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Research Article

Quantitation of Urine Sediment Podocalyxin (PCX) Reflects the Estimated Urinary Podocyte Number (eUPN)

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Keywords

- Urine biomarker; Podocyte injury; Glomerular diseases; Podocalyxin; Estimated urinary podocyte number

Abstract

Introduction: Podocytes are key cells in renal physiology that become injured in many glomerular diseases. Although assessing podocyturia has proven useful in various settings, the urine podocyte number detected by immunostaining is too small compared to the expected cell loss. This study aimed to estimate the original urinary podocyte number by measuring the levels of the protein podocalyxin (PCX).

Methods: PCX quantitation by ELISA was performed in patients with glomerular diseases and normal controls. We calculated the quantity of PCX in a single podocyte (136.1 pg) based on previous research data. Subsequently, the estimated urinary podocyte number (eUPN) was calculated by dividing the sediment PCX level by the single podocyte PCX level. eUPNs were compared between patients and normal controls using the Mann-Whitney U test.

Results: The eUPN was significantly elevated in patients with glomerular diseases than in healthy individuals (mean value, 20.6 cells/mg creatinine vs. 12.9; $p<0.05$). This difference was more pronounced in individuals with diseases, such as lupus nephritis, membranous nephropathy, and diabetic kidney disease, involving podocyte injury. A low eUPN was detected in normal controls. In patients with glomerular diseases, a positive correlation was found between eUPN and proteinuria, albuminuria, urinary alpha-1-microglobulin, urinary beta-2-microglobulin, and urinary n-acetyl-beta-d-glucosaminidase.

Conclusion: The eUPN might be a sensitive and reliable indicator of urinary podocyte loss.

ABBREVIATION

PCX: Podocalyxin; eUPN: Estimated Urinary Podocyte Number; ELISA: Enzyme Linked Immuno Solvent Assay; IF: Immunofluorescence; DKD: Diabetic Kidney Disease; u-sed-PCX: Urinary Sediment PCX; Cre: creatinine; FITC: Fluorescein isothiocyanate; SDS-PAGE: Sodium Dodecyl Sulfate-polyacrylamide Gel Electrophoresis; eGFR: Estimated Glomerular Filtration Rate; FSGS: Focal Segmental Glomerulosclerosis

INTRODUCTION

Glomerulosclerosis in human and experimental glomerular diseases is associated with podocytopenia, a decrease in the number of visceral podocytes that line the glomerular capillaries [1–4]. While apoptosis represents one of the main causes of podocyte loss from the glomeruli, according to biochemical studies [5–7], recent morphological studies have identified mitotic catastrophe as another main mechanism of podocyte death [8,9].

The urinary sediment contains various morphological traces of podocytes, ranging from whole cells to smaller, granular cell debris, shed from the glomerulus [10]. When podocytes in the urinary sediment are examined carefully, various stages of cell destruction can be identified. Large cell debris becomes progressively smaller, and, eventually, the majority of granular structures seem to become entrapped in casts [11].

When evaluated using immunofluorescence (IF), the numbers of urinary podocytes in various glomerular diseases range from 0 to 100 cells/ml [12]. These numbers are too small to explain the loss of podocytes during glomerular sclerosis progression, considering that the normal total number of glomerular podocytes reaches approximately 600,000,000. For example, in the case of diabetic kidney disease (DKD), the number of countable urinary podocytes (approximately 0–10 cells/10 ml or 0-1000 cells/day) [13] seems to be particularly unrepresentative of the real cell loss. Given that in DKD progression, 13% of podocytes are lost every 3 years, this should correspond to a loss of approximately 100,000 cells/day, according to morphological studies [14].

In this study, we aimed to quantitate previously uncountable podocyte cell debris. In this regard, we aimed to estimate the original urinary podocyte number from urinary podocalyxin (PCX, located on the apical podocyte surface and one of podocyte marker) levels.

MATERALS AND METHODS

Patient selection and urine sample collection

Urine samples (10 ml each) from patients with glomerular diseases (N = 118) and DKD (N = 71) were used to quantitate urinary sediment PCX levels (u-sed-PCX) using ELISA. Urine samples were obtained from 64 healthy controls who had laboratory results within normal values. Urine samples were obtained in the morning and stored at −70°C within 2 h of collection until PCX quantitation. The clinical characteristics of the patients and healthy controls are shown in Table 1. This study was conducted in compliance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committees of Yoshida Hospital (approved number 096), Tsukuba University Hospital, Juntendo University Hospital, and Niigata University Hospital. Written informed consent was obtained from all patients.

