NAG is an enzyme of hydrolase class that is abundant in the kidney, predominantly in the lysosomes of proximal tubular cells. The increased excretion of NAG is thought to be a specific marker of functional tubular impairment in many renal pathologies. Likewise KIM-1, NAG has been a useful marker of acute kidney injury (AKI) [97]. A recent study in type 1 diabetes mellitus found that lower levels of urinary NAG were associated with the regression of microalbuminuria [98]. It has not been assessed longitudinally in CKD [95]. In patients with CHF, urinary NAG was associated with an increased risk of death, heart failure hospitalizations and heart transplantation, independent of GFR [99].

IL-18 is a proinflammatory cytokine that is released by the epithelial cells of the proximal tubule within hours of renal injury. It is significantly increased in AKI in comparison to urinary tract infection and nephrotic syndrome [96]. The destabilization of human coronary plaques can be connected to IL-18, which was originally thought to be a factor that promotes interferon-γ synthesis. In addition, in one study it was confirmed that young and middle-aged patients with a recent AMI have higher IL-18 concentration in serum than age- and sex-matched control subjects, showing that concentration of this cytokine is associated with severity of coronary atherosclerosis [100]. In addition, recent evidence suggests that serum IL-18 is an important indicator and predictor of CV death in two-year follow-up among non-diabetic patients suffering from CKD, with history of AMI in the previous year [101].

Fibroblast growth factor-23 (FGF23) is a newly discovered hormone produced in the bone that regulates phosphate and vitamin D metabolism by the kidneys. The main physiological functions of FGF23 are mediated by FGF receptors, generally in the presence of Klotho coreceptors. Decreased phosphorus excretion triggers FGF23 production, which in turn stimulates Klotho coreceptors in the kidneys [102]. CKD progression leads to compensatory elevation of FGF23 levels, resulting in typical CKD manifestations such as hyperphosphatemia, secondary hyperparathyroidism and bone disease, and progression to ESRD [80]. Elevated FGF23 has been associated with LVH, and it has been suggested that FGF23 may induce myocardial hypertrophy through a direct effect on cardiac myocytes [102]. FGF-23 has been independently associated with risk of all-cause death in dialysis and CKD patients, heart failure, CV events and death in the general population [86].

Matrix metalloproteinases (MMPs) are a large family of endopeptidases capable of degrading all components of the extracellular matrix and are therefore responsible for controlling the pathophysiological remodeling of tissues, including CV and renal systems. MMPs are classified according to their structure and substrate specificity, so MMP-2 and MMP-9 belong to the