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Plasma endocan level and prognosis of immunoglobulin A nephropathy

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Abstract

Background: Endocan, previously called endothelial cell–specific molecule-1, is a soluble proteoglycan that is secreted from vascular endothelial cells. Elevated plasma endocan levels were shown to be associated with poor cardiovascular outcomes in patients with chronic kidney disease (CKD). We investigated the clinical relevance of plasma and urine endocan levels in patients with immunoglobulin A nephropathy (IgAN).

Methods: Sixty-four patients with IgAN and 20 healthy controls were enrolled in this study. Plasma and urine endocan levels were measured. Clinical parameters, pathologic grades, and renal outcomes were compared among subgroups with different plasma and urine endocan levels.

Results: Both plasma and urine endocan levels were significantly higher in patients with IgAN than in controls. Elevated serum phosphorus and C-reactive protein were independent determinants for plasma endocan, and elevated C-reactive protein was also an independent determinant for urine endocan levels in multivariate analysis. Plasma endocan level was not significantly different across CKD stages, but patients with higher plasma endocan levels showed adverse renal outcome. Urine endocan levels were also elevated in patients with poor renal function. Cox proportional hazard models showed that high plasma endocan was an independent risk factor for CKD progression after adjusting for the well-known predictors of outcome in patients with IgAN.

Conclusion: This study suggested that plasma endocan might be useful as a prognostic factor in patients with IgAN.

Introduction

Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis in Asian countries, including Korea [1]. The clinical course and renal prognosis of patients with IgAN are quite diverse; nevertheless, approximately 50% of patients eventually progress to end-stage renal disease, which requires renal replacement therapy within 20 years of the initial diagnosis [2]. The well-known risk factors for poor clinical outcome include elevated serum creatinine levels, at first presentation; sustained hypertension; persistent proteinuria; and specific pathologic features, including mesangial hypercellularity; segmental glomerulosclerosis; tubular atrophy; and interstitial fibrosis [3,4]. However, none of these

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markers are sensitive or specific; thus, predicting the risk of disease progression remains controversial. Several studies have described new kidney biomarkers that might predict renal outcome independently, such as kidney injury molecule-1, neutrophil gelatinase–associated lipocalin, and nestin, but these markers should be validated more thoroughly [5–7].

Endocan, also known as endothelial cell–specific molecule-1, is a 50-kDa proteoglycan that is composed of dermatan sulfate and mature polypeptide of 165 amino acids [8]. Unlike other ubiquitous proteoglycans, which are mainly located in the connective tissue, endocan is a soluble molecule, secreted from vascular endothelial cells of various organs, and it can freely circulate in the blood [9]. The exact role of endocan in humans remains to be elucidated. However, it has been reported that elevated plasma endocan levels could serve as an independent risk factor for poor survival in patients with malignancy, chronic kidney disease (CKD), preeclampsia, sepsis, and hypertension [10–14].

Several studies have documented endothelial injury in patients with IgAN by measuring plasma von Willebrand factor and soluble fms–like tyrosine kinase-1 [15,16]. Given that a key element in CKD progression is endothelial injury, we hypothesized that endocan could be linked to endothelial dysfunction, and thus, it may serve as a marker of CKD progression in patients with IgAN [17]. Currently, no study has investigated endocan levels in patients with IgAN. The aim of this study was to evaluate plasma and urine endocan levels in patients with IgAN to determine whether endocan could serve as a marker of clinicopathologic severity and prognosis.

Methods

Patient selection and study design

We retrospectively analyzed 64 patients diagnosed with IgAN based on a renal biopsy, in Kyung Hee University Hospital at Gangdong from June 2011 to October 2014. The diagnosis of IgAN was confirmed by an expert pathologist, based on the following criteria: IgA and/or C3 deposition in the mesangial area observed with immunofluorescence staining and electron-dense material deposited in mesangial and paramesangial regions observed with electron microscopy. Other glomerulopathies that mimicked IgAN, such as systemic lupus erythematosus and Henoch–Schonlein purpura as well as secondary IgAN, were excluded by identifying signs in a careful patient history and laboratory data. We also excluded patients who had superimposed acute kidney injury at the time of renal biopsy. We enrolled 20 additional healthy volunteers; serum creatinine and fasting glucose levels of those were within normal range, urinalysis revealed no proteinuria and hematuria, and blood pressure was normal on routine medical checkup. The Institutional Review Board of Kyung Hee University Hospital at Gangdong approved this study (KHNMC 2008-030). Informed consent was obtained from all patients and healthy controls.

