Original Article

DOES BASELINE PTH INFLUENCE RECOVERY OF BONE MINERAL DENSITY, TRABECULAR BONE SCORE AND BONE TURNOVER MARKERS? A PROSPECTIVE STUDY FOLLOWING CURATIVE PARATHYROIDECTOMY IN PRIMARY HYPERPARATHYROIDISM

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ABSTRACT

Objective: This prospective study was carried out to assess trabecular bone score, bone mineral density (BMD), and bone biochemistry in Indian subjects with symptomatic primary hyperparathyroidism (PHPT), and to study the influence of baseline parathyroid hormone (PTH) on recovery of these parameters following curative surgery.

Methods: This was a 2-year prospective study conducted at a tertiary care centre in southern India. Baseline assessment included demographic details, mode of presentation, bone mineral biochemistry, BMD, trabecular bone score (TBS), and bone turnover markers (BTMs). These parameters were reassessed at the end of the first and second years following curative parathyroid surgery.

Results: Fifty-one subjects (32 men and 19 women) with PHPT who had undergone curative parathyroidectomy were included in this study. The mean (SD) age was 44.6 (13.7) years. The TBS, BTMs, and BMD at lumbar spine and forearm were significantly worse at baseline in subjects with higher baseline PTH (≥250 pg/mL) when compared to the group with lower baseline PTH (<250 pg/mL). At the end of 2 years, the difference between high versus low PTH groups (mean ± SD) persisted only for forearm BMD (0.638 ± 0.093 versus 0.698 ± 0.041 g/cm^2; P = .01). However, on follow-up visits in the first and second year after curative parathyroidectomy, there was no significant difference in BTMs, BMD at the femoral neck, lumbar spine, and TBS between the 2 groups stratified by baseline PTH.

Conclusion: The BMD at the forearm remained significantly worse in individuals with high baseline PTH even at 2 years after surgery, while other parameters including TBS improved significantly from baseline. **(Endocr Pract. 2020;26:1442-1450)**

Abbreviations:
25(OH)D = 25-hydroxyvitamin D; **BMD** = bone mineral density; **BMI** = body mass index; **BTMs** = Bone turnover markers; **CTX** = C-terminal telopeptide of type 1 collagen; **DXA** = dual energy X-ray absorptiometry; **P1NP** = N-terminal propeptide of type 1 procollagen; **PHPT** = primary hyperparathyroidism; **PTH** = parathyroid hormone; **TBS** = trabecular bone score

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a disorder characterized by hypercalcemia with inappropriate secretion of parathyroid hormone (PTH) either from an adenoma or hyperplasia of parathyroid glands (1). In the West,

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due to better screening, there has been a recent increase in the number of patients with normocalcemic hyperparathyroidism, which is defined as a normal albumin corrected total, as well as ionized calcium levels with elevated PTH in the absence of any other cause for secondary hyperparathyroidism such as vitamin D deficiency or kidney disease (2). Although, there has been an increase in detection, treatment, and publications with regards to PHPT in India over the past decade, the incidence of asymptomatic or mild hyperparathyroidism is still low as compared to the West (3). Also, PHPT in the West, tends to be milder as compared to cases reported from the Indian subcontinent. Limited Indian studies have recently reported the changing profile of PHPT from symptomatic and severe ones to milder and asymptomatic types (4-6). Indian subjects differ considerably from their western counterparts in that renal and skeletal manifestations continue to be the common presenting symptoms; there is a considerable delay of about 5 to 7 years before diagnosis, and about two-thirds of patients present before 40 years of age (7). Besides the classic manifestations described, Indian patients are also prone for hyperparathyroidism induced pancreatitis (8), which has rarely been reported in western literature.

Bone mineral density (BMD), markers of bone turnover and trabecular bone score (TBS) following parathyroid surgery have seldom been studied in symptomatic PHPT from the Indian subcontinent. In a retrospective study of Indian patients with PHPT, about three-fourths remained symptom free following curative surgery (9). In a study by Miguel et al (10) involving 32 subjects followed up for a period of 2 years after curative parathyroid surgery, there was an improvement in BMD with a restoration of bone turnover markers (BTMs). Moreover, despite the availability of BTMs and TBS in current day clinical practice, serial changes in these parameters following surgery are not well studied. Hence, we attempted to fill this research gap by prospectively studying the changes in BMD, TBS, and BTMs in Indian subjects with symptomatic PHPT at baseline and following curative parathyroid surgery and also assessing the influence of baseline PTH on bone health recovery.

