used to measure uromodulin levels in urine.[32] Youhanna et al[32] studied the stability of uromodulin in urine samples and showed that the measured concentrations are influenced by spinning, vortexing, and agitation of the sample as well as by conditions and duration of urine storage. A similar interference may influence the measurement of serum uromodulin levels. Therefore, it is absolutely necessary to develop an exact and uniform method for blood collection, centrifugation, and storage of samples, in order to standardize uromodulin measurement.

Several limitations of our study have to be acknowledged. First, this was a cross-sectional study, including patients from a single center and the sample size was not large. Therefore, we cannot specify causality between the concentrations of serum uromodulin levels and kidney function, and more studies have to be performed before generalizing the results. In addition, the reference method for the assessment of GFR was not applied; however the best available model for the estimation of GFR, namely the $CKD\text{-}EPI_{cr\text{-}cys}$ equation, was used. Finally, there is no standardization of the methods used to measure uromodulin levels, which limits the possibility to compare the obtained results with the results of other authors.

In summary, it is known that the pathological process occurring in the kidney tubules or interstitial tissue affects the function of the glomeruli and vice versa. Therefore, GFR is currently considered the best measure of kidney function, reflecting retention of urinary toxins and to some extent impaired regulation of electrolytes, water

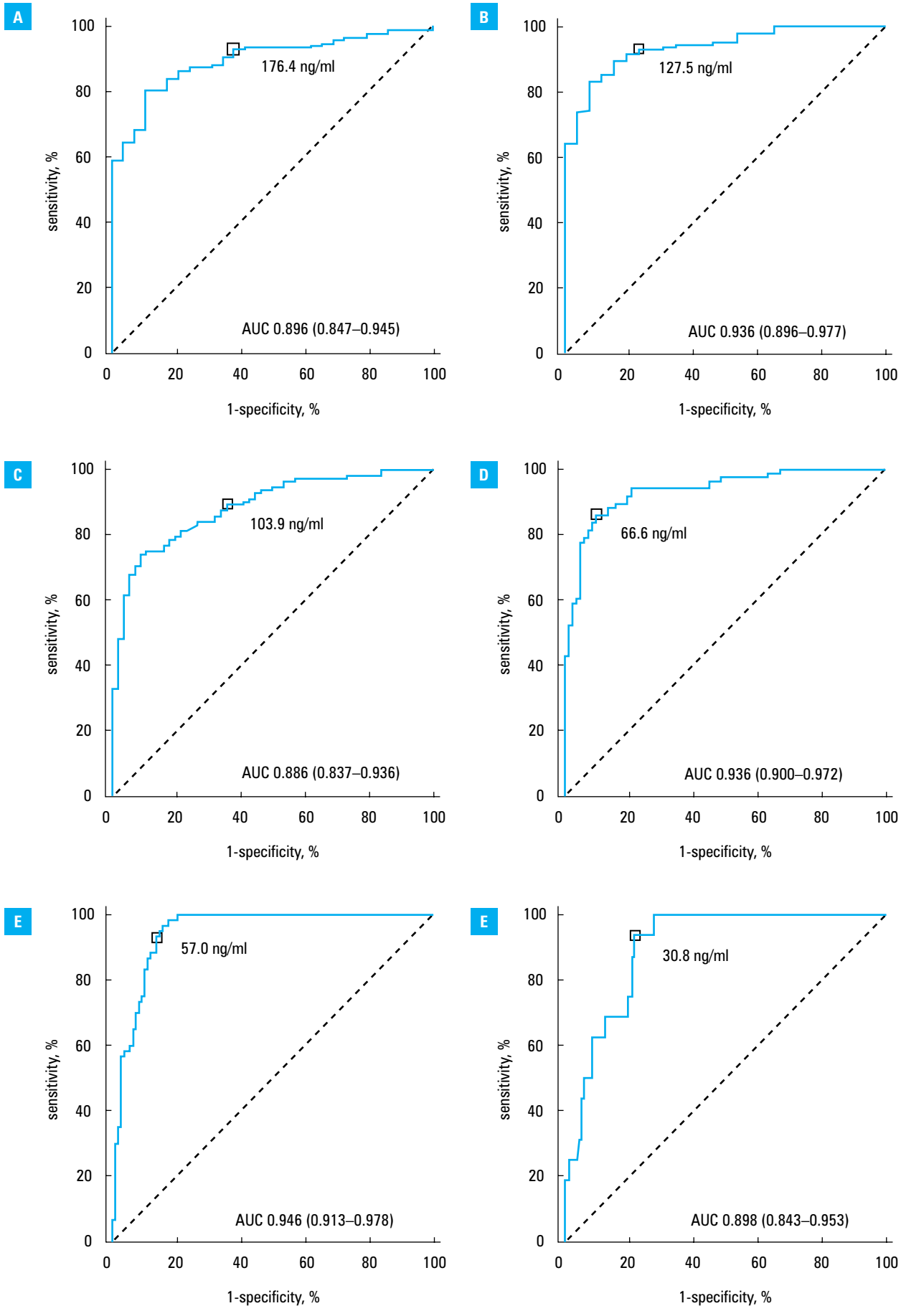

FIGURE 4 **A** – receiver-operating characteristic (ROC) curves showing the accuracy of serum uromodulin level measurements in discrimination between patients with chronic kidney disease (CKD) and controls (**A**), as well as the accuracy for the diagnosis of CKD stage 2 (**B**), stage 3a (**C**), stage 3b (**D**), stage 4 (**E**), and stage 5 (**F**). The selected cut-off points are highlighted. The areas under curve values are reported with 95% confidence intervals.

balance, and hormone production. However, there is still need for novel markers of renal function deterioration, and both serum and urine markers are being studied in this context.[33,34] A strong correlation between serum uromodulin concentrations and eGFR allows us to assume that serum uromodulin levels may potentially be an alternative indicator of renal function with a similarly high diagnostic accuracy. It may be hypothesized that serum uromodulin levels reflect the number or function of renal tubules. Therefore, serum uromodulin measurements may become a method for assessing the number of functioning nephrons independent of nonrenal factors and thus superior to GFR estimation based on serum creatinine. Alternatively, it may complement GFR in the assessment of overall renal function. We believe that this promising hypothesis should be verified in larger prospective studies, including measuring the "true" GFR using a proper clearance method.