Age, sex, height, weight, the presence of diabetes, and systolic and diastolic blood pressures were recorded at the time of admission. Blood samples were drawn for routine laboratory analyses in the fasted state, for measuring hemoglobin, total cholesterol, albumin, creatinine phosphorus, and C-reactive protein (CRP). The estimated glomerular filtration rate (eGFR) was calculated with the equation from the Modification of Diet in Renal Disease study. Patients were classified into different CKD stage groups, according to eGFR. Urine samples were collected on the morning of the day of renal biopsy. Urine was evaluated for the presence of hematuria and proteinuria. Proteinuria was expressed as the urinary protein-to-creatinine ratio (uPCR), calculated as urinary protein/urinary creatinine (g/gCr).

Collection of plasma and urine samples; measurement of endocan levels

Additional samples of plasma were collected on the day of biopsy and stored at −80°C. Urine samples were collected in 50-mL sterile conical tubes. After centrifugation of urine for 20 minutes at 2,000*g* at room temperature, the supernatant was collected in the tube and kept at a −80°C deep freezer. The enzyme-linked immunosorbent assay method was performed with a commercial kit (Boster Biological Technology, Pleasanton, CA, USA) to measure plasma and urine endocan levels. Urine creatinine was measured in the same urine specimens. The urine endocan level was expressed relative to the creatinine concentration: endocan/creatinine (pg/gCr).

Histologic grading of IgAN

The pathologic findings of IgAN were classified with both the Oxford classification and the modified H.S. Lee grading system [18,19]. The 4 pathologic variables of the Oxford classification were defined as the following: mesangial hypercellularity ≤ 0.5 (M0) or > 0.5 (M1); endocapillary hypercellularity absent (E0) or present (E1); segmental glomerulosclerosis absent (S0) or present (S1); and tubular atrophy and/or interstitial fibrosis $\leq 25\%$ (T0), 26–50% (T1), and $> 50\%$ (T2). The H.S. Lee system included 5 grades, defined by the percentage of glomeruli that exhibited crescent/segmental sclerosis (SS)/global sclerosis (GS). These grades were described as the following: grade I, normal or focal mesangial cell proliferation; grade II, diffuse mesangial cell proliferation or $< 25\%$ of glomeruli with crescent/SS/GS; grade III, 25–49% of glomeruli with crescent/SS/GS; grade IV, 50–75% of glomeruli with crescent/SS/GS; and grade V, $> 75\%$ of glomeruli with crescent/SS/GS.

Treatment of IgAN and follow-up

All patients included in this study visited our outpatient clinic regularly every 1–3 months. Patients were treated with an angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) unless proteinuria improved spontaneously to normal range. Patients who showed persistent proteinuria over 1 g/d despite optimal use of ACEi or ARB for 3 months received immunosuppressive agents. Routine laboratory parameters (described previously) were determined for each visit, and all patients were monitored for CKD progression and cardiovascular events, including myocardial infarction, stroke, and death from any cause. CKD progression was defined as more than 50% reduction in eGFR from the value observed at the time of biopsy [20,21].

