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Original Article

Clinical application of neutrophil gelatinase-associated lipocalin in the revised chronic kidney disease classification

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Abstract: Background: A revised classification of chronic kidney disease (CKD) was proposed by the Kidney Disease: Improving Global Outcomes (KDIGO) in 2012. Neutrophil gelatinase-associated lipocalin (NGAL) was considered as one of the most promising biomarkers in clinical nephrology. The aim of this study was to examine the level of NGAL in patients with different impairment of GFR based on the new classification, and to evaluate whether NGAL in serum or urine was associated with different risk categories in CKD patients. Methods: A cross-sectional study was performed in 240 patients with CKD. NGAL, serum cystatin C, β_2-macroglobulin (β_2-MG), urine α_1-macroglobulin (α_1-MG) and albuminuria were tested in patients with various degrees of renal impairment. Results: Good correlation was found between the NGAL and the cystatin C, β_2-MG and the α_1-MG ($r > 0.7$). The level of sNGAL in CKD stage 3b was more than that in CKD stage 3a ($P = 0.025$). The concentration of the NGAL increased progressively with the increasing of risk categories (proposed by the revised CKD classification). The cutoff value of NGAL was calculated from stage 2 to stage 5. ROC analysis showed good AUC (sNGAL > 0.8, uNGAL > 0.7) and high specificity (sNGAL > 87%, uNGAL > 90%) on the cutoff value of NGAL. Conclusion: The results confirm NGAL as a useful biomarker in clinical nephrology which is helpful to diagnosis and evaluate the categories for CKD proposed by the KDIGO.

Keywords: Neutrophil gelatinase-associated lipocalin, KDIGO, chronic kidney disease

Introduction

Chronic kidney disease (CKD) is a devastating illness with an incidence and prevalence rapidly approaching epidemic proportions worldwide [1]. Recently, the KDIGO recommended that CKD is classified based on cause, GFR category, and albuminuria category (CGA). The previous CKD stage 3 was subdivided into two stages (3a and 3b). The level of risk group into 4 levels as low risk, moderately increased risk, high risk, and very high risk categories [2].

Serum creatinine is commonly used to evaluate the impairment in renal function and the progression of CKD [3]. Different low-molecular-weight proteins (range 10-25 kDa) are also used to assess an impairment of GFR [4, 5].

Neutrophil gelatinase-associated lipocalin (NGAL), a 25-kDa small protein, is a member of the lipocalin family that is expressed at low levels in several human tissues and rapidly released from renal tubular cells after various injuring stimuli [6]. Serum and urinary NGAL are arguably the most promising emerging biomarkers for early detection of acute kidney injury [7]. Several recent studies have also defined the role of NGAL in CKD and showed serum and urinary NGAL levels are a marker of kidney disease and severity in CKD [8]. This information suggests that NGAL level may reflect the entity of active renal damage that underlies the chronic impairment condition.

In this study, we test the hypothesis that the serum and urinary NGAL concentration are associated with CKD patients at different functional stages. We compare the correlation between the NGAL and the low molecular weight protein including cystatin C, β_2-MG, α_1-MG and other kidney functional parameters.

The cut-off value of NGAL in revised CKD stages are calculated for predicting the progression of CKD.

Materials and methods

Patient recruitment and selection

CKD patients were referred to our laboratory from nephrology and internal medicine clinics at the Chinese People's Liberation Army General Hospital from September 2011 to December 2012 for functional evaluation of chronic nephropathies diagnosed on the basis of history of renal disease, presence of morphological or laboratory markers of kidney disease, and level of predicted GFR, according to National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines. Inclusion criterions were age > 18 yr and diagnosis of CKD at any stage. Patients were excluded from the study if they had cardiovascular disease (coronary artery disease, myocardial ischaemia, cerebrovascular disease or peripheral artery disease) in the past 3 months, infections requiring admission in the past 3 months, uncontrolled hypertension, or unwillingness to participate in the study. Patients with malignancy, liver, thyroid, or infectious diseases, organ transplantation, immunosuppressive treatment, and pregnancy were excluded in the study. The data of 240 adult CKD patients, affected by different kidney diseases with various degree of impairment of renal function, were analyzed in the present study. The type of glomerulonephritis was reported in the **Table 1**. To avoid inter-observer differences, all patients were recruited by a single investigator.

The study was approved by the Institutional Ethic Committee of the Chinese People's Liberation Army General Hospital, and all participants were given consent before the testing.

