



Bone mineral density changes after parathyroidectomy are dependent on biochemical profile[☆]



Denise Lee, MD^a, Marcella D. Walker, MD^b, Hsin Yi Chen^c, John A. Chabot, MD^a, James A. Lee, MD^a, Jennifer H. Kuo, MD^{a,*}

^a Division of Gastrointestinal/Endocrine Surgery, Columbia University, New York, New York

^b Division of Endocrinology, Department of Medicine, Columbia University, New York, New York

^c Cornell University, Ithaca, New York

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ABSTRACT

Background: Bone mineral density (BMD) has been found to improve after parathyroidectomy (PTX) in patients with primary hyperparathyroidism. There are few data on the effect of PTX on BMD in normocalcemic and normohormonal primary hyperparathyroidism.

Methods: A retrospective analysis of 92 primary hyperparathyroidism patients who underwent PTX between 2004 and 2012 with pre- and post-PTX dual-energy x-ray absorptiometry was performed. Within-person changes in BMD pre- and post-PTX were analyzed using log linear mixed models, stratified by biochemical status.

Results: Bone mineral density increased post-PTX in the whole cohort at the lumbar spine (+2.5%), femoral neck (+2.1%), and total hip (+1.9%) and decreased at the one-third radius (−0.9%). On comparison of BMD changes by profile, BMD increased in those with the typical profile at the lumbar spine (3.2%), femoral neck (2.9%), and total hip (2.9%) but declined at the one-third radius (−1.5%). In contrast, BMD improved only at the femoral neck (4.3%) in the normohormonal group and did not change at any site in the normocalcemic group. The typical group had a greater increase in BMD over time at the femoral neck and total hip compared with normocalcemic patients.

Conclusion: Our results indicate that the skeletal benefit of PTX was attenuated in normocalcemic and normohormonal patients, suggesting that skeletal changes after PTX may depend on biochemical profile.

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Introduction

Primary hyperparathyroidism (PHPT) is characterized by excessive parathyroid hormone (PTH) secretion from one or more of the parathyroid glands. The typical serum biochemical profile includes hypercalcemia and elevated PTH levels. PHPT was first described in the early 20th century sequentially in Europe and the United States. At that time, the disorder came to clinical attention when patients presented with severe skeletal, renal, gastrointestinal, neurological, or constitutional manifestations.^{1,2} Early accounts of the disorder include the frequent occurrence of osteitis fibrosa cystica, a high-turnover skeletal disorder typified by bone pain, fractures, demineralization, fibrosis, cysts, and brown tumors

that rapidly and markedly improved after successful parathyroidectomy (PTX).^{2,3}

Because of the routine screening of calcium, PHPT has evolved from a rare and symptomatic disease to one that, today, is common and most often presents in an asymptomatic fashion when hypercalcemia is identified on routine labs.¹ Although the classic skeletal manifestations of PHPT are rare today, patients often have subclinical skeletal sequelae such as low bone mineral density (BMD) when assessed with dual x-ray absorptiometry (DXA) or vertebral fractures identified by spinal imaging.^{4,5} Current guidelines recommend PTX for patients with PHPT and osteoporosis or vertebral fracture because data from both observational and randomized controlled trials indicate that BMD increases after PTX and the risk of vertebral fracture may decline.^{4,6–8}

Other biochemical forms of PHPT have recently come to clinical attention and are recognized as PHPT or variants of the traditional hypercalcemic form of PHPT in which both PTH and serum calcium are elevated.^{6,9,10} Normocalcemic PHPT is characterized by an elevated serum PTH level with normal serum calcium in patients in whom causes of secondary hyperparathyroidism have

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* Corresponding author: Jennifer H. Kuo, MD, Division of GI/Endocrine Surgery, Columbia University, New York, NY 10032.

E-mail address: jhk2029@cumc.columbia.edu (J.H. Kuo).