Statistical analysis

Statistical analyses were performed with SPSS for Windows, version 20.0 (IBM Corp, Armonk, NY, USA), and P values < 0.05

were considered statistically significant. Normally distributed data are expressed as the mean ± standard deviation or the number of patients and percentage. Plasma and urine endocan levels were described as median and interquartile range (IQR) because these data were nonnormally distributed. Clinical and laboratory parameters were compared between groups with the unpaired *t* test, Mann–Whitney *U* test, or Pearson χ^2 test as appropriate. One-way analysis of variance and linear-by-linear association analyses were used to compare subgroups of patients with different CKD stages. To assess the determinants of plasma and urine endocan, we first used simple regression analysis. Subsequently, the Enter method of multiple regression analysis was performed with all the univariate associates ($P < 0.1$). CKD progression was assessed with the Cox proportional hazard model. We initially performed the Cox analysis only with plasma endocan quartiles. Thereafter, we adjusted for other variables, as follows: model 1: adjusted for age, gender, and diabetes; model 2: adjusted for hypertension and eGFR, plus the variables in model 1; and model 3: adjusted for uPCR plus the variables in model 2.

We used simple correlation analyses to compare plasma endocan and urine endocan levels after log transformation of both endocan levels. Finally, a time-to-event analysis for CKD progression was performed with a log-rank test.

Results

Plasma and urine endocan levels in patients with IgAN

A total of 64 patients were diagnosed with IgAN (mean age, 44.7 ± 16.1 years; 50% male). The baseline clinical characteristics of patients and healthy controls are shown in Table 1. Among the patients with IgAN, 6 had diabetes and 27 had hypertension. The mean creatinine level was 1.64 mg/dL, mean eGFR was 70.42 mL/min/1.73 m^2, and mean uPCR was 1.66 g/gCr. The plasma endocan levels were significantly higher in patients with IgAN than in the control group [198.4 pg/mL (IQR, 109.0–301.6 pg/mL) vs. 111.8 pg/mL (IQR, 35.4–163.7 pg/mL), $P = 0.001$]. The urine endocan levels were also higher in patients with IgAN than in healthy controls [182.6 pg/gCr (IQR, 1.5–909.3 pg/gCr) vs. 0 pg/gCr (IQR, 0–24.2 pg/gCr), $P < 0.001$]. The urine and plasma endocan levels showed positive relationship although the correlation coefficient was low ($r = 0.249$ and $P = 0.047$; Fig. 1). When the patients with IgAN were grouped according to CKD stages, plasma endocan levels were not different among different CKD stages, but urine endocan levels were higher in patients with advanced CKD ($P = 0.501$ and 0.023, respectively; Table 2).

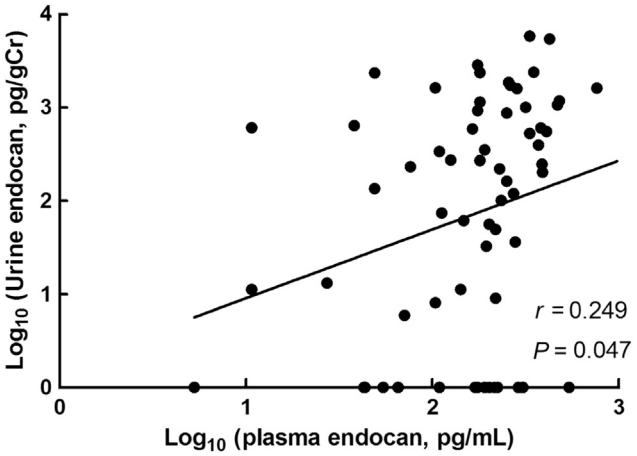

Figure 1. Correlation analysis between plasma endocan and urine endocan level.

Determinants of plasma and urine endocan levels in patients with IgAN

Simple logistic regression analyses demonstrated that serum phosphorus and CRP were positively associated with the plasma endocan level (Table 3). These variables maintained positive association with the plasma endocan level in multiple logistic regression analyses.

The urine endocan level was positively correlated with H.S. Lee pathologic grades, hemoglobin, serum phosphorus, and CRP in simple regression analyses. eGFR showed a negative trend toward significance with urine endocan levels, whereas uPCR showed a positive trend toward significance. In multiple regression analyses, only CRP maintained positive correlation with the urine endocan level.

