**Supplementary Material**

**Supplementary Methods**

From the stored serum samples, we measured inflammatory markers including high-sensitivity c-reactive protein (hs-CRP), IL-6, tumor necrosis factor-α (TNF-α), and interferon-γ (INF-γ). Serum hs-CRP was measured using a UniCel DxC system from Beckman. The inter-assay CV for this assay is 4.9%. Serum IL-6, TNF-α and INF-γ were measured using the luminex platform using Millipore’s reagents. The inter-assay CVs is 18.9%, 18.9% and 19.7% for each analyte.

*25(OH)D:* Total 25(OH)D (sum of 25(OH)D2 and 25(OH)D3) was measured using immunoaffinity purification and liquid chromatography-tandem mass spectrometry. Calibration was confirmed with National Institute of Standards and Technology’s standard reference material 972. [1] The lower limit of detection is 1.6 ng/mL and 2.0 ng/mL for 25(OH)D2 and 25(OH)D3, respectively. The between-assay imprecision (%CV) is 10.3% for 25(OH)D2 and 6.0% for 25(OH)D3.

*1,25(OH)2D:* Serum 1,25(OH)2D levels were also measured using high-performance liquid chromatography–tandem mass spectrometry following immunoaffinity purification of the samples. 1,25(OH)2D2 and 1,25(OH)2D3 levels were reported separately and total 1,25(OH)2D calculated from these values. Limits of detection with this method are 5.6 pg/mL and 6.8 pg/mL for 1,25(OH)2D2 and 1,25(OH)2D3. The inter-assay CVs is 10.1% and 11.0% for each analyte, respectively. This methodology does not detect and does not have interference from paracalcitol or the C-3 epimeric forms of 25(OH)D3 and 1,25(OH)2D3.

1. Phinney  KW. Development of a standard reference material for vitamin D in serum. Am J Clin Nutr. 2008 Aug;88(2):511S-12S.

Supplementary Table 1. FGF23 values at baseline, 12, and 24 months by trajectory group

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| FGF23, pg/mL | Group 1Low stableN = 162 | Group 2Low increasingN = 151 | Group 3Elevated increasingN = 268 | Group 4Elevated decreasingN = 110 | Group 5Elevated stableN = 228 | TotalN = 919 |
| Baseline | 446[221-898] | 602[299-1636] | 2981[1480-6634] | 3641[2208-7332] | 18034[8955-32860] | 2697[735-9897] |
| Month 12 | 270[134-493] | 1212[602-2208] | 5432[3295-9897] | 1480[812-2441] | 24343[14765-36316] | 3295[812-13360] |
| Month 24 | 365[221-897] | 2697[1636-6003] | 7332[3641-14765] | 898[446-1480] | 24343[16318-36316] | 4447[1097-16318] |

Data are presents as median [IQR].

Supplementary Table 2. Odds ratios (95% CI) for variables significantly associated with FGF23 trajectories compared to the elevated stable trajectory