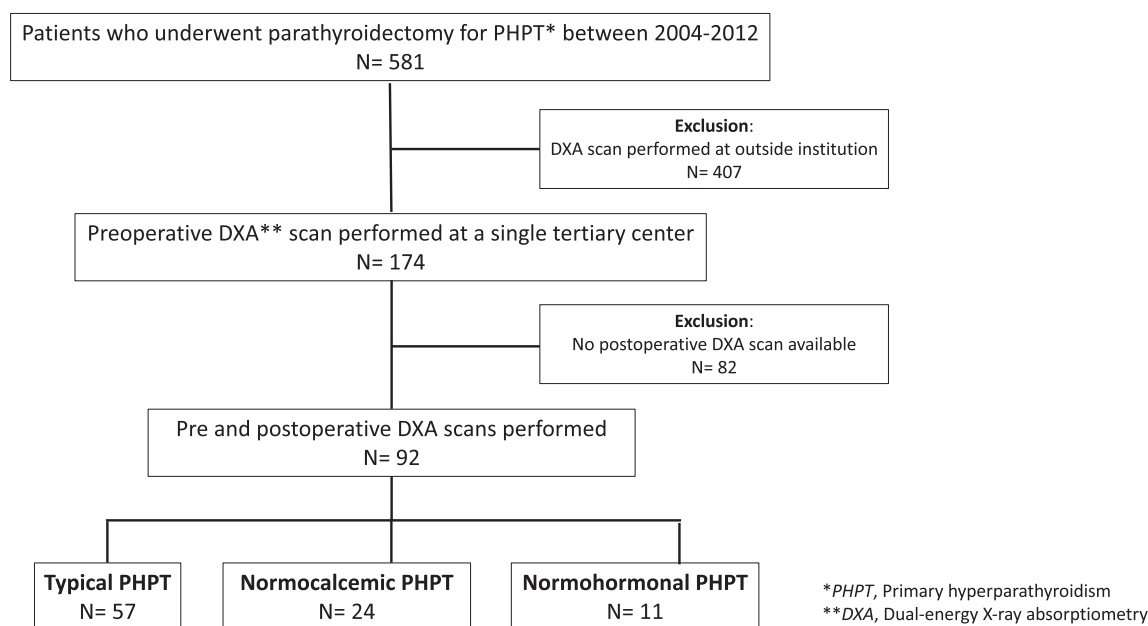


Fig. 1. Diagram of study population inclusion and exclusion criteria.

been excluded. Patients with normocalcemic PHPT have a high prevalence of osteoporosis, fractures, and kidney stones despite the “milder” biochemical phenotype.¹¹ This is most likely due to screening bias when patients presenting with these features have PTH levels evaluated.¹¹ Another recognized biochemical profile is “normohormonal” PHPT, in which calcium is elevated but PTH is inappropriately normal.^{1,12} Guidelines for PTX for the normohormonal form of PHPT follow those for the typical biochemical profile.⁶ In normocalcemic PHPT, PTX is suggested if patients develop hypercalcemia and have other indications for PTX or have worsening of BMD, fracture, or kidney stones regardless of the emergence of hypercalcemia.⁹ However, there are few data regarding BMD changes after PTX in patients with these milder biochemical forms of PHPT. It is unclear if the improvement in BMD in patients with the typical biochemical profile is mirrored in patients with other biochemical profiles. These data are important to obtain because they could change recommendations for PTX.⁴ In this study we investigate the changes in BMD after PTX in patients according to biochemical profile. We hypothesize that patients with milder biochemical profiles of primary hyperparathyroidism will receive the same degree of benefit in bone density after PTX as patients with typical biochemical profiles.

Methods

Patients and data collection

This study was approved by the institutional review board of Columbia University Medical Center or CUMC (Protocol AAAL3823). Between 2004 and 2012, patients with PHPT evaluated at our tertiary referral center for PTX and with complete laboratory data ($N=581$) were considered for inclusion in this study if they had pre- and postoperative DXA. Patients were excluded if they had secondary or tertiary hyperparathyroidism, did not achieve surgical cure (elevated serum calcium or PTH at 6 months postop), had incomplete collection of laboratory values, had DXA at an outside institution ($n=407$), or had no postoperative DXA scan available ($n=82$) (Fig. 1). We excluded patients with outside DXA to avoid combining densitometric data from different densitometer manufacturers and ensure the quality and completeness of DXA informa-

tion. Individual patient clinical data were retrospectively collected from the patient's medical records and analyzed.