Plasma and urine endocan relationships to pathologic parameters

When patients were grouped according to the H.S. Lee grading system, both plasma and urine endocan levels were

Table 1. Baseline clinical characteristics and biochemical parameters of patients with IgA nephropathy and control group

Variables	Control ($n = 20$)	IgA nephropathy ($n = 64$)	*P*
Age (y)	42.9 ± 12.0	44.7 ± 16.1	0.637
Male	12 (60.0)	32 (50.0)	0.434
BMI (kg/m^2)	22.3 ± 2.4	23.2 ± 5.4	0.100
DM	0 (0)	6 (9.4)	0.155
Hypertension	0 (0)	27 (42.2)	< 0.001
Creatinine (mg/dL)	0.8 ± 0.1	1.6 ± 1.8	< 0.001
eGFR (mL/min/1.73 m^2)	105.3 ± 18.5	70.4 ± 34.7	< 0.001
uPCR (g/gCr)		1.7 ± 2.1	
Use of ACEi or ARB		55 (85.9)	
Use of immunosuppressive agents		18 (28.1)	
Plasma endocan (pg/mL)	111.8 (35.4–163.7)	198.4 (109.0–301.6)	0.001
Urine endocan (pg/gCr)	0 (0–24.2)	182.6 (1.5–909.3)	< 0.001

Data are presented as mean ± SD, *n* (%), or median (interquartile range).
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Ig, immunoglobulin; uPCR, urine protein-to-creatinine ratio.

Table 2. Clinical characteristics and biochemical parameters of patients with IgA nephropathy according to CKD stage

Variables	CKD stage 1 ($n = 22$)	CKD stage 2 ($n = 15$)	CKD stage 3 ($n = 18$)	CKD stage 4 ($n = 9$)	P
Age (y)	33.8 ± 12.8	43.0 ± 9.7	53.7 ± 16.2	56.3 ± 15.4	< 0.001
Male	9 (40.9)	5 (33.3)	11 (61.1)	7 (77.8)	0.109
DM	2 (9.1)	0 (0)	2 (11.1)	2 (22.2)	0.339
Hypertension	5 (22.7)	3 (20.0)	14 (77.8)	5 (55.6)	0.001
Oxford classification					
M1	21 (95.5)	10 (66.7)	15 (83.3)	7 (77.8)	0.268
E1	4 (18.2)	4 (26.7)	3 (16.7)	0 (0)	0.294
S1	0 (0)	4 (26.7)	3 (16.7)	3 (33.3)	0.029
T1	1 (4.5)	0 (0)	3 (16.7)	2 (22.2)	0.002
T2	0 (0)	0 (0)	0 (0)	2 (22.2)	
H.S. Lee grade					
I	1 (4.5)	2 (13.3)	1 (5.6)	0 (0)	0.021
II	9 (40.9)	5 (33.3)	5 (27.8)	1 (11.1)	
III	11 (50.0)	7 (46.7)	7 (38.9)	5 (55.6)	
IV	1 (4.5)	1 (6.7)	5 (27.8)	3 (33.3)	
eGFR (mL/min/1.73 m^2)	107.7 ± 16.5	77.0 ± 6.9	46.1 ± 7.3	17.0 ± 10.3	< 0.001
Hemoglobin (g/dL)	13.2 ± 1.4	12.9 ± 1.5	12.6 ± 2.2	10.9 ± 3.0	0.046
Total cholesterol (mg/dL)	185.8 ± 26.7	182.5 ± 35.0	190.2 ± 60.3	192.8 ± 52.8	0.936
Albumin (g/dL)	4.1 ± 0.4	4.0 ± 0.3	3.9 ± 0.5	3.8 ± 0.4	0.100
Phosphorus (mg/dL)	3.4 ± 0.5	3.5 ± 0.4	3.6 ± 0.6	3.9 ± 1.0	0.235
CRP (mg/dL)	0.1 ± 0.1	0.3 ± 0.8	0.6 ± 1.0	0.6 ± 1.3	0.275
uPCR (g/gCr)	0.9 ± 1.0	1.0 ± 0.9	2.3 ± 3.0	3.3 ± 2.5	0.006
Use of ACEi or ARB	18 (81.8)	11 (73.3)	17 (94.4)	9 (100)	0.013
Use of immunosuppressive agents	5 (22.7)	4 (26.7)	8 (44.4)	1 (11.1)	0.784
Plasma endocan (pg/mL)	185.4 (70.8–275.5)	179.9 (70.8–234.5)	261.8 (19.9–375.1)	289.1 (174.5–341.0)	0.501
Urine endocan (pg/gCr)	217.2 (0–939.5)	101.0 (0–337.4)	260.2 (10.5–695.9)	922.1 (0–2380.7)	0.023

