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THE IMPORTANCE OF LABORATORY MEDICINE IN THE MANAGEMENT OF CKD-MBD: INSIGHTS FROM THE KDIGO 2023 CONTROVERSIES CONFERENCE

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ABSTRACT

Laboratory investigations are important in the clinical management and the study of chronic kidney disease-mineral and bone disorder (CKD-MBD)- including CKD-associated osteoporosis. Parathyroid hormone (PTH) is the major hormone in the regulation of bone and calcium balance but is significantly affected in advanced CKD. Knowledge of PTH concentration is important in the assessment of osteoporosis including CKD-associated osteoporosis; however, measurement of PTH in the laboratory is bedevilled by interferences and inter-method differences compounded by

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lack of standardisation of commonly used immunoassays. Vitamin D is important for bone health and its deficiency contributes to the development of osteoporosis. Vitamin D metabolism is impaired in advanced CKD, augmenting the effects of its deficiency on bone health. Lack of consensus on optimal serum 25-hydroxyvitamin D (25-(OH)D) concentrations for bone health, including in the various CKD stages, is compounded by lack of analytical specificity of immunoassays. Liquid chromatography tandem mass spectrometry (LC-MS/MS) assays would help overcome these issues. Ionised calcium measurement is recommended for assessment of serum calcium, especially in CKD. Fibroblast growth factor 23 (FGF23) is important in the homeostasis of phosphate that accumulates in CKD, though this marker is not yet utilized in clinical context. Calculated maximal tubular reabsorption of phosphate normalized to glomerular filtration rate (TmP/GFR) may help in assessment of phosphate homeostasis. Bone specific alkaline phosphatase (BALP) and tartrate-resistant acid phosphatase isoform 5b (TRACP5b), the reference markers of bone formation and resorption for CKD-associated osteoporosis, have been shown to reflect bone turnover by histomorphometry in patients with advanced CKD.

Introduction

The importance of laboratory medicine in the management of metabolic bone disorders cannot be overstated. The recent publication of conclusions from a Kidney Disease : Improving Global Outcomes (KDIGO) Controversies Conference on Chronic kidney disease–mineral and bone disorder (CKD-MBD) [1] provides a comprehensive update on the classification, diagnosis, and management of bone disorders associated with CKD. These conclusions not only advance our understanding of CKD-MBD but also emphasizes the critical role of laboratory investigations in guiding clinical decisions.

CKD is associated with a spectrum of mineral and bone disorders, collectively defined as CKD-MBD, encompassing mineral metabolism disturbances, bone remodeling abnormalities, bone quality impairments and calcification in vasculature and soft tissues. Historically, the term "renal osteodystrophy (ROD)" was used to describe the skeletal aspects of CKD-MBD, such as high or low bone turnover, impaired mineralization, and reduced bone volume. However, the KDIGO 2023 Controversies Conference emphasized that the term "ROD" does not comprise clinical manifestations of bone disease and fosters an overly PTH- and calciumphosphate–centric approach to bone disease management. To overcome this limitation and provide a clearer clinical focus on the severely increased fracture risk in CKD as the main manifestation of ROD, the term "CKD-associated osteoporosis" has been introduced.

CKD-associated osteoporosis is now recognized as a distinct form of osteoporosis, driven by the unique pathophysiological mechanisms of CKD, affecting bone strength, structure, and fracture risk. This shift in terminology aims to prioritize the skeletal aspects of CKD, promoting a more targeted approach to diagnosis and management. The laboratory plays a pivotal role in understanding the pathophysiology of CKD-MBD, identifying mechanisms of bone impairment, and supporting personalized patient management based on precise diagnostic information. Most

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importantly, laboratory parameters can capture the highly dynamic aspects of bone metabolism and are therefore very well suited for longitudinal follow-up in the management of CKD-associated osteoporosis.