Diagnosis of primary hyperparathyroidism and biochemical profiles

Patients were diagnosed with typical PHPT, normocalcemic PHPT, or normohormonal PHPT based on serum biochemistries from each patient's medical record. Biochemistries were measured in different clinical labs. All patients had PTH measured with an intact PTH assay. The 3 biochemical profiles (typical, normocalcemic, and normohormonal) were defined respectively by concomitantly elevated preoperative serum calcium and PTH; normal serum calcium and elevated PTH; and elevated serum calcium and no-suppressed PTH. Ionized serum calcium levels were not routinely measured and not included in this study. Normal values were determined by the individual laboratory reference ranges. When more than one preoperative serum calcium or PTH value was available, the greatest value was used to determine biochemical profile.

Operative procedures

Patients underwent PTX if they both met biochemical criteria for PHPT and were either symptomatic (osteoporosis or history of kidney stones) or asymptomatic but met criteria for PTX based on recommendations outlined by the International Workshop Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism.⁶ Preoperative imaging for localization was obtained at the discretion of the operating surgeon and included cervical ultrasound, sestamibi scan, or 4-dimensional computed tomography scans. The decision to perform a focused PTX or 4-gland exploration was determined by preoperative imaging and intraoperative decision-making. Serial intraoperative PTH levels were obtained in all cases and the operation was terminated when values met the Miami criterion (a 50% decrease in PTH after 10 minutes from the highest pre-excision value).¹³

Criteria for biochemical cure

Patients were determined to have had an operative cure if they achieved normalization of serum calcium and PTH (typical PHPT),

Table 1
Patient demographics and preoperative characteristics.

	Total (N = 92)	Typical (n = 57)	Normocalcemic (n = 24)	Normohormonal (n = 11)	P value
Clinical					
Age, y	66 ± 12.3*	66 ± 11.8	72 ± 12.4	57 ± 14.7	.39
Women	77 (83.7%)	46 (80.7%)	22 (91.2%)	9 (81.8%)	.47
Race					
White	72 (78.3%)	42 (73.7%)	20 (83.3%)	10 (90.9%)	.35
Black	7 (7.6%)	5 (8.8%)	2 (8.3%)	0	.60
Asian	1 (1.1%)	0	1 (4.1%)	0	.24
Unknown/other	11 (12.0%)	9 (15.8%)	1 (4.1%)	1 (9.1%)	.32
Height, cm	164.6 ± 27.4	164.6 ± 34.2	160.0 ± 7.9	157.5 ± 10.1	.97
Weight, kg	67.8 ± 17.7	76.5 ± 18.5	65.4 ± 13.3	61.2 ± 18.7	.49
Nephrolithiasis	9 (9.8%)	8 (14.0%)	1 (4.1%)	0	.20
Biochemical					
Preoperative serum calcium, mg/dL	10.7 ± 0.8	10.9 ± 0.7	9.9 ± 0.3	10.7 ± 0.2	<.001 [†]
Preoperative PTH, pg/mL	118 ± 72.2	149 ± 75	91.5 ± 43	55 ± 14	<.001 [‡]
Preoperative 25-hydroxyvitamin D, ng/mL	31.9 ± 11.9	31.7 ± 12.5	33 ± 10.8	28 ± 11.6	.90
Multigland disease	16 (17.4%)	7 (12.3%)	8 (33.3%)	1 (9.0%)	.056
Bone health					
Osteoporosis	37 (40.2%)	21 (36.8%)	12 (50.0%)	4 (36.4%)	.52
Osteopenia	36 (39.1%)	24 (42.1%)	7 (29.2%)	5 (45.5%)	.50
Preoperative bone mineral density, g/cm ²					
Lumbar spine	0.84 ± 0.2	0.88 ± 0.18	0.80 ± 0.13	0.82 ± 0.10	<.05 [§]
Femoral neck	0.69 ± 0.1	0.71 ± 0.15	0.66 ± 0.11	0.64 ± 0.12	.11
Total hip	0.83 ± 0.2	0.85 ± 0.18	0.81 ± 0.13	0.81 ± 0.19	.14
One-third radius	0.64 ± 0.1	0.65 ± 0.12	0.60 ± 0.09	0.59 ± 0.08	.07
Preoperative T-score					
Lumbar spine	-1.8 ± 1.5	-1.6 ± 1.7	-2.0 ± 1.2	-2.2 ± 0.8	.12
Femoral neck	-1.6 ± 1.2	-1.4 ± 1.2	-1.8 ± 0.9	-1.9 ± 1.0	.13
Total hip	-1.0 ± 1.2	-0.9 ± 1.3	-1.1 ± 1.0	-1.2 ± 1.3	.18
One-third radius	-1.1 ± 1.6	-1.0 ± 1.7	-1.5 ± 1.6	-1.7 ± 1.3	.19
Time between pre- and postoperative DXA scans, mo	23.16 ± 18.2	24.2 ± 19.0	15.5 ± 19.1	24.5 ± 10.7	.87