PCX quantitation by ELISA

After being thawed, urine samples (4 ml each) were centrifuged at 800 × *g* for 5 minutes, and the urine pellet was analyzed using ELISA. To construct a sandwich-type ELISA, the protein G-bound fraction from ascitic fluid was labeled with horseradish peroxidase and used as the capture antibody for ELISA plates [15]. Two clones recognizing the intracellular peptide region of PCX (no. 147 for the capture antibody and no. 5 for the tracer antibody) were chosen for ELISA. To construct a standard curve, Intramembranous PCX was used as a standard antigen. The PCX concentration was standardized relative to the creatinine (Cre) concentration and, thus, expressed in μg/g Cre.

Immunofluorescence

Urine samples were centrifuged at 800 × *g* for 5 min to remove the cellular components, and the supernatant was subsequently centrifuged at 453000 ×*g* for 2 h. After 800 × *g* or 453000 × *g* centrifugation, the precipitates were air-dried on the glass slide, and conventional IF staining was performed using a monoclonal antibody against PCX (clone 22A4) [9] as the primary antibody and a FITC (fluorescein isothiocyanate)-labeled anti-mouse IgG (Cappel, Chester, PA, USA) as the secondary antibody.

Western blotting

Urine samples were first centrifuged at 800 × *g* for 5 minutes, and the resulting supernatant was subsequently centrifuged at 453000 × *g* for 1 h. The sediments of both centrifugations were analyzed using Western blotting to detect PCX. First, proteins were separated with 5–20% sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) (using glomerular lysates as controls) and then transferred onto a polyvinylidene membrane (Millipore, MA, USA). The membrane was first overlaid with

Table 1: Clinical characteristics of patients with glomerulopathy and control subjects.

Condition	N	Age (years)	Gender (male/ female)	SBP (mmHg)	DBP (mmHg)	HbA1c (%)	s-Cre (mg/ dl)	eGFR (mL/min/ 1.73 m^2)	Pro-teinuria (g/gCre)	u-sed-PCX (ug/ gCre)	eUPN (cells/ mgCre)	p-value, u-sed-PCX (eUPN) vs. con-trol
Diabetic ne-phropathy	71	65.4 ± 1.4	46/25	129.3 ± 1.7	77.2 ± 1.2	6.85 ± 0.19	0.93 ± 0.07	67.53 ± 2.32	0.95 ± 0.27	3.59 ± 0.79	26.38 ± 5.80	p = 0.60725
Normoalb-minuric	39	65.1 ± 1.9	25/14	124.9 ± 1.7	77.8 ± 1.4	6.97 ± 0.26	0.76 ± 0.03	75.17 ± 2.25	0.11 ± 0.02	1.55 ± 0.24	11.39 ± 1.76	p = 0.41693
Microalbu-minuric	17	63.8 ± 2.9	12/5	134.4 ± 4.4	75.6 ± 3.2	6.58 ± 0.21	0.82 ± 0.05	70.11 ± 3.71	0.35 ± 0.12	3.67 ± 1.05	20.35 ± 7.71	p = 0.05303
Macroalbu-minuric	15	67.9 ± 3.0	9/6	135.1 ± 4.4	77.4 ± 2.4	6.85 ± 0.60	1.51 ± 0.27	41.31 ± 4.54	3.81 ± 1.00	8.78 ± 3.22	64.51 ± 23.66	p = 0.04109
IgA neph-ropathy	80	32.1 ± 1.2	19/61	113.1 ± 1.8	65.1 ± 1.5		0.77 ± 0.03	85.06 ± 3.20	0.67 ± 0.07	1.97 ± 0.19	14.47 ± 1.40	p = 0.96149
N ephrotic syndrome (MCNS, FSGS)	21	51.5 ± 3.1	13/8	117.3 ± 3.5	68.3 ± 2.0		0.94 ± 0.15	71.75 ± 7.25	4.42 ± 0.75	9.61 ± 2.96	70.61 ± 21.75	p = 0.33021
Lupus ne-phritis	5	35.4 ± 3.3	0/5	116.7 ± 17.6	70.0 ± 6.9		1.13 ± 0.58	84.29 ± 27.16	1.51 ± 0.69	7.14 ± 3.71	52.46 ± 27.26	p = 0.01704
Membranous nephropathy	5	64.2 ± 2.8	2/3	127.6 ± 4.7	77.0 ± 2.4		0.79 ± 0.22	78.52 ± 13.23	4.53 ± 1.72	9.14 ± 2.61	67.16 ± 19.18	p = 0.0254
ANCA related nephritis crescentic glomerulone-phritis	7	48.7 ± 10.9	2/5	142.0 ± 27.2	72.7 ± 3.7		1.64 ± 0.19	30.46 ± 3.34	2.00 ± 0.57	2.11 ± 0.66	15.50 ± 4.85	p = 0.62938
Control group	64	30.9 ± 1.2	46/18	108.4 ± 1.2	64.3 ± 0.9		0.78 ± 0.02	90.91 ± 1.86	0.05 ± 0.003	1.75 ± 0.14	12.86 ± 1.03	

