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temat pracy: *„Wpływ nefrektomii na stężenie sklerostyny i wybrane wskaźniki metabolizmu kostnego”*

**Summary**

 Disturbances of mineral and bone metabolism develop as early as in stage 2 of chronic kidney disease (CKD). Clinically, it translates to increased incidence of cardiovascular events and risk of fractures leading to decreased quality of life. Pathogenesis of this disorder is multifactorial and despite many years of research largely unknown. Traditional biochemical markers of chronic kidney disease and mineral bone disorder (CKD-MBD) such as calcium, phosphorus, parathyroid hormone and vitamin D can remain within normal ranges in early stages of CKD. Therefore the search for biomarkers that might allow earlier diagnosis and would give new insights into CKD-MBD pathogenesis remains the area of many currently conducted research. Growing evidence indicates fibroblast growth factor 23 (FGF-23) and Klotho as key players in maintaining mineral homeostasis. Moreover recently, a lot of attention is paid to inhibitors of Wnt-β-catenin pathway and their associations with skeletal health. Sclerostin is a protein that acts as an antagonist of Wnt-β-catenin pathway and leads to decreased bone formation. Recent studies indicate that sclerostin is associated with bone and cardiovascular complications. As compared with individuals with preserved renal function, CKD patients have elevated levels of sclerostin and FGF-23 and decreased concentrations of Klotho.

 A nephrectomy offers unique clinical model to study effect of acute GFR decline on metabolism of such molecules as sclerostin, Klotho or FGF-23. Up to now there is no data regarding behaviour of bone metabolism markers in response to acute glomerular filtration rate (GFR) decline, as seen in patients undergoing nephrectomy due to urological indications. It might be especially important in light of data reporting altered bone metabolism and increased fracture rates in individuals subjected to nephrectomy.

 The aim of the studies included in this doctoral thesis was to examine the influence of acute GFR decline evoked by nephrectomy on serum sclerostin level and its renal elimination, FGF-23 and Klotho levels. The secondary aim was to assess, whether changes in the concentration of the above molecules are associated with alterations in the markers of bone formation and/or resorption.

 Twenty-nine patients who underwent unilateral nephrectomy (partial or radical) due to urological indications (tumours, cirrhotic kidney, complex renal cysts, pyonephrosis and kidney stones) were enrolled to the study. Nephrectomy resulted in a significant decline in estimated glomerular filtration rate (eGFR) compared with the baseline values and caused around 20 times higher urinary fractional excretion of sclerostin while its serum level remained unchanged. The magnitude of eGFR reduction (ΔeGFR) was associated inversely with change in urinary sclerostin fractional excretion and serum sclerostin level. Moreover nephrectomy significantly decreased sKL level and did not change C-terminal fibroblast growth factor 23 (c-FGF-23) concentration. Simultaneously alterations in bone turnover markers (both formation and resorption) were observed.

 The study showed that in response to moderate eGFR reduction there is increased renal excretion of sclerostin, what enables maintaining constant blood levels of this glycoprotein. As renal function deteriorates, sclerostin accumulation becomes more relevant. Nephrectomy does not increase c-FGF-23 but reduces Klotho concentration. Derangements in bone turnover markers observed in this study may participate in pathogenesis of bone disease after nephrectomy.