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Upregulation of Adipose Tissue (AT) Fatty Acid-Binding Protein 4 (FABP4) in Chronic Kidney Disease (CKD) Patients: Implications for Dysfunctional Vascular Cells

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Objectives: FABP4 is predominantly expressed in AT and has been shown to be elevated in patients with CKD. Although elevated levels of FABP4 have been linked to cardiovascular disease in ESRD patients, the cause of this increase is unclear. The aim of this study was to evaluate the expression of AT FABP4 under uremic conditions and its impact on the function of vascular cells.

Methods: We measured the levels of FABP4 in the blood and urine of CKD patients. The expression of AT FABP4 was analyzed using omental AT obtained from healthy kidney donors and patients with ESRD who received peritoneal catheter insertion. The effect of FABP4 on the function of macrophages and vascular smooth muscle cells (VSMC) was also assessed.

Results: The levels of FABP4 in the blood and urine of CKD patients were inversely correlated with their eGFR. An increase in FABP4 in the blood was detected before its increase in the urine. FABP4 expression was found to be higher in mature adipocytes in visceral AT compared to the stromal vascular fraction (SVF). Adipocytes treated with p-cresol and adipocytes isolated from CKD patients showed higher levels of FABP4 expression compared to healthy individuals. Single-cell RNA sequencing of SVF showed increased FABP4 expression in progenitor cells and macrophages from CKD patients. In THP-1 cells, FABP4 induced more foam cells and increased levels of inflammatory mediators in the presence of palmitic acid. VSMC treated with p-cresol or VSMC isolated from CKD mice showed a pro-calcific phenotype, as indicated by increased calcium content and bone-related gene expression, which was further enhanced by FABP4.

Conclusions: The elevated levels of FABP4 in CKD patients are not solely a result of decreased renal clearance but also due to increased production in AT. These higher levels of circulating FABP4 may be associated with dysfunction in vascular cells.