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Relationship between soluble klotho and longitudinal changes of cardiac structure in CKD patients: Results from the KNOW-CKD Study

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Objectives: The present study aimed to investigate the association between serum klotho and longitudinal changes of cardiac structure from a large-scale Korean CKD cohort.

Methods: We analyzed 645 subjects from KoreaN Cohort Study for Outcome in Patients With Chronic Kidney Disease (KNOW-CKD) cohort whose serum klotho level was measured at enrollment and who performed echocardiographic evaluation both at baseline and at four years. Left ventricular mass index (LVMI) and LV geometry were evaluated. Progressor was defined as those in the upper 50th percentile for changes in LVMI over 4-year period. Subgroup analysis was performed in patients who had no left ventricular hypertrophy (LVH) at baseline. LVH was defined as LVMI $\geq 50\text{g}/\text{m}^{2.7}$ in men and $\geq 47\text{g}/\text{m}^{2.7}$ in women.

Results: The median serum klotho level was 508 (interquartile range: 394-653) pg/mL. Subjects were divided into lower and higher klotho groups (serum klotho <508 , ≥ 508 pg/mL, respectively). During follow-up for 46.2 ± 2.0 months, lower klotho group exhibited a significant increase of LVMI from 40.5 ± 10.3 at baseline to 41.7 ± 11.0 at 4 years ($P = 0.009$), while higher klotho group did not change in LVMI ($P = 0.393$). Lower klotho group showed a significant increase of LVH ($P = 0.036$) and exhibited an increased proportion of concentric hypertrophy ($P = 0.019$) over the 4-year period while higher klotho group did not. However, after adjustment, serum klotho was not independently predictive of being progressors in LVMI in Cox proportional hazards analysis (adjusted HR, 1.00; 95% CI, 0.99-1.00; $P = 0.427$). In the subgroup analysis, 68 (13.6%) patients developed *de novo* LVH. Klotho was not significantly associated with development of *de novo* LVH (adjusted HR, 1.00; 95% CI, 0.99-1.00; $P = 0.847$).

Conclusions: Univariate analysis showed that lower klotho group significantly increased LVMI compared with higher klotho group. However, serum klotho was not significantly associated with development of *de novo* LVH.