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 $25(OH)D_2$ and $25(OH)D_3$) 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 $25(OH)D_2$ and $25(OH)D_3$, respectively. The between-assay imprecision (%CV) is 10.3% for $25(OH)D_2$ and 6.0% for $25(OH)D_3$.

$1,25(OH)_2D$: Serum $1,25(OH)_2D$ levels were also measured using high-performance liquid chromatography–tandem mass spectrometry following immunoaffinity purification of the samples. $1,25(OH)_2D_2$ and $1,25(OH)_2D_3$ 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 $1,25(OH)_2D_2$ and $1,25(OH)_2D_3$. 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 $25(OH)D_3$ and $1,25(OH)_2D_3$.

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 1 Low stable N = 162	Group 2 Low increasing N = 151	Group 3 Elevated increasing N = 268	Group 4 Elevated decreasing N = 110	Group 5 Elevated stable N = 228	Total N = 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
					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)	
$1,25(OH)_2D$	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.