EDITORIAL

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Neutrophil gelatinase-associated lipocalin as a predictor of adverse renal outcomes in immunoglobulin A nephropathy

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Neutrophil gelatinase-associated lipocalin (NGAL) is a 25-kDa protein belonging to the lipocalin family that is associated with human neutrophil gelatinase [1]. It is derived from neutrophils and expressed at low concentrations in various human tissues, including kidney, liver, and spleen [2]. NGAL plays roles in scavenging iron, inhibiting bacterial growth, and promoting epithelial cell growth [3]. Clinical studies have demonstrated the value of plasma and urine NGAL in the diagnosis and prognosis of acute kidney injury (AKI) [4,5].

The role of NGAL in predicting the progression of chronic kidney disease (CKD) has also been demonstrated [6,7]. However, the prognostic value of NGAL in patients with immunoglobulin A (IgA) nephropathy has not been established, and only a few studies of small populations have been published. Recently, *The Korean Journal of Internal Medicine* published two studies on the role of NGAL as a predictor of renal outcome in patients with IgA nephropathy.

Park et al. [8] demonstrated that plasma NGAL was an independent predictor of adverse renal outcomes in patients with IgA nephropathy. They enrolled 91 patients with biopsy-proven IgA nephropathy, and analyzed the correlation of plasma NGAL levels with clinical factors and histological severity. An adverse renal outcome was defined as stage 3 or higher CKD. In their study, plasma NGAL showed good correlations with the estimated glomerular filtration rate, proteinuria, and tubular atrophy/interstitial fibrosis. Furthermore, the plasma NGAL level had a significant predictive value for adverse renal outcomes in a receiver operating characteristic curve analysis (area under the curve = 0.777; $p = 0.001$). An NGAL level exceeding 118.65 ng/mL predicted adverse renal outcomes with 84.6% sensitivity and 68.7% specificity.

Rhee et al. [9] also reported the clinical value of serum and urine NGAL as an independent predictor of renal progression in 121 patients with IgA nephropathy. High serum NGAL was defined as a serum NGAL level exceeding 150 ng/mL. They defined high urine NGAL/creatinine as a urine NGAL/creatinine level higher than the median value for the cohort. In their study, the serum or urine NGAL level alone could not predict renal progression, while the high NGAL group, defined as having elevated levels of both serum and urine NGAL, independently pre-

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dicted renal progression (hazard ratio [HR], 5.56; 95% confidence interval [CI], 1.42 to 21.73; p = 0.014) along with tubular damage (HR, 8.79; 95% CI, 2.01 to 38.51; p = 0.004). In addition, the Kaplan-Meier curve for renal survival showed significantly higher renal progression in the high NGAL group (log rank, p = 0.004).

Both studies suggest that serum or urine NGAL levels at the time of kidney biopsy predict adverse renal outcomes in patients with IgA nephropathy; however, they have several limitations. First, both studies analyzed patients with IgA nephropathy retrospectively. Second, the numbers of enrolled patients were relatively small. In addition, the long-term results need to be confirmed.

Furthermore, the value of NGAL *per se* has several limitations as a biomarker for kidney disease. The cutoff values for NGAL vary according to the timing of the measurement and clinical conditions [5]. The plasma NGAL level is increased in septic patients regardless of the presence of AKI, and septic AKI patients have higher plasma and urine NGAL levels than non-septic patients with AKI [10,11]. The NGAL level cannot differentiate AKI from AKI with CKD because the serum NGAL level is also increased in CKD patients [12]. Cardiomyocytes also express NGAL, and serum NGAL levels are increased in patients with heart failure [13]. In this context, NGAL might be a useful biomarker for kidney disease. However, clinicians should consider comorbid conditions when evaluating NGAL values because several clinical factors can affect serum and urine NGAL levels.

In conclusion, an integrated analysis of combined biomarkers may enhance their predictive value for diagnosis and prognosis. Prospective well-designed studies of larger populations are needed to establish the usefulness of NGAL as a biomarker for kidney disease.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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