Data are expressed as mean ± standard error of the mean.
Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HbA1c: Glycated Hemoglobin; s-Cre: Serum Creatinine; eGFR: Estimated Glomerular Filtration Rate; u-sed-PCX: Podocalyxin Levels in the Urinary Sediment; eUPN: Estimated Urinary Podocyte Number; MCNS: Minimal Change Nephrotic Syndrome

an anti-PCX monoclonal antibody (22A4), followed by an anti-mouse IgG labeled with horseradish peroxidase (Dako Japan Inc, Tokyo, Japan), and finally visualized with diaminobenzidine.

Calculations of the PCX content per single podocyte (pod-PCX) and estimated urinary podocyte number (eUPN)

To calculate the pod-PCX, three formulae were used based on 1) the occurrence rate of glomerulosclerosis with aging, 2) the urinary PCX excretion in patients with IgA nephropathy in a prior publication of ours, and 3) the morphometry of podocyte counts in DKD. The following assumptions were made before calculation: a healthy individual has 1.2 million glomeruli per kidney [16], each normal human glomerulus contains an average of 500 podocytes [14,17], and approximately 1 g/day of Cre is excreted per person per day. These calculations are shown in detail in Figure 1.

Formula 1 (based on glomerulosclerosis due to aging):

Based on autopsy specimens, it is well known that the nephron number decreases with aging. In this regard, the nephron loss rate has been estimated at approximately 6800 nephrons per kidney per year [18]. As the u-sed-PCX level in healthy subjects reflects the normal loss of podocytes, we chose 2.55 ng/mgCre as a cutoff value. The calculated pod-PCX was 98.3 pg/cell.

Formula 2 (based on u-sed-PCX levels in patients with IgA nephropathy):

In a previous study of ours, the podocyte loss in IgA nephropathy was investigated by estimating the glomerular scarring area in repeated biopsies [19]. Considering that the average sclerotic area increased by 10.2 % during the 320 days between the two biopsies, the podocyte loss in that period was calculated as 73 500 000 cells (750 000 000 x 0.102), which corresponds to 229 687.6 podocytes/day (73 500 000/320). Additionally, the average PCX excretion during the 320 days was 35.2 ng/mgCre, resulting in 184.0 pg of PCX per single urinary podocyte.

-Formula 3 (based on diabetic nephropathy):

Pagtalunan et al. studied podocyte loss and progressive glomerular injury in patients with type II diabetes [14]. Using morphometry in renal biopsies, they found a 12.7 % loss in podocyte number during a period of 3 years. Assuming a total podocyte number of 600 000 000, there would be a loss of 69 589 podocytes into the urine per day. The mean U-sed-PCX level measured by ELISA in diabetic patients with macroalbuminuria was 8.78 ng/mgCre. Considering these data, the calculated pod-PCX was 126.1 pg/cell.

The average of the three calculated values, 136.1 pg, was chosen as the pod-PCX.

The eUPN was calculated by dividing the u-sed-PCX level by the pod-PCX.

Statistics

All data were expressed as the mean ± standard error of the mean. Comparisons between groups were performed using the Mann-Whitney U test. The relationship between the groups was analyzed by calculating Spearman's rank correlation coefficients. Statistical analysis was performed using JMP® 14 (SAS Institute Inc., Cary, NC, USA).