Biomarkers for the assessment of bone turnover in CKD patients

The first-line target for the management of CKD-associated osteoporosis is treatment of the abnormalities of mineral metabolism (hyperparathyroidism, hyperphosphatemia, hypocalcemia, and vitamin D deficiency) associated with CKD-MBD which can directly or indirectly influence bone turnover and mineralization. Although bone biopsy remains the gold standard in determining bone turnover in persons with advanced CKD, an increasing number of non-invasive diagnostic tools, including bone turnover markers and bone imaging, are available to support clinicians in the management of CKD-associated osteoporosis. Whilst these biomarkers are useful, their measurement is subject to certain limitations that are continually being refined and improved by ongoing scientific efforts.

1. PARATHYROID HORMONE (PTH)

Secondary hyperparathyroidism is common in CKD and has long been considered amajor feature of CKD-MBD. The degree of hyperparathyroidism increases with the duration and severity of CKD, causing disturbances in bone remodelling and hence bone quality [2]. Over-suppression of PTH, conversely, may cause low turnover which can also impact bone quality and potentially increase propensity to fracture [3,4]. In addition, bone-responsiveness to PTH may be reduced in CKD. Regular measurement of PTH in CKD-MBD is recommended from CKD G3 onwards, although uncertainties remain on optimal treatment of secondary hyperparathyroidism, including targets for PTH in patients with CKD not on dialysis [1]. These uncertainties are compounded by high inter- and intraindividual variability and lack of standardisation of PTH assays and resulting inter-method differences [5,6]. These differences are the reason for defining the PTH target in CKD G5D as 2–9 times the upper limit of normal (ULN), acknowledging that this wide target range only helps avoiding extremes but leaves the clinician with a high degree of uncertainty regarding association of PTH levels within the target with clinical outcomes and skeletal abnormalities [1,2]. The need for standardization of PTH assays has long been recognized by the laboratory profession, aswell as explicitlymandated by KDIGO [1,2]. A higher-order liquid chromatography tandem mass spectrometry (LC-MS/MS) as a candidate referencemethod has recently been published [7] and applied to clinical populations of CKD, including patients receiving haemodialysis (HD), to show that standardization of PTH assays is totally feasible, depending only on the goodwill of the manufacturers [8].

Notwithstanding these promising findings, even currently available commercial 3rd generation PTH assays, which are not widely used, show significant inter-method differences resulting in the

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use of different reference intervals and KDIGO CKD5D targets [2,9] The more widely used 2nd generation ("intact") PTH assays remain largely unstandardized, despite the technical feasibility of achieving harmonization. Indeed, the 7–84 fragment is the only PTH fragment known to exhibit cross-reactivity in intact PTH assays based on spiking studies, yet it has been shown to be absent in humans [10]. For a long time, efforts to standardize PTH assays were hindered by the misconception that 7–84 fragments were circulating in patients, particularly those with CKD, which would have complicated standardization. Furthermore, some authors have questioned the reliability of 2nd and 3rd generation PTH assays, suggesting thatmost circulating PTH is oxidized, especially in patients with CKD receiving HD. Although oxidized PTH is biologically inactive, two independent orthogonal methods using mass spectrometry have demonstrated that no circulating oxidized forms of PTH are present in the blood of patients with CKD, including those receiving HD, likely eliminating this as a potential source of assay interference [11]. The recent work by Cavalier et al. has demonstrated that standardization of PTH assays (both 2nd and 3rd generation) is achievable using a reference LC-MS/ MS method calibrated with internationally recognized reference materials [8]. For this purpose, a panel of commutable serum standards with PTH concentrations determined by a higher-order LC-MS/MSmethod should be established, allowing manufacturers to calibrate their assays against a standardized reference.

Given the significant variability between PTH assays, we strongly recommend that all laboratories performing PTH measurements clearly specify the commercial name of the assay used in their protocols, until full standardization of PTH assays is achieved.