* Continuous variables are expressed as the median ± standard deviation, and remaining variables as number (%).

[†] $P < .05$ for the comparison between normocalcemic and normohormonal groups and between normocalcemic and typical groups.[‡] $P < .05$ for all comparisons among groups.[§] $P < .05$ for the comparison between normocalcemic and typical only.

normalization of calcium (normohormonal), or normalization of serum PTH (normocalcemic) by 6 months postoperatively.

Measurement of bone mineral density

All patients had preoperative and postoperative bone densitometry performed at CUMC within the Metabolic Bone Diseases Unit, measured by an International Society for Clinical Densitometry (ISCD)-certified technician. Areal BMD was measured at the lumbar spine (LS), total hip (TH), femoral neck (FN), and the distal one-third radius using a QDR 4500 instrument (Hologic Inc., Waltham, MA). T- and Z-scores were obtained using the manufacturer's reference norms. *In vivo* precision at this facility is 1.28% at the LS, 1.36% at the TH, and 0.70% for the one-third radius.¹⁴

Statistical analysis

The primary endpoint was the comparison of the average within-person BMD changes before and after PTX, aggregated across the different biochemical groups. Descriptive analyses were performed with analysis of variance for continuous variables and χ^2 -test for categorical variables to determine differences between the 3 biochemical profiles. Log linear mixed models were used to evaluate the change in BMD over time (pre- to post-PTX) as a within-person repeated measure. We controlled for individual patient differences in baseline (pretreatment) BMD due to age, gender, race, and so on through random effects modeling on the intercept. Change in BMD was calculated for each of the skeletal sites measured by DXA.

In the first model, we analyzed the incremental effectiveness of PTX on the change in BMD for each patient over time, controlling for their individual profile. To evaluate whether the change in

BMD was dependent on biochemical profile, an interaction term with the biochemical profile as a categorical variable was used.

A second model was evaluated to determine whether preoperative serum calcium or PTH could predict the change in BMD after PTX by using a log-linear regression model with random intercept to investigate the effect of PTX on BMD while controlling for individual patient-observed average levels of preoperative serum calcium and PTH. All statistical analyses were performed using R software (Version 3.4.2). A 2-tailed P value $< .05$ was considered to indicate statistical significance.

Results

Between 2004 and 2012, 1,137 patients underwent PTX, of whom 581 had complete pre- and postoperative laboratory data. In total, 92 patients were included in this study based on the availability of pre- and post-PTX DXA scans performed at CUMC (Fig. 1). There was no difference in age ($P = 0.95$), sex ($P = 0.70$), preoperative serum calcium ($P = 0.41$), or PTH ($P = 0.93$) between those who were and were not included. Fifty-seven patients met criteria for typical PHPT, 24 for normocalcemic PHPT and 11 for normohormonal PHPT.

Preoperative clinical and biochemical characteristics by biochemical profile

Baseline biochemical, clinical, and skeletal characteristics of the study cohort are summarized in Table 1. There was no difference in age ($P = .39$), sex ($P = .47$), race (white, $P = .35$), weight ($P = .49$), or history of kidney stones ($P = .20$) between the 3 groups with different biochemical profiles. As expected, there was a difference in

preoperative serum calcium and PTH between the typical, normocalcemic, and normohormonal groups (10.9 ± 0.7 , 9.9 ± 0.3 , and 10.7 ± 0.2 mg/dL and 149 ± 75 , 91.5 ± 43 , and 55 ± 14 pg/mL, respectively; both P values $< .001$). Although the calcium level was lower in the normocalcemic group compared with the typical ($P < .001$) and normohormonal ($P < .001$) groups, there was no difference between the latter 2 groups ($P = .19$). PTH levels were highest in the patients with typical PHPT, intermediate in the normocalcemic group, and lowest in the normohormonal group. There were no between-group differences in 25-hydroxyvitamin D level.

