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## **Elevated Heparin is an Independent Risk Factor for the Progression of Coronary Artery Calcification in Patients with Chronic Kidney Disease**

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**Objectives :** Although hepcidin is well known for its role in iron metabolism, recent studies also showed its relationship with cardiovascular events. A previous study demonstrated a positive correlation between hepcidin level and the incidence of atherosclerotic disease. Moreover, elevated hepcidin level was related to increased cardiovascular outcome in dialysis patients. However, the relationship between hepcidin and coronary artery calcification (CAC) in patients with CKD was not well studied. Present study was aimed to investigate the association between hepcidin and CAC progression in patients with non-dialysis chronic kidney disease.

**Methods :** A total of 1,147 CKD (stage 1 to 5) patients were enrolled from the nationwide multicenter prospective observational cohort of KNOW-CKD (KoreaN Cohort Study for Outcomes in Patients With Chronic Kidney Disease). Patients were divided into four groups based on coronary artery calcification (CAC) severity: None (CAC score = 0), Mild (< 100), Moderate (100-300), and Severe (> 300). Primary outcome was CAC progression, which was defined as an annualized percentage change in CAC score  $\geq 0.15$  (15%). An annualized percent change was calculated as follows:  $\{(CAC \text{ score at the end} - CAC \text{ score at the entry}) / (CAC \text{ score at the entry} + 1) + 1\}^{(12 / \text{follow-up months})} - 1$ .

**Results :** The mean age of study subjects was  $52.8 \pm 12.0$  years and 688 (59.7%) were male. Baseline hepcidin levels differed significantly among CAC severity groups ( $14.5 \pm 13.7$ ,  $17.1 \pm 14.9$ ,  $15.4 \pm 13.3$ ,  $13.5 \pm 12.0$ ;  $P=0.04$ ). After log transformation, multivariate analysis showed each 1-unit increase in  $\log(\text{hepcidin}+1)$  associated with higher CAC progression risk (OR 1.95; 95% CI, 1.06-3.60;  $P=0.03$ ). Subgroup analysis revealed no significant association in patients with baseline CAC=0 ( $P=0.29$ ), but significant association in those with baseline CAC>0 (OR 3.15; 95% CI, 1.18-8.39;  $P=0.02$ ).

**Conclusions :** Heparin level may be an independent predictor of CAC progression in CKD patients.