2. VITAMIN D

Vitamin D deficiency contributes to the development of osteoporosis and is an important driver of CKD-associated osteoporosis [1, 12], even if the optimal serum 25- hydroxyvitamin D (25-(OH)D) concentrations for bone health and across different CKD stages remain contentious. Over the past decade, continuous efforts led by the Vitamin D Standardization Program (VDSP) consortium have significantly improved the standardization of 25-(OH)D assays, although complete standardization has not yet been fully achieved [13, 14]. Even more problematic in the context of CKD, is the lack of specificity of immunoassays. These assays often fail to distinguish between vitamin D isoforms (D2 and D3) and their respective metabolites, resulting in variable results and potential misclassification of vitamin D status. This issue is especially critical in the United States, where vitamin D2 has historically been the most commonly prescribed form for patients receiving dialysis. This preference is driven by its availability in standardized, high-dose formulations (e.g., 50,000 IU capsules), inclusion in U.S. Pharmacopeia drug formularies, and higher likelihood of being covered and reimbursed by insurance plans. In contrast, other regions, where vitamin D3 is more commonly used, may be less affected by this problem. Additionally, immunoassays for 25-(OH)D are prone to the influence of the relative concentration and polymorphism of vitamin D-binding protein as well as cross-reactivity with other metabolites, like 24,25-(OH)2D, which further compromise their reliability. To overcome these limitations, LC-MS/MS should be the method of choice for measuring 25-(OH)D, in advanced CKD, particularly patients receiving HD, where

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immunoassays consistently under-recover vitamin D [14]. Properly developed LC-MS/MS assays would provide greater accuracy, specificity, and reproducibility, ensuring clinically reliable results for patient management and delivering precise data for research studies aimed at defining optimal 25-(OH)D targets and dosing strategies in CKD. However, one should be aware that adoption of LC-MSMS methods does not represent the final answer since not all LC-MS/MS methods for 25-(OH)D are necessarily accurate or precise if not appropriately developed and validated. Consequently, we understand that, for pragmatic and practical reasons, many clinical laboratories will continue to measure 25-(OH)D by immunoassays.

Similarly to PTH,we encourage laboratories to specify the commercial name (or LC-MS/MS) of the assay used in their protocols. For LC-MS/MS users, we discourage providing relative concentrations of 25(OH)D2 and 25(OH)D3, but rather the sum of both moieties to avoid confusion in the interpretation of the results.

3. CALCIUM

Calcium is the most abundant mineral in bone and is important for its structure and strength [15]. Maintaining calcium balance is important for bone health but is particularly challenging in CKD, where hypocalcaemia and hypercalcemia are both associated with increased mortality and complications [1]. The active form of calcium in blood is ionized calcium, and the commonly used surrogate measures, total and albumin adjusted calcium, widely reported in research studies, are unreliable, and more so in advanced CKD, mandating the need for the provision of direct measurement of ionized calcium by the laboratories for these patients [1, 16]. It is, however, noteworthy that strict preanalytical conditions are necessary for ionized calcium measurement, which should be performed within 1 h of the sampling. A blood-gas analyser is mandatory, and the ionized calcium concentration should be reported at the pH of the patient, not adjusted to a pH of 7.40.

Besides already mentioned causes of unreliability of albumin-adjusted calcium the method for determining serum albumin also needs to be taken into account. While bromocrersol green (BCG) tends to overestimate albumin, bromocresol purple (BCP) underestimates it [17]. A strategy for reflective testing of ionized calcium is necessary for patients with advanced CKD, in extremes of total calcium or albumin concentrations, and in subjects with suspected primary hyperparathyroidism [16].

4. PHOSPHATE

Hyperphosphatemia is a feature of advanced CKD and may contribute to morbidities of the CKD-MBD syndrome, exacerbating hyperparathyroidism and contributing to bone disease, but most prominently associated with calcification propensity both in vasculature and in soft tissue, associating strongly with adverse cardiovascular outcomes [1,2]. Phosphate lowering therapy is an important aspect of management of advanced CKD, and hence, the provision of laboratory support for the assessment of phosphate homeostasis is important.

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Fibroblast growth factor 23 (FGF23) is a hormone of importance in phosphate homeostasis, which increases early in the development of CKDand associateswith cardiovascular morbidity [18]. However, the role of its measurement in CKD is currently unclear, the main use being in the diagnosis of hereditary hypophosphatemic rickets and diagnosis and follow-up of tumour-induced osteomalacia (TIO) [19].