Laboratory measurements

Blood samples were taken in the morning before any food intake, and the second urine of the day was also collected. In addition to NGAL, cystatin C, β_2-MG, α_1-MG and other commonly tested biochemical parameters such as urea, creatinine, uric acid, serum electrolytes, albumin, hemoglobin, proteinuria and fibrinogen were also tested in all patients according to standard methods in the clinical laboratory. The eGFR was calculated with the CKD-EPI equation [9]. The blood samples were centrifuged immediately at 1500 g and 4°C for 10 min, and the supernatants were stored at -80°C until further use. Ten milliliters of urine sample was mixed with 1 ml of 10 mM Tris buffer, pH8.6, with 0.05% Tween 20 and 0.01% NaN_3 containing protease inhibitors (10 mM benzamidine, 10 mM aminocaproic acid, 20 mM ethylenediamine tetracetate, and aprotinin). This mixture was centrifuged at 3000 rpm for 5 min and stored at -80°C until assayed.

Cystatin C and NGAL were measured by particle-enhanced turbidimetric assay using Cobas c501 automated biochemistry analyzer (Roche, Mannheim, Germany). The NGAL kit was approved for use in serum and urine provided by Kehua Bio-engineering Co., LTD (Shanghai, China). The intra-assay coefficient of variation was 1.9% for 201.6 μg/L and 1.22% for 505.36 μg/L. The inter-assay coefficient of variation was 4.06% for 201.6 μg/L and 2.57% for 505.36 μg/L [10]. β_2-MG and α_1-MG were measured with latex immunonephelometric assay on a Behring Nephelometer II analyzer (Dade Behring, Marburg, Germany). Urinary albumin concentration was measured by immunoturbidimetry. Urinary albumin concentration was expressed as rations to urinary creatinine concentration (uACR). Serum creatinine level was measured by Jaffe's method and urea level was determined by a kinetic test with the urease method.

Statistical analysis

Statistical analyses were performed with SPSS version 15.0 software. Data were presented as mean (SD) or median (25-75th centile) as appropriate. Univariate comparisons of continuous variables among group were also performed using 1-way analysis of variance, unpaired t-tests, or nonparametric Mann-Whitney U tests in case of non-normally distributed variables, and we also compared categorical variables using x^2 test. The diagnostic abilities of the tests were compared using the areas under the curves (AUC). ROC analysis was used to calculate the area under the curve (AUC). The Youden index (sensitivity + specificity-1), an integrative indicator of sensitivity and specificity [11], was used to determine the cutoff value for NGAL identifying the different CKD categories by the revised CKD classification. For all tests, $P < 0.05$ was used to assess the statistical results.

Table 1. Clinical and laboratory data of patients with CKD stratified by eGFR[a]

Variable	All patients	eGFR (mL/min/1.73 m^2)						P[b]
		≥ 90	89-60	45-59	30-44	15-29	< 15	
n	240	48	55	25	30	34	48	
Sex, M/F	142/98	30/18	33/22	10/15	12/18	14/20	32/16	0.32
Age, years	43.15 (14.7)	38.08 (16.6)	42.0 (12.7)	42.5 (10.4)	42.8 (10.6)	47.0 (15.6)	47.4 (16.6)	0.03
BMI, kg/m^2	24.6 (4.0)	24.7 (4.0)	23.5 (3.0)	24.2 (3.8)	26.5 (5.6)	26.4 (3.5)	23.6 (4.7)	0.28
BP, mmHg								
Systolic	137 (21)	138 (21)	134 (24)	137 (21)	136 (19)	138 (18)	140 (20)	0.23
Diastolic	87 (14)	85 (14)	88 (16)	87 (13)	87 (14)	89 (13)	88 (14)	0.2
Scr (μmol/L)	123.5 (79.8, 256.4)	63.9 (12.1)	89.6 (16.3)	122.2 (19.1)	164.4 (31.6)	239.0 (48.4)	648.1 (275.9)	< 0.001
eGFR (mL/mim/1.73 m^2)	48 (20, 85.5)	114.1 (19.8)	74.4 (9.8)	50.8 (4.8)	36.9 (5.8)	22.4 (3.9)	8.6 (2.9)	< 0.001
Urea (mmol/L)	7.6 (5.13, 14.54)	4.6 (1.4)	5.8 (1.9)	7.7 (2.9)	10.5 (5.5)	13.4 (5.9)	22.4 (8.8)	< 0.001
Uric acid (umol/L)	395.2 (126.2)	320.9 (93.9)	344.9 (97.8)	414.9 (117.9)	471.0 (146.9)	425.2 (114.5)	449.0 (126.6)	< 0.001
CysC (mg/L)	1.89 (1.09, 3.00)	0.94 (0.16)	1.40 (0.48)	1.75 (0.37)	2.20 (0.56)	2.70 (0.75)	5.40 (2.08)	< 0.001
sβ2MG (mg/dL)	0.42 (0.24, 1.09)	0.22 (0.08)	0.28 (0.09)	0.39 (0.13)	0.53 (0.16)	1.15 (0.58)	2.33 (1.1)	< 0.001
Ca×P ($mmol^2/L^2$)	2.81 (2.28, 3.29)	2.75 (2.26, 3.16)	2.63 (2.15, 2.96)	2.30 (2.16, 3.08)	2.79 (2.56, 3.12)	3.02 (2.35, 3.36)	3.71 (2.90, 4.65)	0.004
Albumin (g/L)	38.2 (29.3, 41.6)	38.7 (24.4, 41.3)	37.85 (26.73, 41.85)	41.5 (25.65, 44)	36.4 (29.3, 45.1)	35.4 (29.85, 41.33)	37.85 (34.63, 42.65)	0.996
uNGAL (ug/L)	42.5 (15.3, 308)	19 (5.3, 31.7)	17 (6.0, 38)	41 (10.5,124)	41.5 (18.5, 147)	99.5 (33.25, 361.25)	619.5 (378.75, 1148.5)	< 0.001
sNGAL (ug/L)	158 (100, 291.8)	87.9 (42.0)	126.4 (73.4)	159.8 (58.5)	246.0 (106.1)	300.6 (158.2)	574.3 (273.5)	< 0.001
uα1MG (mg/dl)	2.52 (1.4, 4.46)	0.89 (1.90, 2.11)	0.87 (1.2, 2.1)	1.64 (1.89, 2.30)	2.2 (2.85, 4.16)	3.2 (4.1, 5.5)	6.3 (7.18, 10.3)	< 0.001
uβ2MG (mg/dl)	0.40 (0.02, 1.64)	0.02 (0.02, 0.02)	0.02 (0.02, 0.14)	0.45 (0.0213, 0.77)	0.87 (0.28, 1.4)	1.49 (0.83, 2.69)	2.58 (2.01, 3.88)	< 0.001
ACR (mg/mmol)	2.60 (0.34, 4.72)	0.92 (0.13, 2.40)	0.43 (0.10, 2.63)	3.39 (3.08, 4.21)	3.16 (0.49, 4.06)	3.99 (1.25, 7.07)	4.80 (2.84, 10.02)	< 0.001
Primary kidney disease						n		
Chronic renal failure						62		
Primary and secondary glomerulonephritis						110		
Interstitial nephropathy						30		
Diabetic nephropathy						23		
Polycystic kidney disease						15		

