Once more, the administration of cinacalcet (25 mg) just before the HD session caused a significant further decrease in the serum i-PTH levels despite a significant reduction in the plasma Ca^{2+} levels (Figure 1C, Post-HD).

Even if an elevation in PTH levels is transient, it should be avoided that basal high PTH levels increase further at the end of every HD session with a low-Ca dialysate. In addition, a transient decrease in plasma Ca^{2+} levels can stimulate not only PTH secretion but also PG cell proliferation. Over the long term, PG hyperplasias often progress from diffuse to nodular forms. We have demonstrated that calcimimetics are powerful inhibitors of PG cell proliferation in rats with 2HPT, regardless of calcimimetic-induced hypocalcaemia [1,5]. Therefore, we propose that cinacalcet should be administered just before HD sessions to prevent the hyperfunctioning of PG cells that is induced by the transient hypocalcaemia caused by a low-Ca dialysate. This seems to be reasonable because the maximal plasma concentration (C_{max}) of cinacalcet is achieved 4–6 h after its oral administration [2]. Further investigations are clearly required to determine when cinacalcet should be administered, especially in the context of bone metabolism and the gastrointestinal adverse effects.

Conflict of interest statement. Other than N.N. who is a scientist at Kirin Pharma that manufactures and sells cinacalcet in Asia, none of the authors have reported any conflict of interest.

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Vertebral fractures in patients on dialysis: a clinically relevant problem with insufficient investigation

Sir,

Chronic kidney disease mineral and bone disorder (CKD-MBD), previously denominated renal osteodystrophy [1], is a major clinical problem, with increasing prevalence and adverse outcomes, including high bone turnover associated with secondary hyperparathyroidism, low bone turnover or adynamic bone disease, cardiovascular calcifications and bone fractures. The impact of such outcomes on patient morbidity and mortality has not been fully elucidated. We would like to point out a poorly investigated subject, which we feel is of great clinical importance: vertebral fractures in CKD patients.

Studies on the prevalence of fractures in dialyzed patients have focused mainly on hip fractures, while available data on vertebral fractures remain limited and inconsistent, suggesting a prevalence very similar to that of the general population [2,3]. However, improvements in diagnostic methods could be of great importance in better estimating the incidence and prevalence of vertebral fractures [4]. We therefore advocate the adoption of the following approach: the term vertebral fracture (VF) should be used to mean any deformation of the vertebral body following a reduction of one of its dimensions beyond a given threshold (4 mm or 15%). We speak of wedge, biconcave or crush fractures (or deformities) depending on whether the reduction affects the anterior, central or posterior dimension of the vertebra, respectively (Figure 1).

At least two different approaches are suitable for identifying these fractures: one is a semiquantitative visual method, according to Genant [4], which involves an expert radiologist visually identifying the fractures and classifying them, according to the extent of the reduction in the dimension of the vertebral body, as mild (20–25%), moderate (25–40%) or severe (>40%), as illustrated in Figure 1; the other approach is a quantitative morphometric method. In particular, vertebral morphometry (VM) involves the manual or computerized measurement of the anterior, central and posterior dimensions of the dorsal and lumbar vertebral bodies (T4-L5) of the spine using conventional radiological apparatus (MRX: morphometric X-ray radiography) or densitometric apparatus (MXA: morphometric X-ray absorptiometry).

Bone mass, reflected by bone mineral density, bone strength and bone quality should be considered when evaluating bone fractures. The contribution of bone mass to bone strength is of uncertain value in patients with CKD who actually exhibit a wide spectrum of bone quality. Often, bone mineral density has been measured with dual energy X-ray absorptiometry (DEXA), but this approach has been criticized because of the lack of good correlations between DEXA and bone histology in CKD patients. In addition, findings on the correlation of DEXA BMD values to fracture risk in the CKD population are inconsistent. Moreover, in the K-DIGO position statement, there is concern that hip

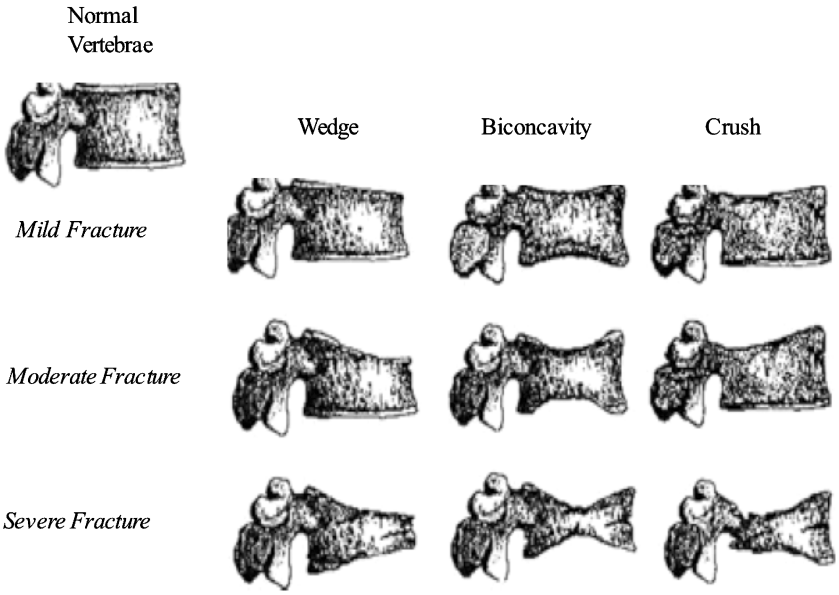

Fig. 1. Types of vertebral deformity depending on whether the reduction concerns the anterior, central or posterior dimension of the vertebra, respectively named wedge, biconcave or crush fractures (or deformities). The severity of the vertebral fracture is estimated, using a semiquantitative visual method according to Genant, as mild, moderate or severe if the reduction in the dimension of the vertebral body is 20–25%, 25–40% or >40%, respectively.

or spine BMD results, without full consideration of the underlying bone pathology, may be misleading and result in the inappropriate administration of anti-osteoporotic therapy in CKD patients [1]. Even in bone biopsy studies, bone mineral density results may not be representative of the vertebral bone architecture, although the universal adoption of the bone turnover, mineralization and volume (TMV) system in future research and publications could help in the diagnostic and therapeutic approach of CKD-MBD [1].

There are contrasting data on the role of PTH as a fracture risk factor in dialyzed patients that would warrant further trials: Block *et al*. suggested that high PTH levels are directly associated with the risk of fracture [5]; on the other hand, Coco *et al*. identified a higher risk of fracture in patients with low serum PTH levels (<195 pg/dL) [6], a finding also reported by Atsumi in a study on the risk of vertebral fractures in a population of 187 males on haemodialysis [2].

In conclusion, nephrologists have so far paid little attention to vertebral fractures in dialyzed patients. Adequate epidemiological studies are consequently needed to provide the clinical evidence that is currently lacking, particularly with a view to preventing fractures and containing the risk of fracture. Randomized controlled studies testing the efficacy of standard anti-osteoporotic therapies on bone fractures are also needed, because some of these drugs are currently not indicated for use in stage 5 CKD patients. In addition, the effects of therapies currently used for control of serum phosphorus, calcium, and PTH on bone fractures and strength are also poorly studied.

We need to do more to prevent and treat vertebral fracture, an invalidating complication of CKD-MBD.

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