Primary hyperparathyroidism (PHPT) is characterised by hyperparathyroid hypercalcaemia with a constantly elevated or inappropriately high plasma concentration of parathyroid hormone (PTH). This hormone, an 84 amino-acid peptide synthesised in the parathyroid glands, is the major regulator of calcium homeostasis and exerts its effects mainly on kidney and bone, where the PTH 1 receptor is expressed. This membrane-bound receptor is activated by the N-terminal end of PTH and causes intracellular activation through a G-protein coupled mechanism. The main stimulus for PTH secretion is low plasma calcium (Ca\(^{2+}\)) levels. In PHPT a continuously elevated PTH stimulates the kidney and bone causing a condition with high bone turnover, elevated plasma calcium and increased fracture risk. If bone resorption is not followed by a balanced formation of new bone, irreversible bone loss may occur in these patients. Medical treatment can help to minimise the loss of bone but the cure of PHPT is by parathyroidectomy. After operation, bone mineral density increases during the return to normal bone metabolism. Supplementation with calcium and vitamin D after operation may improve the normalisation to normal bone metabolism with a secondary reduction in fracture risk.

**Abstract**

Parathyroid hormone (PTH) is produced and secreted by the parathyroid glands and has primary effects on kidney and bone. During the pathological growth of one or more parathyroid glands, the plasma level of PTH increases and causes primary hyperparathyroidism (PHPT). This disease is normally characterised by hyperparathyroid hypercalcaemia. In PHPT a continuously elevated PTH stimulates the kidney and bone causing a condition with high bone turnover, elevated plasma calcium and increased fracture risk. If bone resorption is not followed by a balanced formation of new bone, irreversible bone loss may occur in these patients. Medical treatment can help to minimise the loss of bone but the cure of PHPT is by parathyroidectomy. After operation, bone mineral density increases during the return to normal bone metabolism. Supplementation with calcium and vitamin D after operation may improve the normalisation to normal bone metabolism with a secondary reduction in fracture risk.

**Keywords**

Primary hyperparathyroidism, bone mineral density, parathyroidectomy, vitamin D, PTH, calcium, bone remodelling, fracture

**Disclosure**

The authors have no conflicts of interest to declare.

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Bone Involvement in Primary Hyperparathyroidism and Changes After Parathyroidectomy

In mild to moderate PHPT the general picture concerning BMD is reductions in BMD at all measured sites and reduced weight adjusted BMD compared with controls.16-19 The affection is usually found to be only modest in the spine (mainly trabecular bone) with a more severely affection of the long bones in the appendicular skeleton (mainly cortical bone).20 Accordingly, the low BMD in PHPT is considered to reflect a reversible bone loss due to a high turnover state and increased cortical porosity. However, an irreversible bone loss may occur if the high turnover state causes trabecular perforations or cortical thinning.

New emerging technologies, such as micro-computed tomography (µCT) and high-resolution peripheral quantitative CT (HRpQCT) have provided further insights into 3D microarchitecture of bone.20-23 In a study by Dempster et al. µCT of iliac crest biopsies from PHPT patients showed a well-preserved microarchitecture compared with postmenopausal controls.24 However, they used a very small sample size with only five postmenopausal female controls. With HRpQCT, cortical and trabecular bone can be examined noninvasively with high resolution. Two papers on PHPT patients and controls have described decreased total, cortical and trabecular volumetric BMD (vBMD) in the radius.18,25 The reduced vBMD in the radius seems to have arise from decreases in cortical and trabecular thickness, but, contrary to histomorphometric studies, a decrease in trabecular number and increased trabecular spacing were also found suggesting an irreversible bone loss in both cortical and trabecular bone compartments.18,20

There are few studies that have evaluated fracture in PHPT.20,21 In a study by Vestergaard et al.22 the risk of fracture was almost doubled in PHPT patients compared with controls. The increased risk was observed at all skeletal sites in both the peripheral and the axial skeleton.