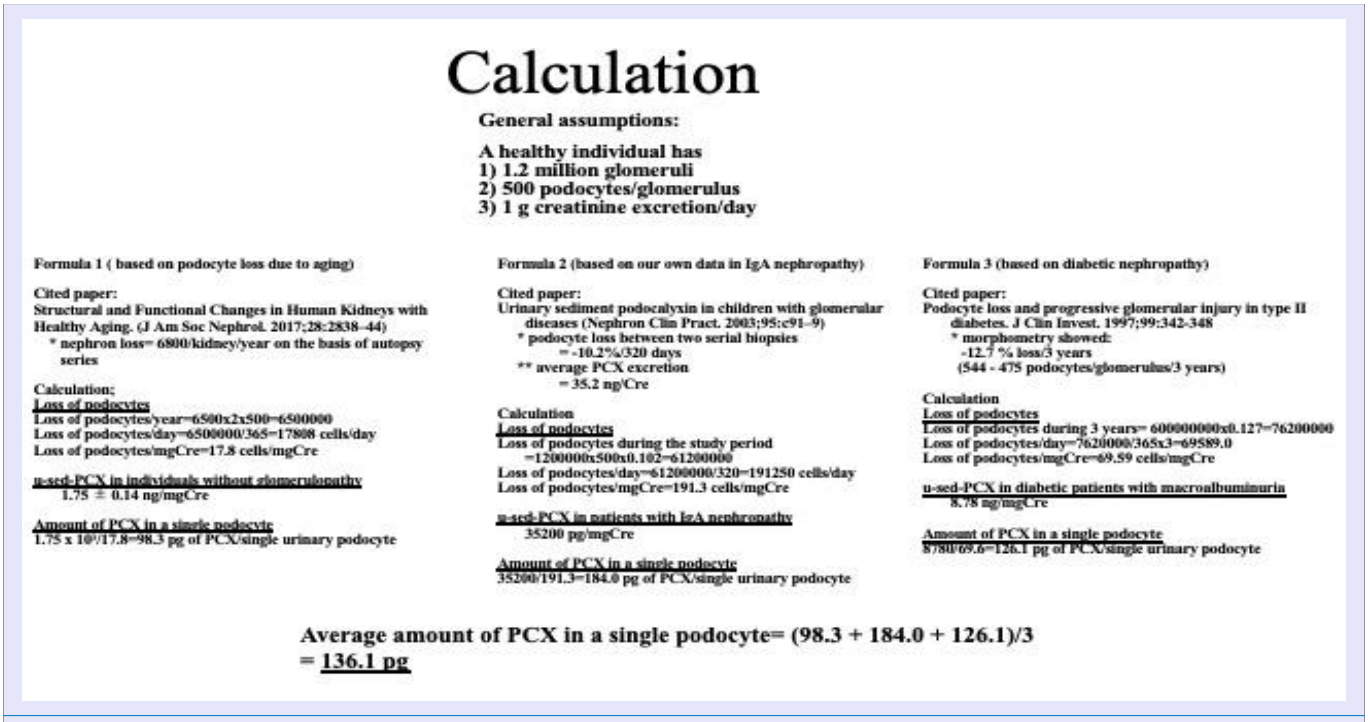

Figure 1 Formulae used for calculating the amount of podocalyxin (PCX) contained in a single podocyte. Cre, creatinine; u-sed-PCX, podocalyxin levels in the urinary sediment.

Differences were considered statistically significant when $p < 0.05$.

RESULTS

Urine IF and Western blotting

After low-grade centrifugation, IF examination of the urine sediment revealed the existence of whole podocytes and large and small cell fragments within and outside casts (shown in Fig. 2A); on the contrary, small granular particles were found in the urine supernatant (Figure 2B). Western blotting showed the presence of PCX in both the urinary sediment and supernatant of patients with glomerular diseases (Figure 2C).

eUPN

As shown in Table 1, the mean eUPN was significantly higher in individuals with glomerular diseases than in healthy subjects. This difference was more pronounced in diseases with marked podocyte injury, such as lupus nephritis and membranous nephropathy. Similarly, the mean eUPN in patients with DKD (including those with macroalbuminuria) was higher than that in normal controls. Conversely, a low eUPN was found in the urine of normal controls.

Correlation of e-UPN with the level of proteinuria and tubular markers

In patients with glomerular diseases, a positive correlation was found between the eUPN and proteinuria, albuminuria, urinary alpha-microglobulin, urinary beta-2-microglobulin, and urinary n-acetyl-beta-d-glucosaminidase. No association was found between the eUPN and other variables, such as the systemic and diastolic blood pressures, HbA1c, total cholesterol, triglycerides, serum Cre level, and estimated glomerular filtration rate (eGFR).