FGF23 can be measured using immunoassays, with both intact FGF23 (iFGF23) assays and C-terminal FGF23 (cFGF23) commercial assays available, most of them for research use only [18]. Inter-assay differences and interferences in immunoassays, lack of an international standard for iFGF23, or an LC-MSMS method to quantify FGF23, are drawbacks for further advances in the clinical application of FGF23 measurement and are for future work in laboratory medicine. Development of an LC–MS/MS method that can quantify both intact FGF23 and its fragments separately, as well as identify possible phosphorylation and glycosylation, would be a step forward. In the meantime, availability of a quality assessment scheme for FGF23 and harmonization of commercial assays would help improve the quality of practice. Current evidence suggests that iFGF23 immunoassays are more sensitive than cFGF23 immunoassays for FGF23 measurement in patients with hypophosphatemia [18].

On the other hand, clinical laboratories should be able to routinely offer an assessment of renal phosphate threshold by way of calculated maximal tubular reabsorption of phosphate normalized to glomerular filtration rate (TmP/GFR) which can be automated using the commonly measured analytes serum phosphate and creatinine as well as urine phosphate and creatinine [20, 21]. TmP/GFR offers a simple measure of renal handling of phosphate in terms of renal phosphate wasting or conservation, which is often deranged in renal dysfunctions associated with mineral and metabolic bone disorders.

5. BONE TURNOVER MARKERS (BTMS)

The 2011 publication of the IOF-IFCC joint WG designated serum procollagen type I N-propeptide (PINP) and β isomerized C-terminal telopeptide of type I collagen (β-CTX-I) as reference BTMs for the assessment of bone formation and resorption, respectively [22]. However, tests for total PINP (tPINP) and β-CTX-I are affected by kidney dysfunction due to accumulation of fragments cleared by the kidney, which may provide inaccurately high concentrations. The updated guidelines published recently by ESCEO, IOF and IFCC designates bone specific alkaline phosphatase (BALP) and tartrate-resistant acid phosphatase isoform 5b (TRACP5b), as reference markers of bone formation and resorption in CKD, as they are not cleared by the kidneys [23]. Further, these markers have been shown to reflect bone turnover by histomorphometry in patients with advanced CKD [23]. It is acknowledged that BALP immunoassays have between 3 and 17 % cross reactivity with liver alkaline phosphatase [24]. Intact PINP is another BTM marker that is not cleared by the kidney; however, the evidence level is stronger for BALP, particularly as relates to clinically relevant outcomes such as fracture [21]. Whilst higher serum BALP has been shown to associate with increased fracture risk in patients with CKD, further studies are warranted [25–28]. Severely increased BALP in the setting of low 25-(OH)D, serum calcium or phosphate and typical

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symptoms (muscle weakness, bone and joint pain) suggest the presence of osteomalacia which, although uncommon, may form a component of bone disease in CKD [1]. The role of BTMs in assessing bone turnover, supporting treatment decisions, and monitoring response to treatment in CKD-associated osteoporosis show great potential, but also requires further study [23].

6. CALCIPROTEIN PARTICLES (CPPS) AND CRYSTALLIZATION TIME (FORMERLY CALCIFICATION PROPENSITY SCORE)

CPPs are protein-mineral complexes that act as a mineral buffer by binding excesses of free calcium and phosphate, thus maintaining concentrations at the solubility level. While primary CPPs prevent soft tissue calcification, secondary CPPs contain large proportions of crystalline hydroxyapatite and may promote vascular calcification and inflammation, particularly in CKD [29]. Several different methods of direct CPP measurement have been developed which differ in their ability to detect total CPP load and to distinguish between primary and secondary CPPs [30]. Crystallization time measures the conversion of primary to secondary CPPs in a standardized supersaturated calcium and phosphate containing solution after addition of patient serum using nephelometric or turbidimetric assays. However, lack of instruments and methods suitable for routine measurement that may be carried out in service laboratories preclude their current use in clinical practice. Elevated CPP levels or shorter crystallization time correlate with cardiovascular risk, making them potential biomarkers of calcification propensity in CKD [31].