[a]Data are mean (SD) or 50th (25th; 75th percentile) for skrewed where appropriate, unless noted otherwise. [b]*P* values are for comparison across all 6 groups from Kruskal-Wallis test, 1-way ANOVA, and x^2 test where appropriate. uNGAL: urinary NGAL; sNGAL: serum NGAL; cysC: cytatin C; $s\beta_2$MG: serum β_2-microglobulin; $u\alpha_1$-MG: urinary α_1-microglobulin; $u\beta_2$-MG: urinary β_2-microglobulin; Scr: serum creatinine; eGFR: estimated glomerular filtration rate; ACR: albuminuria creatinine rate.

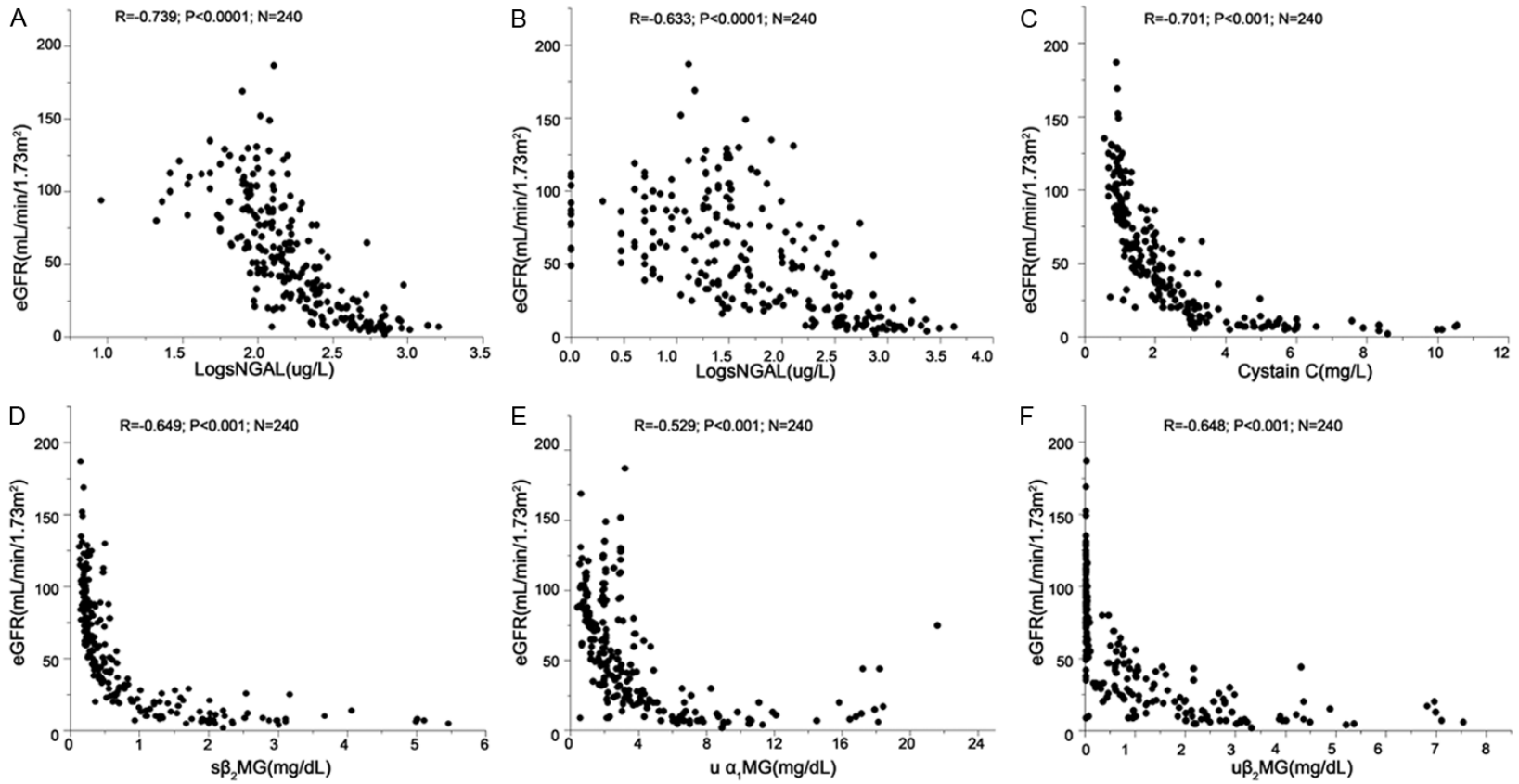

Figure 1. Variable correlations (Pearson coefficient) of estimated GFR (EPI formula). Significant correlation was evidenced with sNGAL (A), uNGAL (B), serum cystatin C (C), β_2-microglobulin (D), and urine α_1-microglobulin (E).