DISCUSSION

In this study, we proposed a new parameter, the eUPN, which may serve as a more accurate marker of urinary podocyte loss than the current IF assessment results. The eUPN was significantly higher in patients with glomerular diseases than in healthy controls.

Counting of the number of urinary podocytes using immunostaining has been used in most of the previous studies in this area. As earlier explained, the resulting podocyte number seems too small compared to the expected loss, according to our calculations. We believe that the eUPN, which has never been reported previously, might be useful for evaluating podocyte injury (especially podocyte detachment) quantitatively. In this regard, evaluating podocyte detachment allows for the introduction of podometrics in the practice of clinical nephrology.

Podocytes are long-living cells that are not easily replaced and are essential for normal kidney functioning [20]. Podocyte

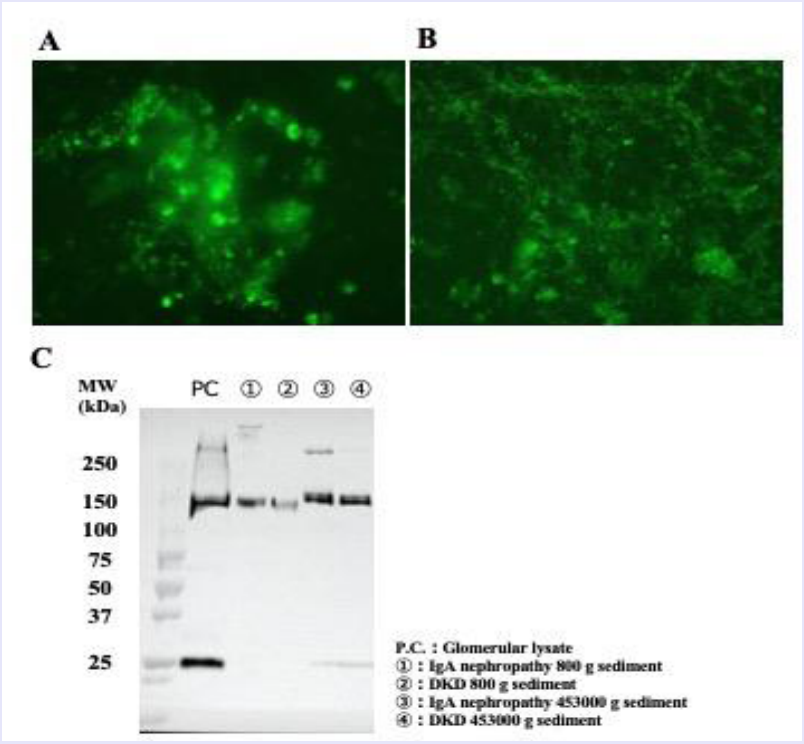

Figure 2 Immunofluorescence of urine sediment (A) and supernatant (B) of a patient with IgA nephropathy (x400). The supernatant was ultra-centrifuged at 453000 × g for 2 h, and the resulting precipitate was subjected to conventional immunofluorescence staining using a monoclonal antibody against PCX (clone 22A4) and a FITC (fluorescein isothiocyanate)-labeled anti-mouse IgG.
(C) Western blotting of the urine of patients with IgA nephropathy (lanes 1 and 3) and diabetic kidney disease (DKD) (lanes 2 and 4). Glomerular lysate (PC) was used as a positive control. Bands at 160-170 kDa were observed, which correspond to podocalyxin.

balance could, therefore, in principle, be considered a zero-sum game (the gains and deficits add up to zero) in which the total podocyte count in an individual is a fixed number that needs to last for a lifetime [21].

PCX can be found in the urine sediment and/or supernatant [11]. Previous studies have revealed that sediment and supernatant PCX have different pathological meanings. Supernatant PCX consists of microparticles originating from injured podocytes; it reflects mild injury, representing an early stage of podocyte death due to apoptosis or mitotic catastrophe. On the contrary, sediment PCX is a sign of severe podocyte injury and involves the detachment of podocytes from the glomerular basal membrane, as well as podocyte death due to apoptosis or mitotic catastrophe. Although sediment PCX is present in much lower quantities than supernatant PCX, its pathological significance is greater since the detachment of podocytes leads to the progression of glomerular diseases such as glomerulosclerosis. In this regard, given that the eUPN is calculated based on sediment PCX levels, it would have similar importance in reflecting podocyte loss from the glomerulus.