Data are presented as mean ± standard deviation, n (%), or median (interquartile range).
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; CRP, C-reactive protein; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; uPCR, urine protein/creatinine ratio.

higher in patients with advanced pathologic grades (H.S. Lee grade III + IV) than in patients with favorable pathologic grades (H.S. Lee grade I + II; Fig. 2). In contrast, there was no significant correlation between Oxford classification variables and plasma and urine endocan levels.

CKD progression in patients with IgAN

Patients with IgAN were followed up for a mean of 25.81 ± 13.29 months. Most patients received an ACEi or ARB (55/64, 85.9%), and 18 patients (28.1%) were treated with additional immunosuppressive agents to reduce proteinuria (Table 1). Patients who exhibited normal or mild decrease in eGFR received less ACEi or ARB (Table 2). In contrast, use of immunosuppressive agents was not different across CKD stages. No cardiovascular events occurred during follow-up; however, 8 patients experienced CKD progression.

CKD progression was evaluated with the log-rank test in patients grouped by plasma and urine endocan levels (Fig. 3). Patients were divided into quartiles, according to the plasma endocan level (< 108.99, 108.99–198.42, 198.42–301.59, and > 301.59 pg/mL), and subsequently divided equally by urine endocan levels (≤ 21.14 and > 21.14 pg/gCr). Based on the plasma endocan level, the rate of reaching CKD progression was significantly higher in patients in the fourth quartile than in patients in the other 3 quartiles ($P = 0.003$; Fig. 3A). The

Table 3. Determinants of plasma and urine endocan levels in patients with IgA nephropathy

Variables	Plasma endocan (pg/mL)						Urine endocan (pg/gCr)					
	Simple regression			Enter method of multiple regression			Simple regression			Enter method of multiple regression		
	Unstandardized β	SE	P	Unstandardized β	SE	P	Unstandardized β	SE	P	Unstandardized β	SE	P
Age (y)	−0.892	0.686	0.198				5.967	8.967	0.508			
DM	−42.19	37.82	0.269				−291.5	493.0	0.557			
Hypertension	−14.83	22.46	0.511				3.743	291.8	0.990			
H.S. Lee grade	14.30	13.80	0.304				348.5	174.7	0.050	335.2	179.8	0.068
eGFR (mL/min/1.73 m^2)	0.090	0.323	0.278				−7.617	4.074	0.066	0.32	4.59	0.944
Hemoglobin (g/dL)	−2.645	5.448	0.629				−174.1	67.11	0.012	−101.0	72.35	0.141
Total cholesterol (mg/dL)	0.190	0.259	0.466				3.573	3.338	0.289			
Albumin (mg/dL)	−11.36	28.36	0.690				−520.7	361.5	0.155			
Phosphorus (mg/dL)	41.43	17.89	0.024	48.44	18.84	0.013	489.7	233.2	0.040	380.2	242.6	0.123
CRP (mg/dL)	33.29	13.24	0.015	40.12	14.54	0.008	450.1	172.4	0.011	411.1	187.2	0.032
uPCR (g/gCr)	7.998	5.220	0.131				121.6	67.08	0.075	−27.79	77.83	0.722

CRP, C-reactive protein; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Ig, immunoglobulin; SE, standard error; uPCR, urine protein/creatinine ratio.

