Table of Contents

Supplementary methods

BTMs: The inter-assay coefficient of variations (CVs) were ≤9% for iPTH, BALP and CTX; ≤5% for intact PINP; ≤10% for 25-hydrovitamin D and TRAP5b; and ≤4% for total PINP. Inter-assay CVs were ≤5% for all biochemistry measured on the same day as the blood sample collection using Roche Cobas c701/702 analyser (Roche Diagnostics, England).

HR-pQCT: The non-dominant side was scanned unless there was a previous fracture or an arterio-venous fistula present. The scans were acquired in the high-resolution mode (image matrix = 1,536 x 1,536) using a source potential of 60 kVp, a tube current of 900 mA, and an integration time of 100 ms. Each scan resulted in the acquisition of a total of 110 image slices (stack height = 9.02mm) at an isotropic resolution of 82 µm. A maximum of one repeat scan at either or both anatomical sites was performed in the event of patient movement. All images were graded by a single operator (MP), and any images with an unacceptable degree of movement artefact were excluded from further analysis. We had to exclude images of 9 radii from controls, 12 radii from CKD, one tibia from control and two tibiae from CKD due to movement artefact. Microarchitectural parameters included trabecular number (Tb.N, 1/mm), trabecular thickness (Tb.Th, mm), trabecular separation (Tb.Sp, mm), bone volume/tissue volume (BV/TV, %) and cortical thickness (Ct.Th, mm). Extended cortical analysis for cortical microstructural bone properties, including cortical porosity (%) and cortical pore diameter (Ct.Po.Dm, µm).

DXA: Lumbar spine scans were assessed by a single operator (MP) for vertebral fracture and other causes leading to falsely high BMD (such as degenerative changes and osteophytes). One lumbar spine scan was excluded due to multiple vertebral fractures and one patient did not have a forearm scan due to previous bilateral wrist fractures.

Transiliac bone biopsy & histomorphometry: To assess bone formation rate (BFR), patients received four days of tetracycline (250mg, four times a day) and after a 10-day intermission, a further two days of demeclocycline (300mg, twice a day). Trans-iliac bone biopsy was performed within 2-4 days of the last dose of demeclocycline. The undecalcified bone sample was placed in 70%, 80%, 90% and 100% ethanol in turn for at least one week in each solution while shielded from light at all time. It was then infiltrated and embedded in LR White medium grade resin. The resin block was sectioned at 6µm thickness and stained with Masson Goldner trichrome.

Supplementary Table 1: Correlation between all bone turnover markers in 43 advanced CKD patients with bone histomorphometry data.

	Intact PINP	Total PINP	bALP	tALP	CTX	TRAP5b
iPTH	0.619	0.523	0.621	0.508	0.567	0.504
Intact PINP		0.813	0.866	0.762	0.732	0.741
Total PINP			0.749	0.698	0.591	0.575
bALP				0.869	0.710	0.672
tALP					0.542	0.548
CTX						0.709

All Spearman's rho correlations are significant at ≤0.001 (2-tailed)

Supplementary Table 2: Diagnostic accuracy of DXA areal BMD Z-scores for identifying advanced CKD patients with low and high bone turnover (N=43).

Areal BMD Z-score	**AUC (95% CI)**
Low bone turnover	
Forearm	0.645 (0.483 – 0.786)
Total hip	0.598 (0.438 – 0.744)
Lumbar spine	0.554 (0.395 – 0.705)
High bone turnover	
Forearm	0.685 (0.523 – 0.819)
Total hip	0.580 (0.420 – 0.729)
Lumbar spine	0.533 (0.375 – 0.686)

Supplementary Table 3: Diagnostic accuracy of HR-pQCT Z-scores for identifying advanced CKD patients with high bone turnover (N=43).

HR-pQCT Z-scores	**Distal radius AUC (95% CI)**	**Distal tibia AUC (95% CI)**
Total vBMD	0.627 (0.450 – 0.782)	0.553 (0.392 – 0.706)
Cortical vBMD	0.569 (0.394 – 0.732)	0.579 (0.417 – 0.729)
Trabecular vBMD	0.625 (0.448 – 0.780)	0.541 (0.381 – 0.696)
Cortical thickness	0.552 (0.377 – 0.717)	0.525 (0.365 – 0.681)
Cortical porosity	0.627 (0.450 – 0.782)	0.548 (0.387 – 0.702)
Cortical BV/TV	0.628 (0.451 – 0.783)	0.576 (0.414 – 0.727)
Trabecular thickness	0.583 (0.407 – 0.744)	0.575 (0.413 – 0.726)
Trabecular number	0.603 (0.427 – 0.762)	0.541 (0.381 – 0.696)
Trabecular separation	0.614 (0.438 – 0.771)	0.533 (0.373 – 0.688)
Trabecular BV/TV	0.628 (0.451 – 0.783)	0.542 (0.382 – 0.697)