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The Predictive Value of LCN2 (NGAL) in Renal Transplant Recipients

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Editorial

Retention parameters (creatinine, urea) signal kidney injury only after a certain degree of irreversible damage. Lipocalin-2 (LCN2), originally described as neutrophil gelatinase associated lipocalin (NGAL)-has been established as an acute kidney injury (AKI) biomarker as it is produced by tubular epithelial cells after hypoxic or other injury [1]. LCN2 may be a more sensitive and thus, an earlier marker of incipient injury than creatinine [2]. Urinary LCN2 was predictive for the need to (re)initiate dialysis after intensive care unit admission [3].

LCN2 transports small hydrophobic molecules such as lipids and steroids [4] and plays a bacteriostatic role by sequestering iron-containing siderophores. Mice lacking LCN2 are more susceptible to bacterial infection [5]. LCN2 as a kidney injury marker is not specific as it is an acute phase protein [6] and its major source is the liver in mice [7] and humans [8]. Furthermore, it can be a product of injured epithelial cells other than the renal tubular epithelium [9]. Thus, urinary excretion (U) or U to plasma (P) ratio may be more informative for kidney injury than plasma levels [10]. However, there is some disagreement whether urinary or plasma NGAL is a better AKI marker [11]. There has been a number of attempts to increase the sensitivity/specificity of LCN2 to detect AKI such as repeated measurements [4,11,12]or normalization of urinary to plasma (U/P) NGAL [8].

Although LCN2 has been established as an AKI marker, the predictive or prognostic value of LCN2 for long term outcome in renal transplant recipients is not clear. Renal transplantation is always accompanied by severe AKI. Since the recognition of severe AKI-induced chronic kidney disease (CKD) [13] AKI markers may have a long-term prognostic relevance. Few papers have investigated LCN2 in this respect. Plasma LCN2 >50 ng/mL was associated with higher frequency of delayed graft function (DGF) [14] and rejection rates after transplantation [4,15]. High serum or urinary NGAL after transplantation was predictive of graft loss at one year [4]. LCN2 is an early and sensitive marker of graft dysfunction due to hypoxia, rejection, calcineurin inhibitor toxicity, occlusion of the urine outflow or infection [4]. LCN2 may not discriminate these causes of tubular injury; however, all of these may significantly shorten graft survival. Thus, LCN2 may predict long term outcome. Although few studies investigated LCN2 in chronic renal fibrosis induced by diabetic nephropathy [16] or primary glomerulonephritis [17], there is very limited data on chronic allograft nephropathy (CAN) or interstitial fibrosis and tubular atrophy (IFTA). A biomarker panel including β2-microblobulin, LCN2, clusterin and KIM-1 in the urine was able to detect CAN [18] and a recent study concluded that LCN2 may predict both DGF and CAN [19].

In conclusion, LCN2 may be a reliable prognostic marker for long term graft outcome, but the possible prognostic value of LCN2 has not been exploited yet.

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