The greater frequency of multiglandular disease in the normocalcemic group compared with the other groups was of borderline significance ($P = .056$). There were no between-group differences in the prevalence of osteoporosis ($P = .52$) or osteopenia ($P = .5$) or median T -scores at any skeletal site (LS, $P = .12$; FN, $P = .13$; TH, $P = .18$; one-third radius, $P = .19$), or median time between pre- and postoperative DXA scans ($P = .87$). Normocalcemic patients had lower absolute BMD at the LS before PTX compared with patients with the typical biochemical profile (0.80 ± 0.13 vs 0.88 ± 0.18 g/cm², $P < .05$), but there were no between-group differences at the FN, TH, or one-third radius.

Changes in BMD after PTX

Figure 2 summarizes the change in BMD over time at all skeletal sites in the whole cohort and stratified by biochemical profile. The post-PTX DXA scan was obtained at a median of 13.4 months after surgery. In the entire cohort, PTX was associated with an increase in BMD at the LS ($2.5 \pm 0.56\%$, $P < .001$), FN ($2.1 \pm 0.62\%$, $P = 0.001$), and TH ($1.9 \pm 0.48\%$, $P < .001$), but a small decrease in BMD at the one-third radius ($-0.9 \pm 0.40\%$, $P = .024$). When stratified by biochemical profile, patients with the typical biochemical profile had a similar increase in BMD at the LS, FN, and TH and decline at the one-third radius: LS ($3.2 \pm 0.70\%$, $P < .001$), FN ($2.9 \pm 0.76\%$, $P < .001$), TH ($2.9 \pm 0.59\%$, $P < .001$), and one-third radius ($-1.5 \pm 0.51\%$, $P = .004$). In contrast, BMD did not change at any skeletal site in the normocalcemic group and improved only at the FN ($4.3 \pm 1.8\%$, $P = .020$) in patients with the normohormonal profile. Comparison of the change in BMD over time between groups revealed that the typical group had an increase in BMD relative to the normocalcemic group at the FN and TH. At the FN, BMD did not change in the normocalcemic group, whereas patients with the typical biochemical profile had an increase in BMD (-0.6% vs $+2.9\%$ respectively, $P = .012$); thus, the group with the typical profile had a $+3.5\%$ increase in BMD post-PTX relative to their normocalcemic counterparts. Similarly, at the TH, BMD did not change in the normocalcemic group, whereas there was an increase in the typical group (-0.2% vs $+2.9\%$ respectively, $P = .004$)—an overall $+3.1\%$ relative increase in BMD post-PTX in typical patients compared with normocalcemic patients.

Predictors of BMD change over time

As outlined in Table 2, PTX is associated with a change in BMD over time at all skeletal sites. Our results indicate that there is a significant interaction between baseline serum calcium and time (after PTX). The change in BMD over time (after PTX) was modified by baseline serum calcium. There was an additional 2.9% increase in BMD at the FN over time (after PTX) for a 2SD higher serum calcium level preoperatively, compared with a calcium level at the mean level.

Discussion

In this analysis, we found that BMD response to PTX in patients with PHPT varied by preoperative biochemical profile.