METHODS

This was a prospective study carried out in a tertiary care centre in southern India and was conducted over a period of 4 years (September 1, 2015, to August 31, 2019). Recruitment of patients was done during the first 24 months and they were followed up once a year for the next 2 years.

Study Subjects

Patients diagnosed with symptomatic PHPT due to a single gland involvement, undergoing curative parathyroidectomy with a histopathologic diagnosis of parathyroid adenoma were recruited in the study. The subjects included had concordant parathyroid involvement on Sestamibi and ultrasound scans on preoperative evaluation. The study flowchart with inclusion and exclusion criteria is shown in Figure 1. This study was approved by the institutional review board (Research and Ethics committee; IRB No: 9004; dated 04.08.2014). All study subjects provided written informed consent at recruitment into the study.

Assessment

Patients were assessed at baseline before surgery and at the end of the first year and second year following surgery. Clinical baseline assessment included demographic details, mode of presentation, bone mineral biochemistry, BMD, TBS, and BTMs. Weight was recorded in kg using an electronic scale, and standing height was measured to the nearest cm with a stadiometer, with subjects wearing light indoor clothing without shoes. Fasting (overnight for 8 hours) venous blood samples were

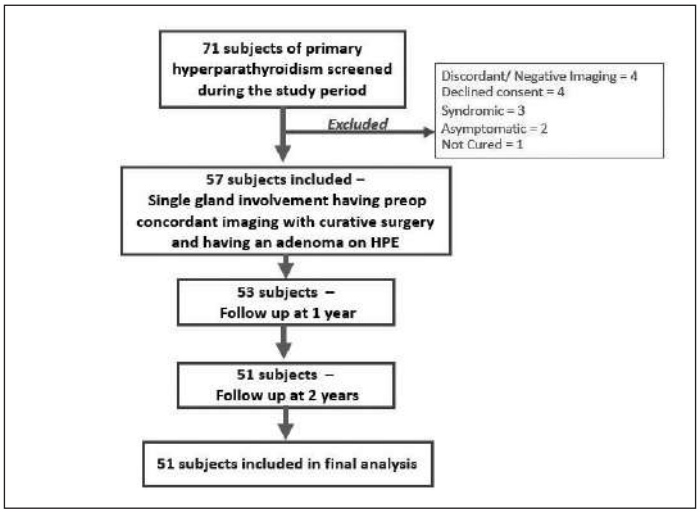

Fig. 1. Study flow chart. *HPE* = histopathologic examination.

collected for the measurement of serum calcium (normal, 8.3 to 10.4 mg/dL), phosphate (normal, 2.5 to 4.5 mg/dL), alkaline phosphatase (normal, 40 to 125 U/L), albumin (normal, 3.5 to 5.0 g/dL), creatinine (normal, 0.6 to 1.4 mg/dL), 25-hydroxyvitamin D (25[OH]D; normal, 30 to 75 ng/mL), and intact PTH (normal, 8 to 50 pg/mL). Serum calcium, phosphate, albumin, creatinine, and alkaline phosphatase were measured using colorimetric methods with Beckman coulter (Beckman coulter AU 5800). An iced sample for intact PTH was collected and estimated by chemiluminescence assay (Advia Centaur XPT immunoassay system, New York, NY) and 25(OH)D was measured using a electrochemiluminescence assay (Roche Cobas 6000- Immunoassay system, Mannheim, Germany). The following BTMs were measured using a electrochemiluminescence immunoassay on a Roche elecsys Modular E170 analyzer: plasma C-terminal telopeptide of type 1 collagen (CTX; normal, 142 to 584 pg/mL in men, 137 to 573 pg/mL in premenopausal women, and 226 to 1088 pg/mL in postmenopausal women), N-terminal propeptide of type 1 procollagen (P1NP; normal, 16.9 to 42.4 ng/mL in men, 15.1 to 58.3 ng/mL in premenopausal women, and 16 to 73.9 ng/mL in postmenopausal women), and osteocalcin (normal, 9.39 to 61.56 ng/mL). PHPT was defined as the presence of hypercalcemia with elevated or inappropriately normal PTH (1). Study subjects with 25(OH)D deficiency (defined as 25(OH)D <20 ng/mL) were treated with cholecalciferol pre-operatively, which was continued following parathyroid surgery (1,000 to 2,000 units/day).