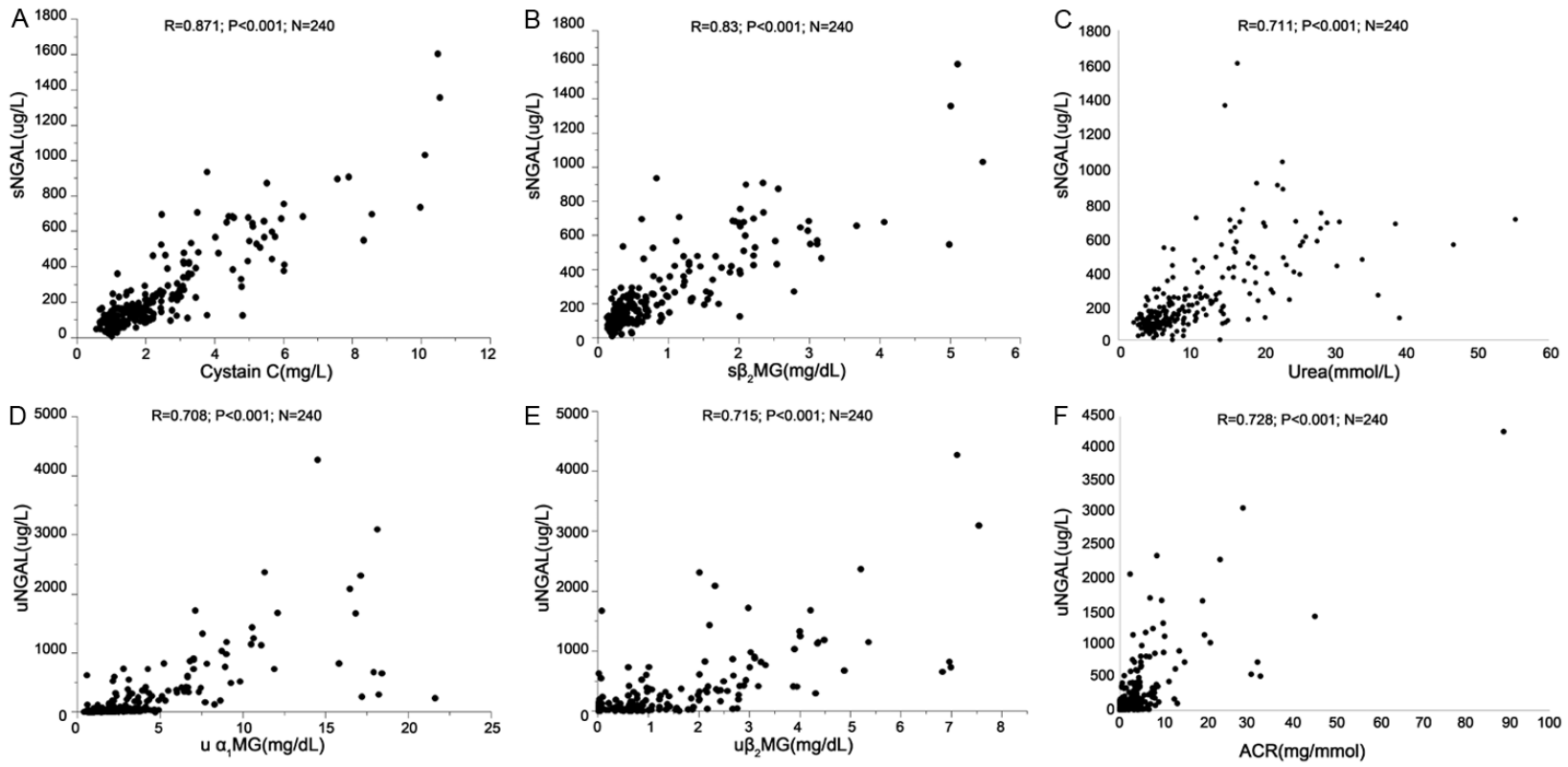

Figure 2. The correlation analyses among the tested parameters in CKD patients. Correlations were analyzed between sNGAL and serum cystatin C (A) (r = 0.871, $P < 0.001$), sNGAL and serum β_2-MG (B) (r = 0.83, $P < 0.001$), sNGAL and Urea (C) (r = 0.711, $P < 0.01$), uNGAL and urine α_1-MG (D) (r = 0.708, $P < 0.001$), uNGAL and urine β_2-MG (E) (r = 0.715, $P < 0.001$), uNGAL and Albuminuria creatinine ration (F) (r = 0.728, $P < 0.001$).

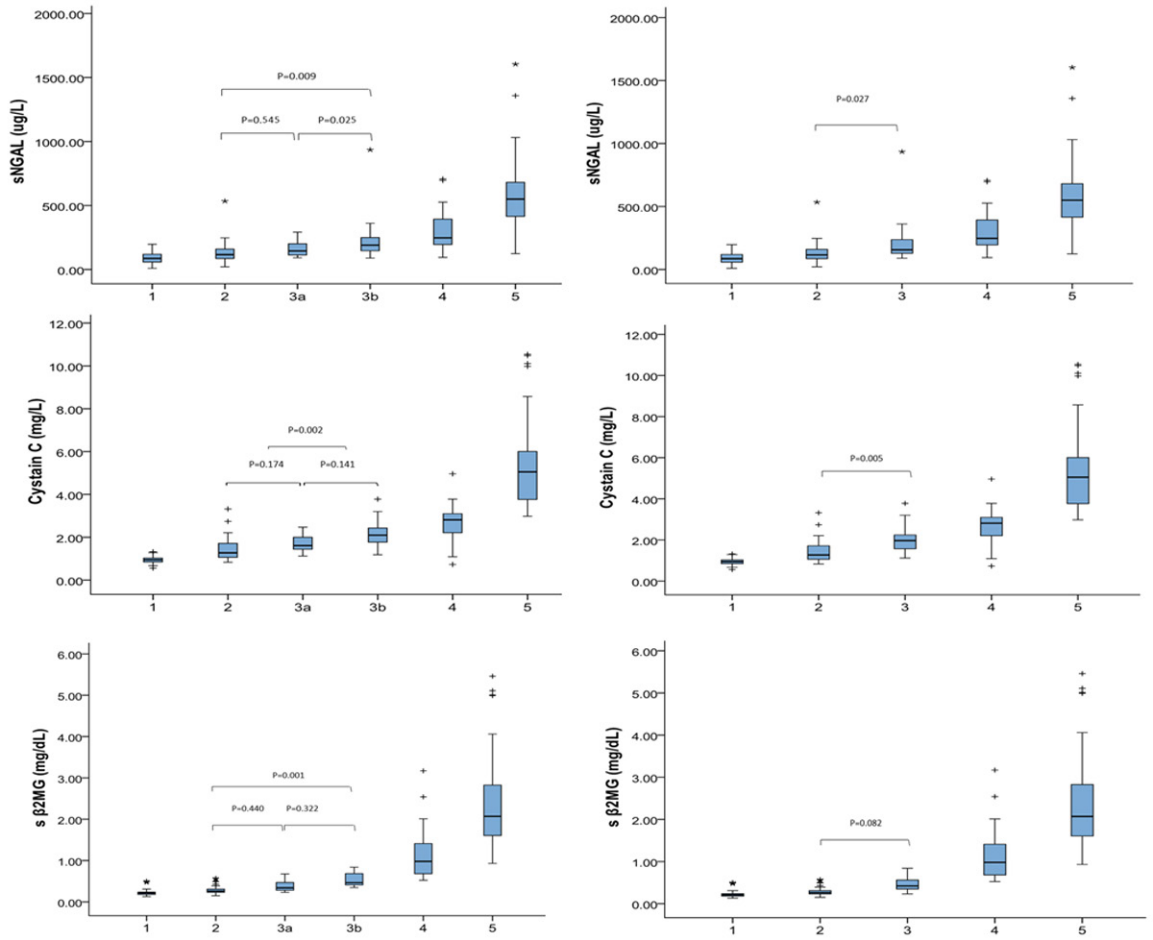

Figure 3. sNGAL, cystatin C, and β_2-MG in the GFR category of CKD. There was a significantly statistical difference between the stage 3a and the stage 3b by serum NGAL. There was a significantly statistical difference between the stage 2 and the stage 3 by serum NGAL, cystatin C.