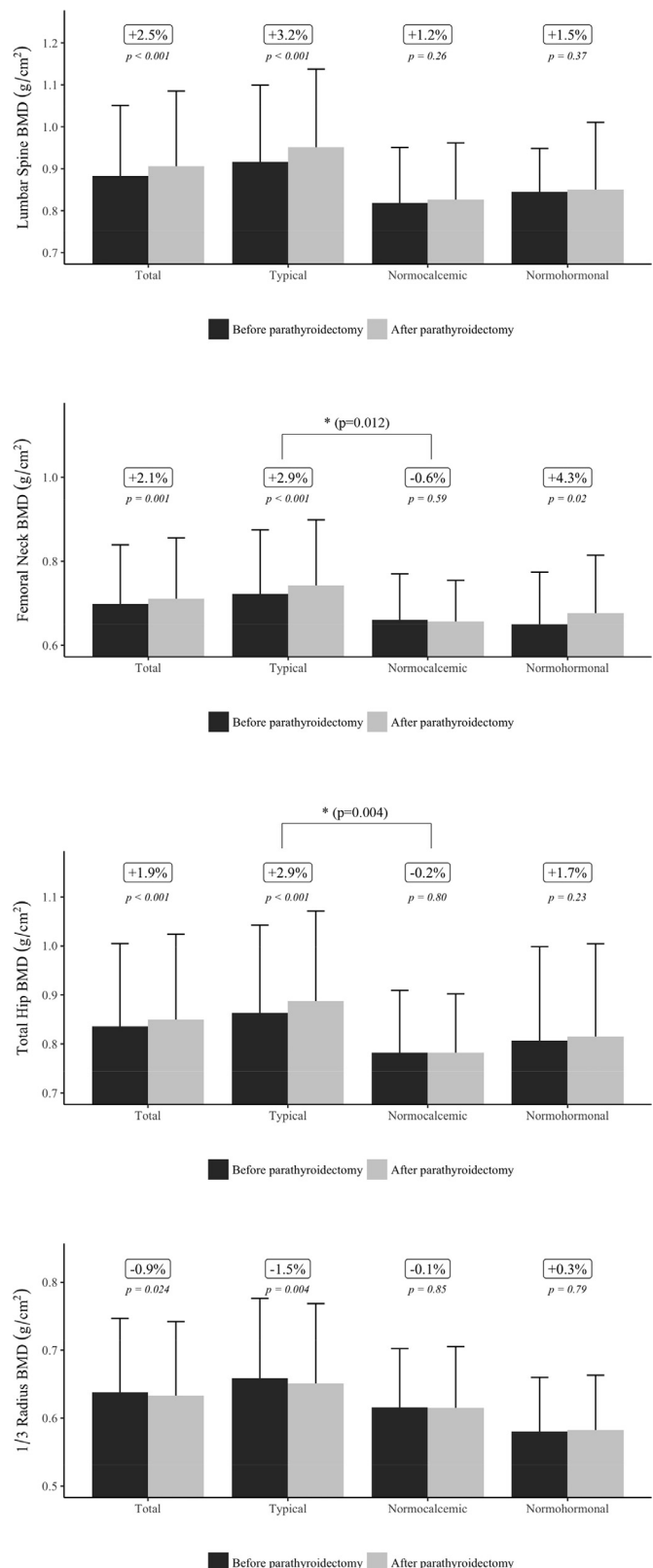


Fig. 2. Percentage changes in BMD before and after parathyroidectomy at all sites. *Statistically significant difference in change in BMD over time when compared with typical biochemical profile, $P = .048$. BMD = bone mineral density.

Table 2
Predictors of change in bone mineral density over time after parathyroidectomy.

Explanatory variable	BMD change	95% CI	P value
Lumbar spine			
Time (after PTX)	+2.5%	(1.4%, 3.5%)	<.001*
Baseline serum calcium × time	+1.0%	(−1.5%, 3.4%)	.44
Preoperative PTH × time	+0.7%	(−1.8%, 3.2%)	.58
Femoral neck			
Time (after PTX)	+2.0%	(0.8%, 3.2%)	.001
Baseline serum calcium × time	+2.9%	(0.2%, 5.5%)	.04
Preoperative PTH × time	−1.7%	(−4.4%, 1.0%)	.22
Total hip			
Time (after PTX)	+1.9%	(0.9%, 2.8%)	<.001
Baseline serum calcium × time	+1.6%	(−0.5%, 3.6%)	0.13
Preoperative PTH × time	+0.6%	(−1.4%, 2.7%)	0.55
One-third radius			
Time (after PTX)	−0.9%	(−1.8%, −0.2%)	0.02
Baseline serum calcium × time	−0.7%	(−2.5%, 1.1%)	0.46
Preoperative PTH × time	−0.6%	(−2.6%, 1.4%)	0.56

* P values in boldface indicate significant differences.
CI, confidence interval.

