# Does Secondary Renal Osteopathy Exist in Companion Animals?

Gilad Segev, DVM*, Hagar Meltzer, DVM, Anna Shipov, DVM

**KEYWORDS**

• Dog • Cat • Mineral density • Quality • Bone • Hyperparathyroidism

**KEY POINTS**

- Renal secondary hyperparathyroidism is common in dogs and cats with chronic kidney disease.
- Renal osteodystrophy occurs in dogs and cats with chronic kidney disease and bone quality is reduced in these animals.
- In the cortical bone, material properties, bone geometry, and mechanical properties are affected.
- Bone mass is reduced in cancellous bone of animals with chronic kidney disease.

## INTRODUCTION

### *Renal Secondary Hyperparathyroidism*

Secondary hyperplasia of the parathyroid glands, resulting in increased parathyroid hormone (PTH) blood concentration, is an inevitable consequence of chronic kidney disease (CKD) in human and veterinary patients. The pathophysiology of this multifactorial syndrome, known as renal secondary hyperparathyroidism (SHPT), is complex. Progressive loss of functional nephrons leads to a decrease in the glomerular filtration rate, resulting in phosphorus retention, which promotes PTH secretion, by a direct stimulatory effect on the parathyroid gland, and more importantly, by binding free calcium, resulting in decreased ionized calcium concentration. PTH decreases phosphorus reabsorption in the renal tubules and restores normophosphatemia, but only to a certain point. As the disease progresses and glomerular filtration rate continues to decline, phosphorus retention becomes more severe and further triggers PTH secretion, which in turn promotes bone resorption and release of calcium and phosphorus to the circulation.[1,2] Vitamin D also plays a pivotal role in the pathophysiology of renal SHPT. Calcitriol, the active

The authors have nothing to disclose.
Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, Hertzel Street, Rehovot 76100, Israel
* Corresponding author.
*E-mail address:* gilad.segev@mail.huji.ac.il

Vet Clin Small Anim 46 (2016) 1151–1162
http://dx.doi.org/10.1016/j.cvsm.2016.06.006 **vetsmall.theclinics.com**
0195-5616/16/$ – see front matter 

form of vitamin D, is formed by 1α-hydroxylation of 25-hydroxy-cholecalciferol in the kidney. Decreased functional renal mass and phosphorous retention result in decreased 1α-hydroxylase activity, hereby limiting calcitriol production. Calcitriol, in addition to promoting intestinal calcium absorption, is a major suppressor of PTH secretion. Therefore, reduced calcitriol levels contribute to the progression of renal SHPT, by promoting hypocalcemia and by decreasing the inhibitory effect of calcitriol on PTH secretion.[1,2] An additional, more recently identified key player in the development of renal SHPT, is fibroblast growth factor (FGF)-23, a hormone produced mainly by osteoblasts and osteocytes, which promotes renal phosphorous excretion. FGF-23 is secreted in response to hyperphosphatemia, early in the course of CKD. It downregulates 1α-hydroxylase activity, thus further decreasing calcitriol levels and worsening renal SHPT.[3,4] Increased serum FGF-23 concentration has been demonstrated as one of the earliest metabolic derangements in patients with CKD, often elevated while patients are still normophosphatemic and have normal PTH concentrations.[5]

#### *Prevalence of renal secondary hyperparathyroidism in patients with chronic kidney disease*

In humans, renal SHPT develops early in the course of CKD, and has been reported to affect 40% and 80% of patients with stage III and IV CKD, respectively.[6] Renal SHPT is also prevalent among cats and dogs with CKD. A 20-fold increase in PTH concentration was documented in a study of dogs with experimental CKD compared with healthy dogs.[7] A more recent study demonstrated SHPT is a common metabolic complication, documented in 76% and 84% of dogs and cats with naturally occurring CKD, respectively, and is present in all animals with International Renal Interest Society (IRIS) CKD stage IV disease.[8,9] In another survey, renal SHPT was documented in 47% of asymptomatic cats, being the only biochemical evidence of CKD.[9] PTH concentrations were higher in nonazotemic cats that subsequently developed azotemia within 12 months compared with cats that remained nonazotemic, and the increase in PTH occurred before changes in plasma calcium or phosphorous concentrations were detected.[10] FGF-23 blood concentration also increases in cats with CKD and were positively correlated with the IRIS stage.[11]

### *Bone Abnormalities Associated with Renal Secondary Hyperparathyroidism*

#### *Renal osteodystrophy*

Persistently elevated PTH concentration increases bone resorption by activating osteoclasts, thereby leading to an imbalance in the bone remodeling process and consequently to decreased bone quality. This phenomenon is generally referred to as renal osteodystrophy (ROD), a complex disorder of bone, resulting from the individual and combined actions of metabolic and hormonal abnormalities that occur in CKD. ROD was defined by the National Kidney Foundation as a constellation of bone disorders, present or exacerbated by CKD, that lead to abnormal mineral metabolism, bone fragility, and fractures.[12] The definition was refined by the "Kidney Disease: Improving Global Outcomes Committee," and a new term, CKD–mineral and bone disorder was coined to refer more broadly to the skeletal and extraskeletal manifestations of the mineral disorders in CKD. The broader CKD–mineral and bone disorder is defined as a systemic disorder of mineral and bone metabolism caused by CKD and manifested by either one or a combination of (1) abnormalities of calcium, phosphorous, PTH, or vitamin D metabolism; (2) abnormalities of bone turnover, mineralization, linear growth, volume, or strength; or (3) vascular or other soft tissue calcification.[13,14]