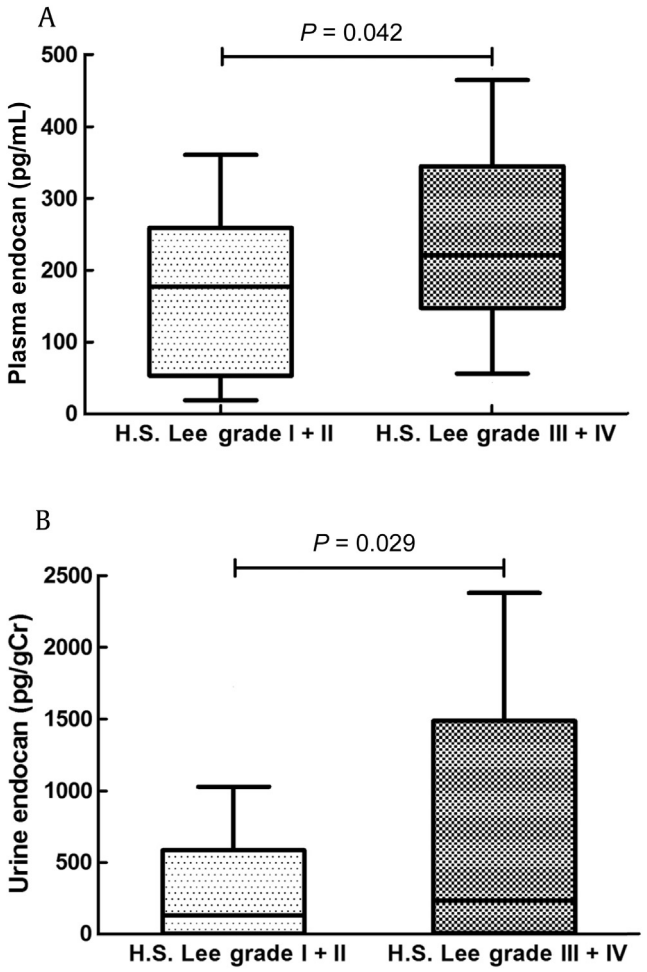

Figure 2. Box-and-whisker plots. Plasma (A) and urine (B) endocan levels are shown according to H. S. Lee pathologic grading.

proportion of patients who experienced CKD progression was slightly higher in patients with high urine endocan than in those with low urine endocan (cutoff: 21.14 pg/gCr, median value), but the difference was not significant ($P = 0.138$; Fig. 3B).

Cox proportional hazard model analyses were performed for patients with IgAN. We found that plasma endocan in the highest quartile was an independent risk factor for CKD progression, after adjusting for baseline clinical characteristics (model 1) and well-known predictors of outcome (models 2 and 3; Table 4).

Discussion

In the present study, we demonstrated that a high plasma endocan level was an independent risk factor for rapid deterioration of renal function. This finding was unexpected because plasma endocan levels were not elevated in patients with IgAN, and they did not vary significantly among patients with different CKD stages. In contrast, urine endocan was not significantly associated with renal outcome, although it was elevated in patients with IgAN, and it was correlated with poor renal function. Poor renal prognosis in patients with high plasma endocan levels could partly be explained by its correlation with pathologic severity. Another explanation for these findings could be that high plasma endocan levels might reflect vascular endothelial injury. Some previous studies supported this hypothesis with demonstrations that endothelial dysfunction contributed to IgAN pathogenesis and CKD progression [15–17].

Endocan formation and secretion is a tightly regulated process. It mainly occurs in the vascular endothelium of lungs and kidneys [22]. To date, many cytokines and growth factors are known to affect the level of plasma endocan. Importantly, tumor necrosis factor-α, interleukin-1β, and lipopolysaccharides strongly upregulated the expression of endocan messenger RNA [8]. In contrast, interferon-γ blocked the effect of tumor necrosis factor-α on endocan messenger RNA [23]. In addition, vascular endothelial growth factor, which plays an important role in the pathogenesis of cancer neoangiogenesis, was shown to induce endocan expression [24].