Recent studies have revealed the central role of the podocyte as both a regulator of glomerular development and a determinant of progression to glomerulosclerosis. All glomerular diseases can be encompassed within a spectrum of podocytopathies with predictable outcomes based on podocyte biology influenced by temporal, genetic, and environmental factors [22]. Nephrotic syndrome-causing diseases, such as minimal change disease, focal segmental glomerulosclerosis (FSGS), lupus nephritis, and membranous nephropathy, are the most representative podocyte diseases among these glomerular diseases. It is worth noting that significantly high eUPNs were found in diabetic patients with macroalbuminuria; this seems logical since DKD is a glomerular disease characterized by significant podocyte injury. Taking the findings mentioned above together, it seems reasonable to consider eUPN as a reliable biomarker of overall podocyte injury and, particularly, of podocyte detachment from the glomerulus.

Our findings revealed that, although at a very low level, u-sed-PCX was also found in healthy individuals. This indicates that low-grade podocyte loss is a normal process. Although the podocyte loss per day or in a short time may not seem high, its long-term impact is far from negligible since this is a continuing process. In this regard, the slow eGFR decline associated with aging might be a consequence of gradual podocyte loss. Since aging is thought to be the major driver of progression to end-stage kidney disease, including the eUPN in podometrics [21] might represent a very useful strategy in the practice of clinical nephrology.

Albuminuria and proteinuria can be manifestations of kidney dysfunction by causing (i) high concentrations of small proteins in the blood, (ii) an increase in hemodynamic factors, (iii) glomerular endothelial injury, (iv) glomerular basement membrane disorganization, (v) podocyte dysfunction and/or detachment, (vi) defective tubular reuptake of filtered proteins, and (vi) combinations of the above; among these points, glomerular capillary disorders (such as in iii], iv], and v]) constitute a major determinant of kidney dysfunction. Additionally, the normal urine contains significantly large amounts of proteins at baseline, some of which are produced by the kidney. Therefore, proteinuria and albuminuria are moderately sensitive but nonspecific markers of kidney dysfunction. On the contrary, the eUPN is both a specific marker of podocyte injury and a more sensitive marker of kidney dysfunction. Furthermore, u-sed-PCX is a very time-specific indicator of ongoing podocyte injury. On the contrary, albuminuria and proteinuria are not specific to the time the injury occurred on the glomerular capillary wall but rather reflect overall glomerular dysfunction.

Although the eUPN is a marker of podocyte injury that seems to accurately reflect podocyte detachment and glomerular disease progression, a very serious limitation may impair its application in clinical practice. It relates to sample handling before the PCX quantitation. A good biomarker should fulfill several requirements, such as high sensitivity, specificity, accuracy, and throughput, ease of obtaining a sample, simplicity of quantitation, and good reproducibility. In this regard, the fact that urine has to be spun down to obtain the sediments represents a disadvantage for sample collection to count eUPN.

Although eUPN is a specific indicator of ongoing podocyte injury, a single measurement does not provide information concerning glomerular disease progression. Thus, it is necessary to repeat u-sed-PCX assessments and calculate the cumulative eUPN value (the total number of podocytes detached during that period) [23].

CONCLUSION

In this study, we found that eUPN provides information on the rate of podocyte detachment. Thus, this parameter might constitute a sensitive and reliable indicator of glomerular disease progression in the practice of clinical nephrology, providing a better understanding of disease course, an appropriate choice for therapy, and a better assessment of the treatment.

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REFERENCES

1. Kim YH, Goyal M, Kurnit D, Wharram B, Wiggins J, Holzman L, et al. Podocyte depletion and glomerulosclerosis have a direct relationship in the PAN-treated rat. Kidney Int. 2001; 60: 957– 968.

2. Lemley KV, Abdullah I, Myers BD, Meyer TW, Blouch K, Smith WE, et al. Evolution of incipient nephropathy in type 2 diabetes mellitus. Kidney Int. 2000; 58: 1228–1237.

3. Lemley KV, Lafayette RA, Safai M, Derby G, Blouch K, Squarer A, et al. Podocytopenia and disease severity in IgA nephropathy. Kidney Int. 2002; 61: 1475–1485.

4. Meyer TW, Bennett PH, Nelson RG. Podocyte number predicts long-term urinary albumin excretion in Pima Indians with type II diabetes and microalbuminuria. Diabetologia. 1999; 42: 1341–1344.