Contribution statement DF conceived the idea for the study. M. Kuźniewski, BS, and WS contributed to the design of the study. M. Kuźniewski coordinated the funding. EW-S, BP-H, PJ, and PM recruited the patients and collected clinical data. DF and M. Kapusta performed laboratory measurements. PD and DF analyzed the data. DF, AF, and PD drafted the manuscript. All authors edited and approved the final version of the manuscript.

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ARTYKUŁ ORYGINALNY

Stężenie uromoduliny w surowicy koreluje z szybkością filtracji kłębuszkowej u pacjentów z przewlekłą chorobą nerek

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SŁOWA KLUCZOWE

dokładność diagnostyczna, przewlekła choroba nerek, stężenie uromoduliny w surowicy, wskaźnik filtracji kłębuszkowej

STRESZCZENIE

WPROWADZENIE Wydalanie uromoduliny z moczem wiąże się z występowaniem chorób nerek. Jednak stężenia uromoduliny w surowicy nie były dotychczas intensywnie badane u pacjentów z przewlekłą chorobą nerek (PChN), a opublikowane wyniki badań są niejednoznaczne.

CELE Celem badania była ocena stężenia uromoduliny w surowicy u pacjentów z PChN oraz analiza użyteczności diagnostycznej oznaczania uromoduliny w surowicy w klasyfikacji zaawansowania PChN.

PACJENCI I METODY Do badania obserwacyjnego włączono 170 pacjentów z PChN pozostających w 1–5 stadium choroby, niepoddawanych zabiegowi przeszczepienia nerki, oraz 30 osób zdrowych. Oceniono stężenia kreatyniny, cystatyny C oraz uromoduliny w surowicy, zaś oszacowaną wielkość przesączania kłębuszkowego (*estimated glomerular filtration rate* – eGFR) oszacowano na podstawie równania 2012 CKD-EPI$_{kr\text{-}cys}$ (Chronic Kidney Disease Epidemiology Collaboration creatinine-cystatin equation).

WYNIKI Stężenie uromoduliny w surowicy było znacząco niższe u pacjentów z PChN w porównaniu z grupą kontrolną oraz wykazywało silną ujemną korelację z markerami retencji nerkowej (tj. kreatyniną i cystatyną C w surowicy) oraz silną dodatnią korelację z eGFR. Ujemna, hiperboliczna zależność między stężeniami kreatyniny a uromoduliny w surowicy była analogiczna do znanej zależności między stężeniem kreatyniny w surowicy a eGFR. Analiza krzywych ROC wykazała wysoką dokładność diagnostyczną oznaczania stężenia uromoduliny w surowicy w klasyfikacji stopnia zaawansowania PChN.

WNIOSKI Stężenia uromoduliny w surowicy są silnie skorelowane z wartościami rekomendowanego wskaźnika funkcji nerek, jakim jest eGFR. Ponieważ uromodulina jest produkowana wyłącznie przez komórki kanalików nerkowych, oznaczanie stężenia uromoduliny w surowicy u pacjentów z PChN może być alternatywnym sposobem oceny ilości czynnych nefronów.

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