Previous studies provided conflicting results on the biologic roles of plasma endocan in the control of inflammation. One experiment with human umbilical vein endothelial cells demonstrated that elevated endocan could trigger systemic inflammation through the upregulation of vascular cell adhesion molecule-1, intercellular adhesion molecule-1, and E-selectin [25]. All these molecules can cause leukocyte adhesion and migration into vascular endothelium. They also observed increases in the activation of mitogen-activated protein kinase and nuclear factor-kappa B, which implied that endocan mediated an inflammatory response through a complex mechanism. In contrast to those findings, Béchard et al [26] showed that endocan could bind directly to lymphocyte function–associated antigen-1 (LFA-1), a major integrin in human monocytes and lymphocytes. The interaction between leukocyte LFA-1 and vascular endothelial intercellular adhesion molecule-1 is a pivotal process in leukocyte adhesion and migration. Thus, endocan binding to LFA-1 suggested a mechanism for the anti-inflammatory effect of endocan. It remains to be clarified whether, *in vivo*, endocan plays a proinflammatory or anti-inflammatory role.

Recently, Yilmaz et al [11] reported a positive correlation between plasma endocan levels and CKD stages. They suggested that plasma endocan may serve as a predictor of mortality and cardiovascular events. That finding was not consistent with our results. We detected no differences in plasma endocan levels among different CKD stages. This discrepancy might not only be related to the number of studied patients and degree of renal dysfunction but also explained by a difference in the underlying etiologies of CKD. Arman et al [27] investigated the effects of glycemic regulation on serum endocan levels in patients with diabetes and found that the degree of glycemic control could influence the serum endocan levels. In the previous study [11], the most common cause of CKD was diabetes. Thus, high plasma endocan levels in patients with advanced CKD might result from poor glycemic control, rather than the CKD stage. In future studies, the degree of glycemic control (i.e., hemoglobin A1c) should be assessed to investigate this possibility.

To our knowledge, this study was the first to investigate urine endocan levels in renal disease. Interestingly, urine endocan was undetectable in 65% of controls, and the remaining individuals showed very low levels of urine endocan. In contrast, most patients with IgAN had variable levels of urine endocan. These findings implied that endocan was involved in