5. Stieger N, Worthmann K, Schiffer M. The role of metabolic and

haemodynamic factors in podocyte injury in diabetes. Diabetes Metab Res Rev. 2011; 27: 207–215.

6. Schiffer M, Bitzer M, Roberts IS, Kopp JB, ten Dijke P, Mundel P, et al. Apoptosis in podocytes induced by TGF-beta and Smad7. J Clin Invest. 2001; 108: 807–816.

7. Ziyadeh FN, Wolf G. Pathogenesis of the podocytopathy and proteinuria in diabetic glomerulopathy. Curr Diabetes Rev. 2008; 4: 39–45.

8. Liapis H, Romagnani P, Anders HJ. New insights into the pathology of podocyte loss: mitotic catastrophe. Am J Pathol. 2013; 183: 1364–1374.

9. Hara M, Oohara K, Dai D-F, Liapis H. Mitotic Catastrophe Causes Podocyte Loss in the Urine of Human Diabetics. Am J Pathol. 2019; 189: 248–257.

10. Hara M, Yamamoto T, Yanagihara T, Takada T, Itoh M, Adachi Y, et al. Urinary excretion of podocalyxin indicates glomerular epithelial cell injuries in glomerulonephritis. Nephron. 1995; 69: 397–403.

11. Hara M, Yanagihara T, Hirayama Y, Ogasawara S, Kurosawa H, Sekine S, et al. Podocyte membrane vesicles in urine originate from tip vesiculation of podocyte microvilli. Hum Pathol. 2010; 41: 1265–1275.

12. M Hara, T Yanagihara, T Takada, M Itoh, M Matsuno, T Yamamoto, et al. Urinary excretion of podocytes reflects disease activity in children with glomerulonephritis. Am J Nephrol. 1998; 18: 35–41.

13. Nakamura T, Ushiyama C, Suzuki S, Hara M, Shimada N, Ebihara I, et al. Urinary excretion of podocytes in patients with diabetic nephropathy. Nephrol Dial Transplant. 2000; 15: 1379–1383.

14. Pagtalunan ME, Miller PL, Jumping-Eagle S, Nelson RG, Myers BD, Rennke HG, et al. Podocyte loss and progressive glomerular injury in type II diabetes. J Clin Invest. 1997; 99: 342–348.

15. Hara M, Yamagata K, Tomino Y, Saito Y, Hirayama Y, Ogasawara S, et al. Urinary podocalyxin is an early marker for podocyte injury in patients with diabetes: establishment of a highly sensitive ELISA to detect urinary podocalyxin. Diabetologia. 2012; 55: 2913–2919.

16. Puelles V, Hoy W, Hughson M, Diouf B, Douglas-Denton R, Bertram J. Glomerular number and size variability and risk for kidney disease. Curr Opin Nephrol Hypertens. 2011; 20: 7–15.

17. Venkatareddy M, Wang SQ, Yang Y, Patel S, Wickman L, Nishizono R, et al. Estimating podocyte number and density in histologic sections. J Am Soc Nephrol. 2014; 25: 1118–1129.

18. Hommos MS, Glassock RJ, Rule AD. Structural and Functional Changes in Human Kidneys with Healthy Aging. J Am Soc Nephrol. 2017; 28: 2838–2844.

19. Kanno K, Kawachi H, Uchida Y, Shimizu F, Uchiyama M. Urinary sediment podocalyxin in children with glomerular diseases. Nephron Clin Pract. 2003; 95: c91–99.

20. Wanner N, Hartleben B, Herbach N, Goedel M, Stickel N, Zeiser R, et al. Unraveling the role of podocyte turnover in glomerular aging and injury. J Am Soc Nephrol. 2014; 25: 707–716.

21. Kikuchi M, Wickman L, Hodgin JB, Wiggins RC. Podometrics as a Potential Clinical Tool for Glomerular Disease Management. Semin Nephrol. 2015; 35: 245–255.

22. Wiggins RC. The spectrum of podocytopathies: a unifying view of glomerular diseases. Kidney Int. 2007; 71: 1205–1214.

23. Hara M, Yanagihara T, Kihara I. Cumulative excretion of urinary podocytes reflects disease progression in IgA nephropathy and Schönlein-Henoch purpura nephritis. Clin J Am Soc Nephrol. 2007; 2: 231–238.

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