The BMD at the left femoral neck, distal one-third of the left radius, and lumbar spine (L1-L4) were determined using a Hologic dual energy X-ray absorptiometry (DXA) machine (Discovery-A series). The right femur and right distal radius were used for evaluation of BMD in subjects who had fractures involving the left side. TBS (L1-L4) measurements were performed using TBS iNsight Software version 3 (Med-Imaps, Bordeaux, France). BMD of subjects were compared with normative BMD data of Caucasian population. A CV of 2% was noticed for BMD measurements at the lumbar spine and forearm and 3% at the femoral neck during the study period. A TBS ≥1.350 was considered as normal (11). Based on the severity of hyperparathyroidism using the median baseline value of PTH (250 pg/mL), the BMD, TBS, and BTMs were compared at baseline and on follow-up.

Statistical Analyses

Normality was assessed using histograms for continuous variables. Data for categorical variables were presented as frequency and percentage and for continuous variables as the mean (SD) or median. The chi-square test or Fisher exact test was used for comparison of categorical variables and independent Student's *t* tests for continuous variables. A linear mixed-effect model was applied and a repeated-measures approach was used for within-group comparisons across all time points (baseline, 12, and 24 months following surgery). All statistical tests were 2-tailed, and a *P* value <.05 was considered significant. The statistical software SPSS 16.0 for Windows (IBM Corp., Armonk, NY) was used for the analyses.

RESULTS

Fifty-one subjects (32 men and 19 women including 4 postmenopausal women) with PHPT who had undergone curative parathyroid surgery were included in the study. The mean (SD) age was 44.6 (13.7) years. The mean (SD) body mass index (BMI) (kg/m^2) at baseline, at the end of 1 year and 2 years were 24.5 (3.9), 25.3 (3.7), and 25.7 (3.6) in men, and 24.8 (3.4), 25.9 (3.5), and 26.3 (3.4) in women respectively, and this increment was statistically significant in both men and women (*P*<.05). The most common clinical presentation was renal (37.3%) in the form of renal calculi, followed by skeletal involvement in the form of osteoporosis or fractures (35.3%). Two patients had features suggestive of brown tumors on radiology. Among the study subjects, 11.8% had pancreatitis at the time of presentation. Seventy one percent of the study cohort had vitamin D deficiency (<20 ng/mL) at baseline. The median PTH at baseline was 250 pg/mL. The baseline characteristics of the study subjects in high PTH (≥250 pg/mL) and low PTH (<250 pg/mL) groups are shown in Table 1. Following surgery, serum calcium, phosphate and albumin were measured in all subjects. Two patients developed hypocalcemia transiently and 4 patients developed hungry bone syndrome which recovered in 4 weeks following treatment with calcium and calcitriol. Postoperatively, all subjects were continued on 1,000 mg of elemental calcium and 1,000 to 2,000 IU of cholecalciferol daily. Bone mineral biochemistry, BTMs, and DXA parameters (BMD and TBS) at baseline and on follow-up in men and women are shown in Table 2, Table 3, and Table 4, respectively. The findings were not significantly different between premenopausal and postmenopausal women, probably due to the small proportion of postmenopausal women (4/19) in the study. Also, there was no significant difference in findings between men and women and also in subjects with and without vitamin D deficiency at baseline. In both men and women, there was a significant improvement in calcium, phosphate, 25(OH)D, PTH, BTMs, BMD, and TBS over 2 years following surgery.