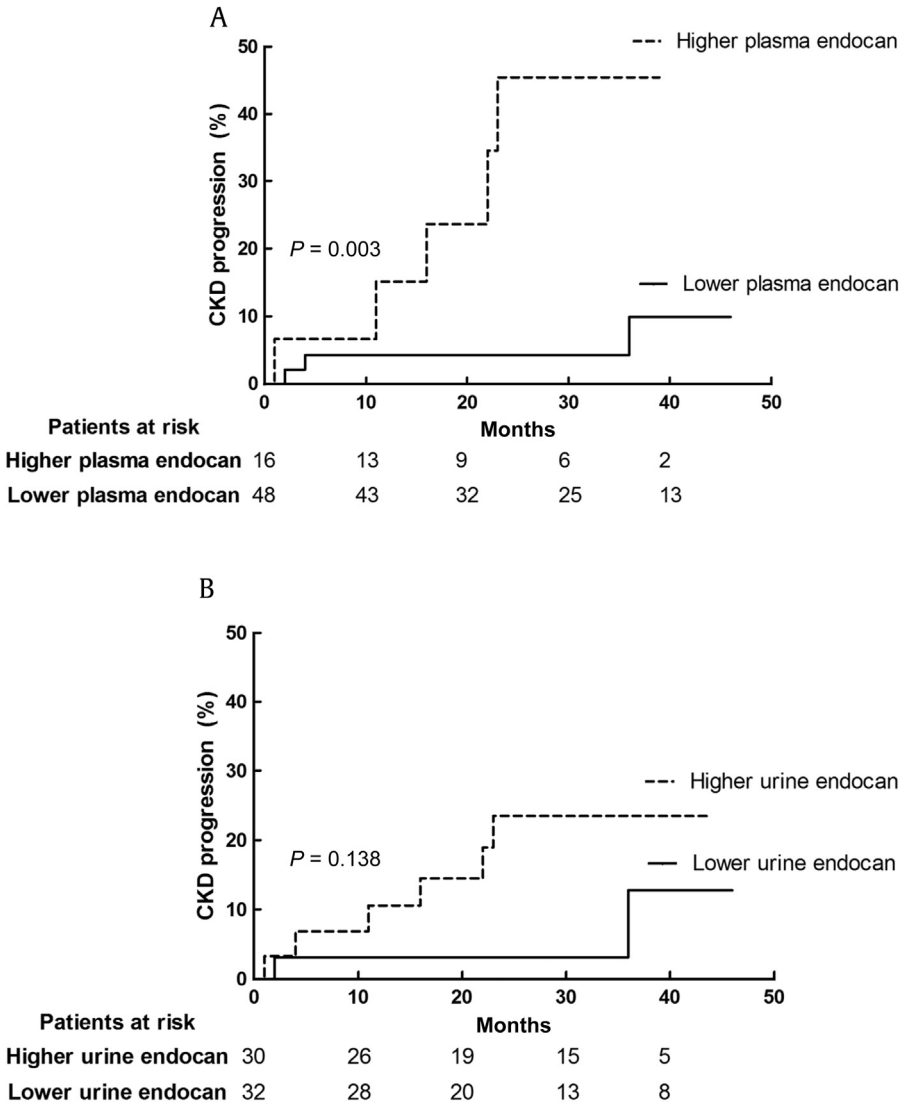

Figure 3. Renal outcomes according to plasma (A) and urine (B) endocan levels.

important pathophysiologic processes in the kidney. Normally, the negatively charged basement membrane in a healthy glomerulus can prevent endocan from passing through the glomerular filtration barrier because of the presence of dermatan sulfate, an important component of endocan, which is also highly negatively charged [8]. Thus, any glomerular injury that disrupted the glomerular basement membrane could permit circulating plasma endocan to leak into the urine. Alternatively, endocan may leak into the urine from renal tubules. Indeed, immunohistochemistry staining in healthy control biopsies showed endocan expression in renal tubular epithelium [9]. In our study, urine endocan levels were not related to the degree of a tubulointerstitial injury, suggesting that urine endocan leaked through a disrupted glomerular barrier, rather than through damaged tubulointerstitial cells. Because there are scarce data about the metabolism and excretion of endocan after secretion into blood, thorough investigations are mandatory to confirm this hypothesis.

Table 4. Cox proportional hazard model for risk of CKD progression according to plasma endocan quartiles (first + second + third quartiles vs. fourth quartile)

Models	CKD progression	
	Hazard ratio (95% confidence interval)	*P*
Unadjusted	8.73 (2.01–37.88)	0.004
Adjusted		
Model 1	14.48 (2.35–89.27)	0.004
Model 2	16.01 (1.67–154.18)	0.016
Model 3	17.69 (1.78–174.4)	0.014

Model 1 was adjusted for age, gender, and diabetes mellitus.
Model 2 was adjusted for model 1 plus hypertension and estimated glomerular filtration rate.
Model 3 was adjusted as model 2 plus urine protein/creatinine ratio.
CKD, chronic kidney disease.

The main limitations of this study were the relatively small numbers of enrolled patients and healthy controls. Also, the follow-up was relatively short, particularly for evaluations of clinical events including the occurrence of cardiovascular disease. Another limitation was that some patients regularly took medications that might have influenced endothelial activity at

the time of plasma and urine sampling. Some antihypertensive agents (e.g., ARBs and calcium channel blockers) and some lipid-lowering agents are known to reduce plasma endocan levels [28,29].

In conclusion, our results demonstrated that, among patients with IgAN, those with high plasma endocan levels tended to show advanced pathologic grades and rapid decline in eGFR. Further studies are needed to validate whether endocan levels could serve as a marker of poor renal prognosis.

Conflicts of interest

All authors have no conflicts of interest to declare.

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