FGF23 in Type 2 Diabetic Patients: Relationship With Bone Metabolism and Vascular Disease

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The relationship between fibroblast growth factor (FGF) 23 and vascular disease is well established in chronic kidney disease (CKD). Regarding serum FGF23 and bone fragility, there is contradictory data. Type 2 diabetes (T2D) is associated with higher rates of cardiovascular disease and fractures despite high bone mineral density (BMD), so the evaluation of FGF23 and its relationship with bone and cardiovascular disease in T2D is of interest. Our hypothesis was that serum FGF23 may be related to cardiovascular disease and bone metabolism (BMD, osteoporosis, and fractures) in T2D.

We performed a cross-sectional study including 68 T2D subjects and 45 subjects without diabetes. We analyzed the relationship between circulating FGF23, bone metabolism, cardiovascular events, and intima-media thickness (IMT).

There were no differences in FGF23 according to group. In the entire cohort, subjects with prevalent fracture and osteoporosis had lower FGF23 (20.9 $\pm$ 8.3 vs. 51.4 $\pm$ 38.9 pg/mL and 29.5 $\pm$ 15.6 vs. 52.4 $\pm$ 40.6 pg/mL, $P < 0.05$). In T2D, serum FGF23 was related to serum phosphorus ($r = 0.484$), lumbar spine T-score ($r = 0.300$), and femoral neck T-score ($r = 0.252$) and was inversely related to age ($r = -0.496$) ($P < 0.05$ for all). Differences according to osteoporosis, abnormal IMT, and diabetic nephropathy are shown in Fig. 1. In T2D, after linear regression analysis the main determinants of serum FGF23 were age ($\beta = -0.406$), glomerular filtration rate ($\beta = -0.206$), serum phosphorus ($\beta = 0.299$), osteoporosis ($\beta = -0.235$), and abnormal IMT ($\beta = -0.253$) ($P < 0.05$ for all).

Our results showed a stronger correlation between FGF23 and BMD than previously found in elderly nondiabetic males (1,2). Serum FGF23 may reflect the osteocyte number, and T2D subjects have higher BMD. On the other hand, a different relationship between FGF23 and parathyroid hormone in diabetes has been reported apart from the presence of CKD (3), which may indicate a differentiated regulation and possibly different effects of FGF23 on bone metabolism in T2D compared with nondiabetic populations.

In our study, subjects with previous fractures have lower FGF23 concentrations, but no differences in T2D were found. Circulating FGF23 has been linked to fracture risk (4), although in another study FGF23 and hip fracture risk was not related (2). We consider that the relationship between FGF23 and fracture risk is not established.

T2D patients with abnormal IMT had lower FGF23, and abnormal IMT remained associated with FGF23 after linear regression analysis. However, FGF23 and established cardiovascular disease or aortic calcification was not related. Our findings may indicate a role in the development of atherosclerosis in T2D. Supporting the association between FGF23 and preclinical vascular disease, higher FGF23, even within the normal range, is independently associated with impaired vasoreactivity and increased arterial stiffness in the general population (5).

In summary, serum FGF23 is related to BMD and preclinical vascular disease in T2D patients. Our study suggests that effects of FGF23 in T2D may differ from other populations, although it must be confirmed in larger studies.

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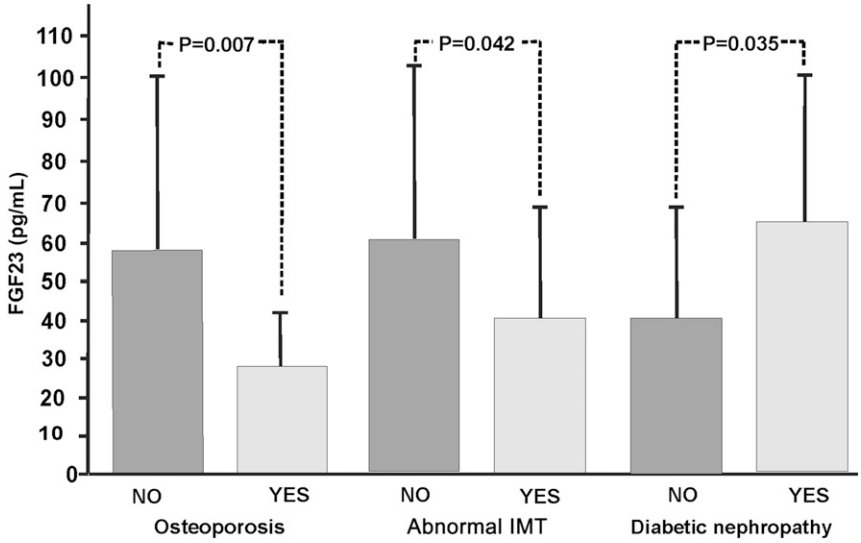

Figure 1—Serum FGF23 in T2D group ($n = 68$) by osteoporosis diagnosis, abnormal IMT, and diabetic nephropathy.

the integrity of the data and the accuracy of the data analysis.

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