Impact of Baseline PTH on Serial BMD, TBS and BTMs at Each Follow-Up Visit

The impact of high versus low baseline PTH (<250 vs. >250 pg/mL) on BMD, TBS, bone biochemistry, and BTMs is shown in Table 5. The TBS, BTMs, and BMD at lumbar spine and forearm were significantly worse at baseline in subjects with higher PTH (>250 pg/mL). On follow-up visits at first and second year after curative parathyroid-

Table 1
Demographic Details and Bone Biochemistry

Variable	PTH <250 pg/mL (N = 26)	PTH ≥250 pg/mL (N = 25)	*P* value
Males:females	1:1	3.1:1	NS
Age (years)	45.4 (11.1)	45.5 (13.7)	NS
BMI (kg/m^2)	23.6 (2.9)	25.8 (4.2)	.03
Calcium (mg/dL)	11.5 (1.6)	12.1 (1.3)	NS
Phosphate (mg/dL)	2.6 (0.7)	1.9 (0.6)	.001
25-hydroxyvitamin D (ng/mL)	16.3 (6.3)	15.6 (6.1)	NS
PTH (pg/mL)	163.9 (39.1)	736.6 (491.5)	<.001
Alkaline phosphatase (U/L)	118.5 (45.3)	227.4 (127.3)	<.001
CTX (pg/mL)	1,198 (450)	2,327 (1277)	<.001
P1NP (ng/mL)	170 (146)	410 (308)	.01
Osteocalcin (ng/mL)	62.6 (50.2)	150.8 (101.9)	<.001

Abbreviations: BMI = body mass index; CTX = C-terminal telopeptide of type 1 collagen; P1NP = N-terminal propeptide of type 1 procollagen; PTH = parathyroid hormone.

Table 2
Biochemical Parameters at Baseline and on Follow-Up

Males (N = 32), mean (SD) age = 45.4 (12.1) years, mean (SD) BMI = 24.5 (3.9) kg/m^2

Variable	Baseline mean (SD)	Year 1 mean (SD)	Year 2 mean (SD)	*P* value			
				ANOVA	Paired Student's *t* test		
					Baseline vs. year 1	Baseline vs. year 2	Year 1 vs. year 2
Calcium (mg/dL)	11.9 (0.9)	9.2 (0.7)	9.1 (0.3)	.0001	.0001	.0001	1
Phosphate(mg/dL)	2.1 (0.6)	3.1 (0.5)	3.2 (0.4)	.0001	.0001	.0001	.506
Creatinine(mg/dL)	1.1 (0.2)	0.9 (0.3)	0.9 (0.3)	.083	.6	.7	1
25(OH)D (ng/mL)	15.3 (6.8)	22.5 (8.9)	26.3 (5.7)	.0001	.004	.0001	.010
PTH (pg/mL)	540 (392)	50 (44)	56 (16)	.0001	.001	.001	1

Females (N = 19), mean age (SD) = 45.6 (12.9) years, mean (SD) BMI = 24.8 (3.4) kg/m^2

Variable	Baseline mean (SD)	Year 1 mean (SD)	Year 2 mean (SD)	*P* value			
				ANOVA	Paired Student's *t* test		
					Baseline vs. year 1	Baseline vs. year 2	Year 1 vs. year 2
Calcium (mg/dL)	11.3 (1.7)	9.1 (0.7)	9.5 (0.4)	.0001	.0001	.002	.011
Phosphate(mg/dL)	2.5 (0.6)	3.6 (0.9)	3.7 (0.5)	.0001	.0001	.0001	.801
Creatinine(mg/dL)	0.9 (0.3)	0.9 (0.3)	0.8 (0.2)	.26	1	1	.498
25(OH)D (ng/mL)	18.8 (11.1)	35.3 (13.1)	31 (8.1)	.004	.002	.003	.218
PTH (pg/mL)	446 (178)	50.6 (47)	49 (21)	.0001	.004	.005	.122

Abbreviations: 25(OH)D = 25-hydroxyvitamin D; BMI = body mass index; PTH = parathyroid hormone.