Results

Clinical and laboratory data

The average age of patients was 43.15 ± 14.7 years old. **Table 1** shows the clinical characteristics 240 patients in 6 groups according to stages of eGFR as defined in the Kidney Disease: Improving Global Outcomes (KDIGO) for CKD [12]. sNGAL and uNGAL concentrations increased progressively with the decreasing of eGFR.

NGAL, cystatin C, α_1-MG and β_2-MG vs. eGFR

In univariate analysis (**Figure 1**), the eGFR was found to be inversely correlated with cystatin C (R = -0.701, $P < 0.01$), serum β_2-MG (R = -0.649, $P < 0.001$), urine β_2-MG (R = -0.649, $P < 0.001$), urine α1-MG (R = -0.529, $P < 0.001$), and log sNGAL (R = -0.739, $P < 0.001$) and log uNGAL (R = 0.633, $P < 0.001$). On the contrary, any significant correlation was described between eGFR and other parameters, such as age, gender, BMI, cholesterol, triglycerides, CRP, or proteinuria ($P > 0.05$).

Cystatin C, β_2-MG, urea, ACR and α_1-MG vs. NGAL

The correlation analyses among serum and urinary kidney functionary parameters in CKD patients are presented in **Figure 2**. A good correlation was found between uNGAL and urinary α_1-MG (r = 0.708, $P < 0.01$), uNGAL and urine β_2-MG (r = 0.715, $P < 0.01$), uNGAL and urine ACR (R = 0.728, $P < 0.01$) respectively. The sNGAL was also found to be directly correlated to serum cystatin C (r = 0.871, $P < 0.01$), serum urea (r = 0.711, $P < 0.01$) and serum β_2-MG (r = 0.83, $P < 0.01$), respectively.

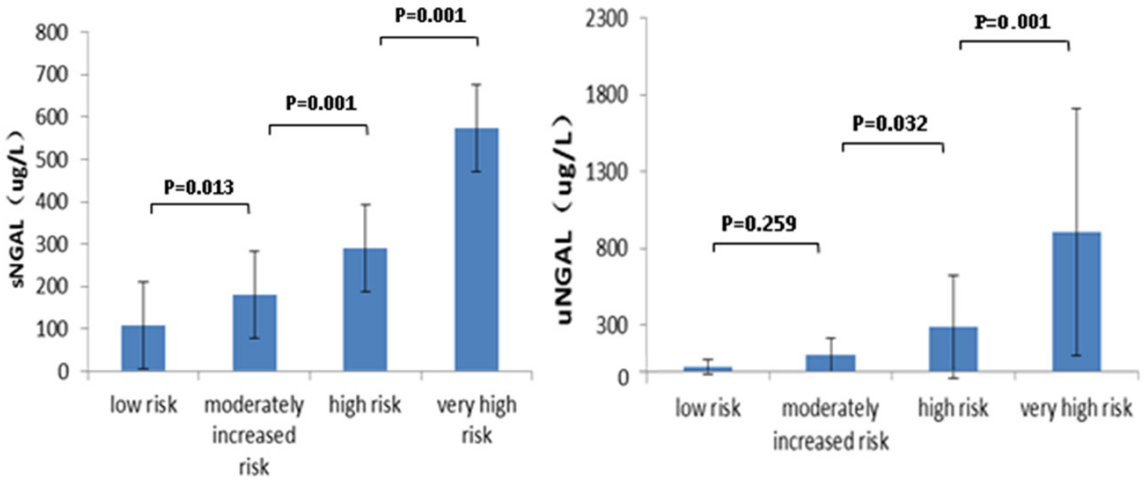

Figure 4. Levels of NGAL in the GFR and albuminuria categories of CKD. The sNGAL levels showed the significantly statistical difference among the 4 risk categories. The uNGAL levels showed the significantly statistical difference between the very high risk category and high risk category.