Although patients with the typical biochemical profile of hypercalcemia and elevated PTH had improvements in BMD at the LS, FN, and TH, there was no change in BMD at any skeletal site after PTX in the normocalcemic group and only an improvement at the FN in the normohormonal group. To our knowledge, this is the first study to assess BMD changes in both patients with the normocalcemic and those with the normohormonal profiles of PHPT; it is also the largest overall comparison of typical PHPT to these “milder” biochemical profiles, to date, and the only study to assess BMD changes in these phenotypes in the United States. Further, this is the only study to assess the biochemical factors that predicted BMD response to PTX in those with such profiles. These findings suggest that PHPT patients with a “milder” biochemical profile may not receive as robust of a skeletal benefit from PTX as the typical group. Our data further indicate that it may be the degree of hypercalcemia, rather than the degree of PTH elevation, that determines extent of BMD gains post-PTX because only groups with hypercalcemia improved. Our model assessing predictors of the change in BMD also supports that the degree of elevation of preoperative calcium is associated with post-PTX change in BMD, though it was not consistent across all skeletal sites. This finding may help explain why normocalcemic patients exhibited no change in BMD after PTX, whereas hypercalcemic patients (typical profile) did.

Our results contrast with those of Koumakis et al.¹⁵ Their study compared BMD changes 1-year post-PTX in normocalcemic and hypercalcemic patients with PHPT. The normocalcemic group in their study, like the hypercalcemic group, had a modest increase in BMD at the LS and FN (1.9%–2.3%) and a decrease at the one-third radius.¹⁵ The reasons for the difference in BMD response in the normocalcemic groups at the LS and FN between studies is not clear, but the majority of patients in this previous study (92%) had osteoporosis and there was a high rate of fragility fracture, which might account for the difference. Because of the limited size of the normocalcemic and normohormonal groups in our study, however, we cannot completely rule out a type II error.

The BMD improvement we observed at the LS and hip site in patients with the typical biochemical profile is consistent with both observational and randomized studies.^{4,7} Although most studies suggest the one-third radius does not improve after PTX or may take many years to improve, we noted a decline at that site.^{4,7,16} Because our analysis assessed BMD at a median of 13.4 months post-PTX, it is possible that stable BMD or an improvement at the radius may have been observed with longer follow-up.

Similar to the study by Koumakis et al.,¹⁵ our results imply that patients with normocalcemic PHPT are more likely to have

multiglandular disease than patients with either typical or normohormonal profiles. As noted in their prior report, this could indicate that normocalcemic PHPT may have a different pathophysiological mechanism compared with the other 2 profiles. Lowe et al.¹¹ also suggested that patients with normocalcemic PHPT may not be just an antecedent of typical asymptomatic PHPT.

Our study has several limitations. First, data were collected retrospectively and thus could be subject to selection bias, confounding, or differential follow-up between groups. The similar characteristics of our overall cohort to those of previous cohorts recruited in our prospectively enrolled studies, however, is reassuring in this regard, as is the similar median follow-up among groups.¹⁷ In addition, given the evolution of criteria for diagnosis of normocalcemic PHPT over the enrollment period, we did not routinely obtain ionized calcium levels in our study nor did all patients have all secondary causes of hyperparathyroidism eliminated that are now suggested, such as a history of hydrochlorothiazide and lithium use, hypercalciuria, and malabsorption syndromes.¹⁸ Although we cannot exclude misclassification of some participants, our study does provide meaningful real-world data from prevailing clinical surgical practice during the study period. Because of the retrospective nature of this study, DXA was obtained at different time points relative to PTX, and we cannot exclude the possibility of greater BMD improvement with longer follow-up. Our study also has several strengths. We studied a relatively large cohort of patients with PHPT, assessed both the normocalcemic and normohormonal biochemical profiles of PHPT, and assessed predictors of the post-PTX change in BMD. Further, to our knowledge it is the only study to assess BMD changes in normocalcemic PHPT after PTX in the United States. Because of the variability in PHPT disease presentation by geographic location, data from other countries are not necessarily applicable to the United States.

Conclusion

Although PTX remains the only definitive treatment for PHPT and results in increased BMD in patients with a typical profile of hypercalcemia and elevated PTH, our findings indicate that the benefit of PTX may be attenuated in patients with normocalcemic and normohormonal PHPT. Further work is needed to determine optimal evidence-based guidelines for PTX in PHPT patients with “atypical” biochemical profiles.

Acknowledgments

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Discussion

Dr. Barry Inabnet (New York, NY): Denise, great presentation and a great study.