Table 3
Bone Turnover Markers at Baseline and on Follow-Up

Males (N = 32), mean (SD) age = 45.4 (12.1) years, mean (SD) BMI = 24.5 (3.9) kg/m^2							
				***P* value**			
					Paired Student's *t* test		
Variable	**Baseline mean (SD)**	**Year 1 mean (SD)**	**Year 2 mean (SD)**	**ANOVA**	**Baseline vs. year 1**	**Baseline vs. year 2**	**Year 1 vs. year 2**
CTX (pg/mL)	1,944 (763)	654 (254)	437 (107)	.0001	.0001	.0001	.001
Osteocalcin (ng/mL)	122 (54)	41 (28)	53 (37)	.0001	.0001	.0001	.072
P1NP (ng/mL)	323 (176)	111 (62)	137 (72)	.0001	.003	.011	.705
Alkaline phosphatase (U/L)	206 (123)	105 (44)	88 (23)	.0001	.002	.0001	.078
Females (N = 19), mean age (SD) = 45.6 (12.9) years, mean (SD) BMI = 24.8 (3.4) kg/m^2							
				***P* value**			
					Paired Student's *t* test		
Variable	**Baseline mean (SD)**	**Year 1 mean (SD)**	**Year 2 mean (SD)**	**ANOVA**	**Baseline vs. year 1**	**Baseline vs. year 2**	**Year 1 vs. year 2**
CTX (pg/mL)	1,482 (442)	615 (320)	402 (246)	.0001	.010	.003	.009
Osteocalcin (ng/mL)	81 (71)	29 (18)	44 (36)	.002	.019	.031	.2
P1NP (ng/mL)	175 (85)	91 (68)	89 (57)	.041	.054	.07	1
Alkaline phosphatase (U/L)	150 (118)	94 (59)	79 (27)	.006	.059	.077	.507

Abbreviations: BMI = body mass index; CTX = C-terminal telopeptide of type 1 collagen; P1NP = N-terminal propeptide of type 1 procollagen.

Table 4
Bone Mineral Density and TBS at Baseline and on Follow-Up

Males (N = 32), mean (SD) age = 45.4 (12.1) years, mean (SD) BMI = 24.5 (3.9) kg/m^2							
				***P* value**			
					Paired Student's *t* test		
Variable	**Baseline mean (SD)**	**Year 1 mean (SD)**	**Year 2 mean (SD)**	**ANOVA**	**Baseline vs. year 1**	**Baseline vs. year 2**	**Year 1 vs. year 2**
Lumbar spine (g/cm^2)	0.855 (0.152)	0.958 (0.144)	0.966 (0.231)	.002	.0001	.033	1
Femoral neck (g/cm^2)	0.676 (0.112)	0.739 (0.103)	0.770 (0.100)	.0001	.0001	.0001	.0001
Forearm (g/cm^2)	0.604 (0.107)	0.669 (0.096)	0.677 (0.089)	.0001	.0001	.0001	.826
TBS	1.192 (0.146)	1.248 (0.118)	1.272 (0.085)	.0001	.0001	.0001	.044
Females (N = 19), mean age (SD) = 45.6 (12.9) years, mean (SD) BMI = 24.8 (3.4) kg/m^2							
				***P* value**			
					Paired Student's *t* test		
Variable	**Baseline mean (SD)**	**Year 1 mean (SD)**	**Year 2 mean (SD)**	**ANOVA**	**Baseline vs. year 1**	**Baseline vs. year 2**	**Year 1 vs. year 2**
Lumbar spine (g/cm^2)	0.833 (0.137)	0.889 (0.138)	0.937 (0.137)	.0001	.004	.0001	.007
Femoral neck (g/cm^2)	0.654 (0.100)	0.674 (0.091)	0.695 (0.092)	.0001	.061	.005	.016
Forearm (g/cm^2)	0.593 (0.063)	0.639 (0.051)	0.644 (0.055)	.0001	.0001	.001	.921
TBS	1.207 (0.125)	1.272 (0.086)	1.302 (0.988)	.001	.036	.008	.197

Abbreviations: BMI = body mass index; TBS = trabecular bone score.