Table 2. Diagnostic performance of NGAL, Cystatin C, β_2-MG and α_1-MG to confirm the stages of kidney impairment

	AUC for GFR < 60 mL·min·(1.73 m^2)$^{-1}$	AUC for GFR 60-89 vs GFR > 90 mL·min·(1.73 m^2)$^{-1}$
sNGAL	0.903 (0.861-0.936)	0.819 (0.750-0.876)
uNGAL	0.834 (0.784-0.884)	0.701 (0.616-0.765)
CysC	0.945 (0.918-0.973)	0.899 (0.841-0.941)
sβ2MG	0.937 (0.901-0.972)	0.900 (0.842-0.942)
uβ2MG	0.788 (0.686-0.890)	0.711 (0.618-0.872)
uα1MG	0.861 (0.782-0.941)	0.753 (0.679-0.818)

uNGAL: urinary NGAL; sNGAL: serum NGAL; cysC: cytatin C; sβ_2-MG: serum β_2 -microglobulin; uα_1-MG: urinary α_1-microglobulin; uβ_2-MG: urinary β_2-microglobulin.

sNGAL, cystatin C, and β_2-MG in the GFR category of CKD

The results showed that there was a significant difference between the stage 3b and the stage 2 ($P < 0.05$) with the serum markers NGAL, cystatin C and β_2-MG, but not that between stage 3a and stage 2 (**Figure 3**). There was a significantly statistical difference between the stage 3a and the stage 3b by serum NGAL only. As the previous GFR category, there was a significantly statistical difference between the stage 2 and the stage 3 by serum NGAL, cystatin C, with the *P* value 0.027 and 0.005, respectively, but no significantly statistical difference between the stage 2 and the stage 3 by serum β_2-MG ($P = 0.082$).

NGAL in the GFR and albuminuria categories of CKD

The KDIGO guideline encompassed the levels of risk for CKD. By the GFR categories and the albuminuria categories, the levels of risk can be identified and grouped into low risk, moderately increased risk, high risk and very high risk 4 categories (**Figure 4**). The sNGAL levels showed the significantly statistical difference among the 4 risk categories. The concentration of the sNGAL in the 4 risk categories were 108.9 ± 62.2 μg/L (low risk), 180.5 ± 54.5 μg/L (moderately increased risk), 289.7 ± 154.3 μg/L (high risk), 574.3 ± 273.5 μg/L (very high risk), respectively. There was not a statistical difference between the low risk category and the moderately risk category with the uNGAL. The concentration of the uNGAL in the 4 risk categories were 31.7 ± 49.1 μg/L (low risk), 107 ± 106.5 μg/L (moderately increased risk), 290.4 ± 337 μg/L (high risk), 905.7 ± 806 μg/L (very high risk), respectively.

Diagnostic performance

The ROC analysis was used to evaluate the diagnostic performance of the tested markers in the staging of kidney impairment. **Table 2** demonstrated that all serum and urine markers showed a similar diagnostic meaning or area under the ROC curve to estimated GFR < 60 Ml min^{-1} (1.73 m^2)$^{-1}$ (0.903, 0.834, 0.945, 0.937,

Table 3. Cutoff values of the NGAL in the GFR categories of CKD

Parameters	Stages	AUC[#]	95% CI	Sensitivity (%)	Specificity (%)	Youden index	Cutoff value (μg/L)	*P*
sNGAL	2	0.819	0.75-0.876	71.4	87.5	0.587	128.5	< 0.001
	3a	0.903	0.861-0.936	73.1	92.7	0.658	189.5	
	3b	0.936	0.905-0.966	78.4	94.2	0.92	222	
	4	0.921	0.883-0.959	75.3	95.6	0.709	259	
	5	0.948	0.916-0.979	85.1	91.1	0.76	317.5	
uNGAL	2	0.701	0.616-0.765	49.5	95.8	0.453	82.5	< 0.001
	3a	0.834	0.784-0.884	61.6	90	0.515	100.5	
	3b	0.869	0.824-0.914	66.7	92.7	0.59	165.5	
	4	0.923	0.889-0.958	70.4	94.3	0.65	254.5	
	5	0.958	0.935-0.981	91.5	91.7	0.83	316.5	

[#]The AUC was determined for stage 2: all patients with CKD stage 2 and higher vs. CKD stage 1; stage 3a: all patients with CKD stage 3a and higher vs. CKD stage 1, and 2; stage 3b: all patients with CKD stage 3b and higher vs. CKD stage 1, 2, and 3a; stage 4: all patients with CKD stage 4 and stage 5 vs. CKD stage 1 + stage 2 + stage 3a + stage 3b; stage 5: patients with CKD stage 5 vs. other CKD stage patients.

0.861, and 0.788 for sNGAL, uNGAL, Cytatin C, $s\beta_2$-MG, $u\alpha_1$-MG and $u\beta_2$-MG, respectively) or to diagnose middle deterioration of renal function, estimated GFR 60-89 vs ≥ 90 mL min^{-1} (1.73 $m^2)^{-1}$ (0.819, 0.701, 0.899, 0.900, 0.753, and 0.711, respectively) (**Table 2**).