I call these patients with an atypical biochemical diagnosis kind of a “back-door diagnosis,” and often they drop in through bone density analysis, and that’s how then the astute clinician begins investigating and realizes perhaps they have primary hyperparathyroidism. But your data suggest we shouldn’t be operating on those patients with normocalcemic hyperparathyroidism, and on top of that they are more likely to have multiglandular disease. What do you recommend for us?

Dr. Denise T. Lee: That’s an excellent question and actually a very difficult one to answer. As you said, a lot of these patients are referred to us because they have osteoporosis. They are identified by their metabolic bone disease.

What I would recommend to patients after these findings is that they can certainly undergo parathyroidectomy, but they should recognize that their improvement in bone mineral density may actually be more attenuated, and it may be actually slower to manifest. Our follow-up was a median of 13 months, and it could be that we did not capture an actual improvement that may have been apparent had we been able to follow patients for a longer period of time.

Dr. Nancy Perrier (Houston, TX): Denise, congratulations on some great data—a wealth of information there. Can you take that data set and stratify it by sex to tell us whether there’s a difference in the bone mineral density with hypercalcemia or parathyroid hormone level related to sex because of the estrogen levels and other factors of timing? Do you have that information?

Dr. Denise T. Lee: Excellent question. We were able to control for different clinical variables such as sex, multigland disease, the percent of patients with kidney stones, etc. We essentially saw that there is no other clinical factor that had an effect on bone mineral density other than the preoperative calcium level.

Dr. Sanziana Roman (San Francisco, CA): I have more of a comment, and it might be a little controversial. In my heart, I never really believed that normocalcemic hyperparathyroidism was an actual pathological state. I actually have always thought that it is more of a physiological state that is in response to having poorer bone mineral density and osteoporosis. In fact, we give people Forteo to treat it. So isn’t it really an endogenously generated situation caused by elevating the PTH, and perhaps that’s why people actually have hyperplasia, because this is a compensatory mechanism rather than a pathological state? I wonder if you could comment.

Dr. Denise T. Lee: That is an excellent point. There is much to be studied in terms of a better understanding of the pathophysiology and the natural history of normocalcemic primary hyperparathyroidism. I believe that there’s not much known about it, and it’s been hypothesized that this may actually be a biphasic disease where patients presenting with a normocalcemic phase actually later progressed to typical primary hyperparathyroidism. There are longitudinal studies following patients with normocalcemic disease that suggest that maybe it is a precursor for those who would develop symptomatic primary hyperparathyroidism. They certainly do have higher rates of multigland disease, which is less consistent with going on to develop typical primary hyperparathyroidism. So there’s a lot to be further understood about this pathophysiology.

Dr. Rosemarie Metzger (Weston, FL): Great presentation. What was the length of time from surgery to when you next measured their bone mineral density? You alluded to the average length of follow-up being approximately 13 months. I was wondering if these tests were being done prior to that time. Perhaps you may not have been catching all of the effect that surgery may have been having. Did you also control for patients who were on any type of antiresorptive agents both preoperatively and in the postoperative setting?

Dr. Denise T. Lee: Our median follow-up was 13 months after parathyroidectomy, and that median follow-up was for patients with a DEXA scan done postoperatively.

In terms of the question about assessing for patients who had been on antiresorptive medications, unfortunately, given the retrospective nature of this study, we weren’t able to ascertain which patients may have still been on the antiresorptive medications prior to undergoing surgery or how soon after surgery they may have been restarted, but that would certainly be an important aspect to look at in the future.

Dr. Toni Beninato (New York, NY): Congratulations on a well-done study.

I just question the small number of patients in the normocalcemic and normohormonal groups. I know that you did not see a difference in bone mineral density in those patients. While I think I agree with your conclusions, are you sure the study was adequately powered to make that particular conclusion?

Dr. Denise T. Lee: That’s certainly a very good point. That’s one of the reasons why we did the secondary analysis where we stratified patients according to their preoperative calcium and PTH levels rather than just looking at the biochemical profiles beforehand.



We certainly acknowledge that there were a small number of patients in each of these biochemical groups. However, our study size was fairly similar to what has been previously reported in the literature. There's only one other study that we are aware of right now

that assessed changes in normocalcemic patients after parathyroidectomy. This study was published in France in 2014, and they had only 39 patients with normocalcemic disease I believe.