|  |  |
| --- | --- |
| Predictor | FGF23 Trajectory  |
| Low Stable | Low Increasing | Elevated Increasing | Elevated Decreasing | Elevated Stable |
| Age | 1.06(1.03 – 1.08) | 1.04(1.02 – 1.06) | 1.01(1.00 – 1.03) | 1.03(1.01 – 1.05) | Reference |
| Female | 0.34(0.20 – 0.59) | 0.43(0.26 – 0.73) | 0.79 (0.52 – 1.19) | 0.72(0.42 – 1.24) | Reference |
| Black | 1.23(0.69 – 2.19) | 1.33(0.75 – 2.34) | 0.96(0.61 – 1.49) | 1.40(0.78 – 2.52) | Reference |
| Current smoking | 1.12(0.52 – 2.42) | 1.11(0.57 – 2.19) | 1.25 (0.75 – 2.10) | 0.80 (0.37 – 1.72) | Reference |
| Dialysis vintage | 1.02(0.96 – 1.09) | 1.01(0.96 – 1.07) | 0.95(0.91 – 1.00) | 1.02 (0.97 – 1.08) | Reference |
| Diabetes | 2.58(1.51 – 4.41) | 1.96(1.18 – 3.28) | 1.32(0.86 – 2.03) | 1.26(0.74 – 2.16) | Reference |
| Cardiovascular Disease | 1.17(0.65 – 2.11) | 1.12(0.64 – 1.94) | 1.77(1.11 – 2.82) | 0.96(0.54 – 1.70) | Reference |
| High Kt/V | 2.53(1.54 – 4.17) | 1.33(0.83 – 2.13) | 1.41(0.96 – 2.07) | 1.54(0.94 – 2.52) | Reference |
| High Flux | 1.61(0.99 – 2.63) | 1.43(0.90 – 2.29) | 1.22(0.83 – 1.79) | 2.64(1.60 – 4.38) | Reference |
| Catheter as vascular access | 0.20(0.07 – 0.56) | 0.43(0.14 – 1.23) | 0.86(0.34 – 2.19) | 0.33(0.12 – 0.92) | Reference |
| Residual kidney function | 2.76(1.59 – 4.77) | 2.05(1.18 – 3.57) | 1.42 (0.86 – 2.36) | 1.64 (0.92 – 2.95) | Reference |
| Markers of Mineral Metabolism |
| Calcium | 0.31(0.23 – 0.42) | 0.41(0.53 – 0.83) | 0.66(0.53 – 0.83) | 0.77(0.58 – 1.02) | Reference |
| Phosphorus | 0.44(0.37 – 0.53) | 0.53(0.45 – 0.62) | 0.75(0.67 – 0.84) | 0.83(0.72 – 0.95) | Reference |
| 25(OH)D | 0.87(0.55 – 1.39) | 0.90(0.58 – 1.40) | 0.94(0.66 – 1.35) | 0.53(0.33 – 0.84) | Reference |
| 1,25(OH)2D | 0.94(.074 – 1.22) | 0.91(0.72 – 1.15) | 0.85(0.70 – 1.03) | 1.07 (0.84 – 1.37) | Reference |
| PTH | 1.00 (0.99 – 1.00) | 1.00 (0.99 – 1.00) | 1.00(0.99 – 1.01) | 1.00 (0.99 – 1.00) | Reference |
| Vitamin D analog use | 0.46(0.27 – 0.77) | 0.62 (0.38 – 1.02) | 0.75(0.50 – 1.13) | 0.65 (0.39 – 1.10) | Reference |
| Inflammatory Markers |
| Albumin | 1.84(0.83 – 4.10) | 1.42 (0.65 – 3.07) | 1.31 (0.70 – 2.46) | 1.83 (0.81 – 4.14) | Reference |
| CRP | 1.06(0.84 – 1.32) | 1.04(0.84 – 1.29) | 0.93 (0.78 – 1.11) | 0.98(0.78 – 1.23) | Reference |
| IL-6 | 0.71(0.54 – 0.90) | 0.70(0.53 – 0.90) | 0.85(0.69 – 1.04) | 0.83(0.63 – 1.10) | Reference |
| TNF-α | 1.04 (0.73 – 1.49) | 0.81 (0.59 – 1.12) | 1.10 (0.85 – 1.45) | 0.83 (0.59 – 1.17) | Reference |
| IFN-γ | 0.66 (0.45 – 0.98) | 0.96 (0.67 – 1.41) | 1.05 (0.80 – 1.38) | 0.97(0.67 – 1.41) | Reference |

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; 1,25(OH)2D, 1,25-dihydroxyvitamin D; PTH, parathyroid hormone; FGF23, fibroblast growth factor 23; CRP, c-reactive protein; IL-6, interleukin-6, TNF-α, tumor necrosis factor-alpha; IFN-γ, interferon-gamma.