Table 5
Influence of Low Versus High PTH at Diagnosis on BMD, Bone Biochemistry and BTMs at Baseline and on Follow-Up

Variable	Baseline		*P* (Group 1 vs. Group 2 at baseline)	Year 1		*P* (Group 1 vs. Group 2 at year 1)	Year 2		*P* (Group 1 vs. Group 2 at year 2)
	Group 1[a] N = 26 mean (SD)	Group 2[b] N = 25 mean (SD)		Group 1[a] N = 26 mean (SD)	Group 2[b] N = 25 mean (SD)		Group 1[a] N = 26 Mean (SD)	Group 2[b] N = 25 Mean (SD)	
Femoral neck, g/cm^2	0.699 (0.090)	0.656 (0.128)	.17	0.726 (0.084)	0.743 (0.162)	.63	0.737 (0.075)	0.751 (0.130)	.66
Lumbar spine, g/cm^2	0.894 (0.136)	0.790 (0.132)	.008	0.993 (0.130)	0.919 (0.157)	.73	0.980 (0.140)	0.931 (0.247)	.40
Forearm, g/cm^2	0.648 (0.069)	0.556 (0.106)	.001	0.686 (0.06)	0.616 (0.108)	.006	0.697 (0.041)	0.638 (0.093)	.01
TBS	1.23 (0.16)	1.16 (0.08)	.02	1.27 (0.09)	1.26 (0.12)	.86	1.27 (0.06)	1.31 (0.10)	.13
Calcium, (mg/dL)	11.5 (1.6)	12.1 (1.3)	NS	9.1 (0.8)	9.3 (0.7)	NS	9.4 (0.5)	9.2 (0.4)	NS
Phosphate, (mg/dL)	2.6 (0.7)	1.9 (0.6)	.001	3.4 (0.9)	2.9 (0.7)	.03	3.6 (0.6)	3.2 (0.4)	.008
PTH, (pg/mL)	163.9 (39.1)	736.6 (491.5)	.001	40.7 (32.1)	66.7 (40.5)	.01	52.1 (17.7)	56.5 (18.3)	NS
25(OH)D, (ng/mL)	16.3 (6.3)	15.6 (6.1)	NS	29.1 (12.1)	24.8 (12.2)	NS	28.7 (7.9)	26.2 (7.8)	NS
P1NP, ng/mL	170 (146)	410 (308)	.01	85 (67)	110 (91)	.56	88 (50)	123 (109)	.24
CTX, pg/mL	1,198 (450)	2,327 (1,277)	.001	542 (356)	726 (478)	.12	408 (249)	440 (185)	.62
Osteocalcin, ng/mL	62 (50)	150 (101)	.001	31 (21)	43 (33)	.26	45 (34)	55 (34)	.46
ALP, (U/L)	118 (45)	227 (127)	.001	81 (29)	119 (56)	.01	72 (17)	97 (25)	.01

Abbreviations: 25(OH)D = 25-hydroxyvitamin D; ALP = alkaline phosphatase; BMD = bone mineral density; BTM = bone turnover marker; CTX = C-terminal telopeptide of type 1 collagen; P1NP = N-terminal propeptide of type 1 procollagen; PTH = parathyroid hormone; TBS = trabecular bone score.
[a]Group 1: individuals with baseline PTH <250 pg/mL; [b]Group 2: individuals with baseline PTH ≥250 pg/mL.

ectomy, there was no significant difference in BMD at the femoral neck, lumbar spine, and TBS between the 2 groups stratified by baseline PTH. The forearm BMD remained significantly lower in the group with baseline PTH >250 pg/mL at all 3 time points (baseline, first, and second follow-up visits) as compared to the low PTH group (<250 pg/mL).

Impact of Baseline PTH on Change in BMD, Change in TBS, and Change in BTMs from Initial Presentation to the End of the Follow-Up

The change in BMD at the femoral neck was significantly greater in the high baseline PTH group (>250 pg/mL) as compared to the subjects with baseline PTH <250 pg/mL (0.095 [0.079] vs. 0.038 [0.035] g/cm^2; P = .025). In addition, the decrement in BTMs (CTX, osteocalcin, and alkaline phosphatase) was significantly higher in the group with high baseline PTH as compared to the group with low baseline PTH (change in CTX: –1,886 [1,226.1] vs. –789.9 [629.3] pg/mL; P = .001), change in osteocalcin: –95.8 [92.9] vs. –17.0 [19.9] ng/mL; P = .001, and change in alkaline phosphatase: –130.1 [122.9] vs. –46.9 [21.5] U/L; P = .001). There was no significant difference in the change in TBS, P1NP, or BMD at the lumbar spine and forearm in the above groups.