Conclusions

Laboratory medicine plays a critical role in the diagnosis and management of CKD-associated osteoporosis and CKD-MBD. The advances in PTH standardization, improved vitamin D assessment using LC-MS/MS, and recognition of ionized calcium as the preferred measure in CKD highlight the urgent need for accurate and reliable biomarkers in clinical practice. The adoption of BALP and TRACP5b as reference bone turnover markers ensures more accurate assessment of bone metabolism in CKD, while emerging biomarkers such as CPPs may enhance risk stratification for vascular calcification. Despite these advances, further standardization and validation of assays remain essential to improve diagnostic accuracy, treatment decisions, and patient outcomes in CKD-MBD.

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Use of Large Language Models, AI and Machine Learning

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References

1. Ketteler M, Evenepoel P, Holden RM, Isakova T, Jørgensen HS, Komaba H, et al. Conference participants. Chronic kidney diseasemineral and bone disorder: conclusions from a kidney disease: improving global outcomes (KDIGO) controversies conference. Kidney Int 2025;107:405–23.

2. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl 2017; 7:1–59.

3. Malluche HH, Porter DS, Monier-Faugere MC, Mawad H, Pienkowski D. Differences in bone quality in low- and high-turnover renal osteodystrophy. J Am Soc Nephrol 2012;23:525–32.

4. Jansz TT, Goto NA, van Ballegooijen AJ, Willems HC, Verhaar MC, van Jaarsveld BC. The prevalence and incidence of vertebral fractures in end-stage renal disease and the role of parathyroid hormone. Osteoporos Int 2020;31:515–24.

5. Sturgeon CM, Sprague S, Almond A, Cavalier E, Fraser WD, Algeciras- Schimnich A, et al. IFCC working group for PTH. perspective and priorities for improvement of parathyroid hormone (PTH) measurement - a view from the IFCC working group for PTH. Clin Chim Acta 2017;467:42–7.

6. Cavalier E, Vasikaran S, Bhattoa HP, Heijboer AC, Makris K, Ulmer CZ. The path to the standardization of PTH: is this a realistic possibility? A position paper of the IFCC C-BM. Clin Chim Acta 2021;515:44–51.

7. Farré-Segura J, Le Goff C, Lukas P, Cobraiville G, Fillet M, Servais AC, et al. Validation of an LC-MS/MS method using solid-phase extraction for the quantification of 1-84 parathyroid hormone: toward a candidate reference measurement procedure. Clin Chem 2022;68:1399–409.

8. Cavalier E, Farré-Segura J, Lukas P, Gendebien AS, Peeters S, Massonnet P, et al. Unveiling a new era with liquid chromatography coupled with mass spectrometry to enhance parathyroid hormone measurement in patients with chronic kidney disease. Kidney Int 2024; 105:338–46.

9. Dupuy AM, Bargnoux AS, Morena M, Lauret E, Souberbielle JC, Cavalier E, et al. Moving from the second to the third generation roche PTH assays: what are the consequences for clinical practice? Clin Chem Lab Med 2018;57:244–9.

Published in : Clinical Chemistry and Laboratory Medicine (2025)
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Status : Postprint (Author's version)

10. Gao P, D'Amour P. Evolution of the parathyroid hormone (PTH) assay– importance of circulating PTH immunoheterogeneity and of its regulation. Clin Lab 2005;51:21–9.

11. Kritmetapak K, Losbanos LA, Hines JM, O'Grady KL, Ulmer CZ, Vesper HW, et al. Chemical characterization and quantification of circulating intact PTH and PTH fragments by high-resolution mass spectrometry in chronic renal failure. Clin Chem 2021;67:843–53.

12. Peacock M. Effect of calcium and vitamin d insufficiency on the skeleton. Osteoporos Int 1998;8:S45–51.

13. Cavalier E, Makris K, Heijboer AC, Herrmann M, Souberbielle JC. Vitamin D: analytical advances, clinical impact, and ongoing debates on health perspectives. Clin Chem 2024;70:1104–21.