Changes in Bone Remodelling and Bone Mass after Surgery

Changes in bone turnover and bone structure have been evaluated by histomorphometry in a study by Steiniuche et al.23 comparing iliac crest biopsies before and 3 years after parathyroidectomy (PTX). Reduced bone turnover, but no changes in trabecular structure, were observed.23 Activation frequency, bone formation rate and amount of osteoid surfaces all decreased following PTX. Furthermore, there was a small increase in relative cortical width and a decrease in cortical porosity.

Measurements of low BMD in PHPT with a T-score <−2.5 at any site was an indication for PTX in the 2002 International Guidelines of asymptomatic PHPT and has not changed.20,24 In most patients there will be an immediate BMD increase in the spine and hip following surgical cure of PHPT, while BMD of the forearm only improves at a slower rate.25,26 In a meta-analysis, the mean (95% confidence interval (CI)) BMD increase 1 year after PTX was 4.2% (2.6;5.9) in the spine and 3.5% (1.4;5.5) in the femoral neck.27 Most of the change in BMD arises from a decrease in the PTH-induced bone turnover with secondary refilling of remodelling spaces.28 In previous studies by our group, most of the postoperative BMD increase was seen in the first 6 months of a 3-year study period after successful cure by PTX.29 However, during the following 2.5 years, BMD increased continually at the spine, hip and forearm (see Figure 3). We know that patients with young age and high preoperative plasma levels of PTH and ionised calcium (Ca2+) have the highest BMD increases postoperatively, whereas gender does not seem to affect the postoperative BMD increase.29 On the other hand, the increase in BMD is impaired in patients with reduced kidney function.30,31 In patients with renal failure the hyperparathyroidism is often secondary to kidney disease and these patients are not covered in the present paper.

Long-term data on patients with mild PHPT who have been followed without PTX have shown that BMD measurements were stable for up to 10 years.32 A significant BMD decrease was reported from 10–15 years after diagnosis but although the decrease in BMD seems to be minimal in untreated PHPT patients for many years, there is without doubt a stable BMD increase after PTX. In the same observational study, patients had significant BMD increases 1 year after PTX in the spine, femoral neck and forearm.

In a study from Hansen et al.33 assessing effects of PTX by HRpQCT scans, trabecular vBMD and trabecular number increased following PTX whereas trabecular spacing decreased. In contrast to the changes...
in the forearm, HRpQCT scans of the distal tibia have not revealed significant microarchitectural abnormalities in PHPT patients, and no major changes after PTX have been observed. Accordingly, it may be that weight-bearing (tibia) and non-weight-bearing (radius) bone is affected differentially in PHPT. Collectively, there is evidence of improved microarchitecture in both cortical and trabecular bone after PTX. The main increase in BMD following PTX seems to arise from a lowering of bone turnover causing refilling of the remodelling spaces with increased mineralisation.

The shift from a high to a low bone turnover state following PTX leads to improved microarchitecture in both cortical and trabecular bone after PTX. The main increase in BMD following PTX seems to arise from a lowering of bone turnover causing refilling of the remodelling spaces with increased mineralisation.

Up to 1 year after surgery the risk of fractures was increased in the study by Vestergaard et al., but thereafter the risk returns to the level of controls. In the same study, there was no difference in fracture-free survival between PHPT patients who were operated or not. However, we do not have evidence from randomised trials with fracture as endpoint and the fracture risk in asymptomatic PHPT without a BMD decrease may not be equally increased. To meet the increased risk of fracture in these patients, a treatment with anti-osteoporotic medication after PTX may be necessary if the postoperative BMD increase does not improve the fracture risk sufficiently.

**Conclusion**

Constantly elevated PTH levels in PHPT induce an increased bone turnover with a decreased BMD and an increased fracture risk. The affection varies in different compartments and at different skeletal sites. The decreased BMD is mainly due to a reversible bone loss and refilling of remodelling spaces following surgical cure increases BMD in both trabecular and cortical bone leading to a normalisation of fracture risk. The return to normal bone metabolism after operation may be improved with calcium and vitamin D supplementation.

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4. Parfitt AM, Misreception? Calcium leaves bone only by resorption and enters only by formation, Bone, 2003;33:259–63.
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