The cutoff value of the NGAL in the GFR categories of CKD

Receiver operating characteristic (ROC) curves was used to determine the cut-off value for NGAL in the GFR categories of CKD. The cut-off value of the sNGAL was 128.5 mg/L for 2 stage, 189.5 mg/L for 3a stage, 222 mg/L for 3b stage, 259 mg/L for 4 stage, 317.5 mg/L for 5 stage, respectively. The cut-off value of the uNGAL was 82.5 mg/L for 2 stage, 100.5 mg/L for 3a stage, 165.5 mg/L for 3b stage, 254.5 mg/L for 4 stage, 316.5 mg/L for 5 stage, respectively. The cut-off value of sNGAL was highly accurate for the AUC > 0.90 among the stage 3a to 5 (**Table 3**).

Discussions

The CKD classification system encompasses cause of CKD, GFR category, and albuminuria category [3, 12]. In this study, we intended to evaluate whether NGAL in serum or urine was associated with different risk categories in CKD patients based on the new classification.

In the study, the NGAL, cystatin C, β_2-MG, α_1-MG showed good correlation with eGFR. Median concentrations of the 4 markers progressively increased across stages of CKD as defined by the revised CKD guidelines. The result was accordance with the report that NGAL could inhibit the rise of serum creatinine and blood urea nitrogen, alleviate kidney injury, and reduce renal tubular epithelial cells apoptosis [13]. The four markers demonstrated similar diagnostic performance and accuracy for identifying a mild deterioration of renal function, GFR 60-89 vs ≥ 90 mL min^{-1} (1.73 $m^2)^{-1}$.

In this study, there was a correlation between the uNGAL with the ACR (r = 0.728). It is likely that increased albuminuria and NGAL reflects a different underlying pathophysiology in CKD. Albuminuria is a useful biomarker for glomerular injury. Significant glomerular injury is often noted in the microalbuminuric stage. Nodular glomerulosclerosis is the most prominent pathological manifestation in advanced nephropathy. The late pathological is tubulointerstitial fibrosis for the chronic kidney disease. Tomonaga Y et al. demonstrated that when albuminuria exceeds 10 mg/g creatinine and eGFR decreases to values below 105 ml/min/1.73 m^2, uNGAL concentrations increase with decreasing eGFR and increasing albuminuria [14].

It is important to dividing stage 3 based on data supporting different outcomes and risk profiles into categories 3a and 3b [15]. Bhavsar NA, et al. found that concentration of urinary NGAL was associated with incident CKD stage 3 [16]. Interestingly, the results of this study

showed a significant difference between the stage 3b and the stage 2 ($P < 0.05$) with the serum markers NGAL, cytatin C and β_2-MG, but not that between stage 3a and stage 2 (**Figure 3**). Furthermore, there was a significant difference between the stage 3b and 3a ($P = 0.025$) only with sNGAL. The results suggest that it is helpful for the sNGAL to differentiate the stage 3a or 3b.

Levels of risk can be identified and grouped into 4 categories in CKD patient by the revised CKD KDIGO guideline. The data showed a significant difference between the 4 risk categories with the sNGAL. Though no significantly statistic difference observed between the moderately increased risk category and low risk category, the concentration of uNGAL showed obvious difference among the 4 risk levels. The study indicated that the sNGAL could be used to predict CKD risk levels. Recent evidence suggests that NGAL may even be involved as a mediator of CKD progression [17]. In fact, the NGAL knockout mouse has markedly reduced renal lesions seen in CKD progression [17]. The role of NGAL in CKD is not completely understood. Some studies suggest that NGAL up regulation promotes apoptosis [18], whereas others suggest that NGAL aids in cell survival [19]. Liu K.D. et al. suggest uNGAL was an independent risk factor of progression among patients with established CKD of diverse etiology [20].

The cutoff value of NGAL was calculated from stage 2 to stage 5 with the ROC analysis in the study. Bolignano *et al*. reported the optimum cut-off of 435 mg/L for sNGAL and 231 mg/L, which patients were likely to develop renal failure [8]. This was in agreement with our proposed cut-off value for sNGAL (stage 4 vs. 259 mg/L, stage 5 vs. 317.5 mg/L) and uNGAL (stage 4 vs. 254.5 mg/L, stage 5 vs. 316.5 mg/L). The study indicated that the sNGAL showed better diagnosis performance than that of the uNGAL in stage 2-3. It was considered that sNGAL was significantly correlated with the severity of renal damage and the progression of renal function deterioration [21]. The uNGAL showed the same diagnosis performance as the sNGAL in stage 4 and stage 5. The finding was also agreement with the hypothesis that patients with greater uNGAL levels more frequently required dialysis [22].

Limitations of the study include no direct measure of GFR and a single baseline measurement of each marker.

In conclusion, our study results showed that NGAL is an effective biomarker for CKD patients. Serum NGAL showed better diagnosis performance in patients with stage 2-5 CKD, while urine NGAL showed the same diagnosis performance as the sNGAL in patients with stage 4 and 5 CKD. Large scale, longterm follow-up studies are required to validate the role of the NGAL level in diagnosis and evaluate the categories for CKD proposed by the KDIGO.

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Disclosure of conflict of interest

None.

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