14. Dirks NF, Cavalier E, Heijboer AC. Vitamin d: marker, measurand and measurement. Endocr Connect 2023;12:e220269.

15. Clarke B. Normal bone anatomy and physiology. Clin J Am Soc Nephrol 2008;3:S131–9.

16. Ong GS, Walsh JP, Stuckey BG, Brown SJ, Rossi E, Ng JL, et al. The importance of measuring ionized calcium in characterizing calcium status and diagnosing primary hyperparathyroidism. J Clin Endocrinol Metab 2012;97:3138–45.

17. Labriola L, Wallemacq P, Gulbis B, Jadoul M. The impact of the assay for measuring albumin on corrected ('adjusted') calcium concentrations. Nephrol Dial Transplant 2009;24:1834–8.

18. Heijboer AC, Cavalier E. The measurement and interpretation of fibroblast growth factor 23 (FGF23) concentrations. Calcif Tissue Int 2023;112:258–70.

19. Kritmetapak K, Kumar R. Phosphatonins: from discovery to therapeutics. Endocr Pract 2023;29:69–79.

20. Payne RB. Renal tubular reabsorption of phosphate (TmP/GFR): indications and interpretation. Ann Clin Biochem 1998;35:201–6.

21. Peacock M. Phosphate metabolism in health and disease. Calcif Tissue Int 2021;108:3–15.

22. Vasikaran S, Eastell R, Bruyère O, Foldes AJ, Garnero P, Griesmacher A, et al. IOF-IFCC bone marker standards working group. Markers of bone turnover for the prediction of fracture risk and monitoring of osteoporosis treatment: a need for international reference standards. Osteoporos Int 2011;22:391–420.

23. Bhattoa HP, Vasikaran S, Trifonidi I, Kapoula G, Lombardi G, Jørgensen NR, et al. Update on the role of bone turnover markers in the diagnosis and management of osteoporosis: a consensus paper from the european society for clinical and economic aspects of osteoporosis, osteoarthritis and musculoskeletal diseases (ESCEO), international osteoporosis foundation (IOF), and international Federation of clinical chemistry and laboratory medicine (IFCC). Osteoporos Int 2025;36: 579–608.

Published in : Clinical Chemistry and Laboratory Medicine (2025)
DOI: 10.1515/cclm-2025-0802
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24. Jean G, Souberbielle JC, Zaoui E, Lorriaux C, Mayor B, Hurot JM, et al. Total and bone-specific alkaline phosphatases in haemodialysis patients with chronic liver disease. Clin Biochem 2012;45:436–9.

25. Kashgary A, Attiah FOA, AlKhateeb NA, Abdulaziz NH, Alsaif BA, Aljuhani AF, et al. Incidence of bone fractures among patients on maintenance hemodialysis. Ren Fail 2023;45:2224456.

26. Matias PJ, Laranjinha I, Azevedo A, Raimundo A, Navarro D, Jorge C, et al. Bone fracture risk factors in prevalent hemodialysis patients. J Bone Miner Metabol 2020;38:205–12.

27. Iimori S, Mori Y, Akita W, Kuyama T, Takada S, Asai T, et al. Diagnostic usefulness of bone mineral density and biochemical markers of bone turnover in predicting fracture in CKD stage 5D patients–a single-center cohort study. Nephrol Dial Transplant 2012;27:345–51.

28. Maruyama Y, Taniguchi M, Kazama JJ, Yokoyama K, Hosoya T, Yokoo T, et al. Higher serum alkaline phosphatase is associated with the incidence of hip fracture and mortality among patients receiving hemodialysis in Japan. Nephrol Dial Transplant 2014;29:1532–8.

29. Feenstra L, Reijrink M, Pasch A, Smith ER, Visser LM, Bulthuis M, et al. TransplantLines investigators. Calciprotein particle counts associate with vascular remodelling in chronic kidney disease. Cardiovasc Res 2024;120:1953–66.

30. Miura Y, Kurosu H, Kuro-O M. Quantification of calciprotein particles (CPPs) in serum/plasma samples using a fluorescent bisphosphonate. Methods Mol Biol 2023;2664:333–41.

31. Bundy JD, Cai X, Mehta RC, Scialla JJ, de Boer IH, Hsu CY, et al. CRIC study investigators. Serum calcification propensity and clinical events in CKD. Clin J Am Soc Nephrol 2019;14:1562–71.