DISCUSSION

This is the first study from southern India which evaluated the longitudinal changes in BMD, TBS, and BTMs in subjects with symptomatic PHPT following curative parathyroidectomy. In the entire study cohort, the BMD at all 3 sites, TBS, and bone BTMs showed significant improvement over 2 years following curative parathyroidectomy. There was also an increase in BMI on follow-up in both sexes. On comparing various parameters between groups stratified by PTH, it was observed that the BMD at the forearm remained significantly lower in the group with higher PTH at all 3 time points.

PHPT in many parts of India is still an underdiagnosed and symptomatic disease of "bones, stones, abdominal groans, and psychic moans" (7). In this study, most subjects presented in the fifth decade of life and this is comparable to previous Indian studies (3,7,11). PHPT is known to occur more commonly in women. However, the majority of the patients in our study were men, which is probably due to a more health-seeking behavior among them in the Indian society. In our study, we found no difference in clinical presentation and bone mineral parameters between men and women. The gender differences that have been described in patients with PHPT, may vary among different ethnicities (12).

Renal manifestations in the form of renal calculi were the most common mode of presentation followed by skeletal involvement. These results correlate with other studies where renal and bony involvement continue to be the most common manifestations at presentation (13). Pancreatitis as a presenting feature is still reported in Indian literature (8,14). One-tenth of the study subjects presented with acute pancreatitis.

There was a significant increase in BMI in both men and women over 2 years after curative surgery. Thorsen et al (15) noticed that patients with PHPT gained about 4.5 kg of weight over 24 months (62.8 ± 3.3 kg to 67.4 ± 3.8 kg) in a prospective study. However, in another study (16), there was no increase in BMI noted. The increase in BMI in our study subjects probably indicate the improvement in overall health status after successful parathyroid surgery. There was a decline in the PTH and calcium levels and an improvement in serum phosphate on follow-up after surgery in both sexes.

There was a significant progressive improvement in BMD at all sites and TBS which was more pronounced in the first year after surgery. This has been previously reported in several studies (16,17). In a study of 34 subjects following parathyroidectomy, there was no significant increase in BMD at the femoral neck (10). In another study by Tay et al (18), in obese and nonobese subjects following curative parathyroid surgery, significant improvements in BMD at the lumbar spine and femoral neck were observed.

In the present study, subjects with more severe hyperparathyroidism had lower BMD at the lumbar spine and forearm at baseline. On follow-up, this difference persisted only at the distal forearm after 2 years. This is a novel observation, which has not been described before and needs further validation. In patients with PHPT, the cortical bones (forearm) are more affected than the cancellous bones (lumbar spine). The femur being a combination of both cortical and cancellous bone is moderately affected. However after curative surgery, the recovery in the forearm has been noticed to be inferior compared to the femoral neck. The lack of difference in the BMD at the femoral neck at baseline between subjects with and without severe PHPT may be attributed to the small sample size.

TBS is a novel tool that can be applied to DXA images and utilizes gray-level textural analysis, to predict trabecular microarchitecture (19). Studies in cadaveric bones have shown significant correlations between TBS and 3-dimensional trabecular microarchitecture measurements by microcomputed tomography and fracture risk (10). In a study by Silva et al (20), it was shown that TBS had the potential to identify subjects with PHPT and abnormalities in trabecular bone not captured by lumbar spine BMD. TBS has also been shown to be associated with vertebral fractures regardless of BMD, age, BMI, and gender. As compared to BMD, it has better accuracy in detecting vertebral fractures in subjects with PHPT. (21). In our study subjects, there was a significant improvement seen in TBS following surgery. Previous studies have not consistently demonstrated improvement in bone microarchitecture

indices following curative parathyroid surgery (10,13). However, Cusano et al (22), showed significant improvement in bone microarchitecture assessed by high resolution quantitative computed tomography (QCT) following parathyroidectomy.

There was a significant decrease in BTMs including CTX, P1NP, ALP, and osteocalcin during follow-up. A high turnover state seen in PHPT settles after successful parathyroid surgery. A decline in the BTMs can be used as a surrogate marker for improvement in bone health (15). In patients with PHPT, there is an increase in osteoclastic activity which is partially compensated by high osteoblastic activity and this is reflected by high levels of both markers of bone resorption and formation, respectively. After surgery, a transient elevation of serum alkaline phosphatase and osteocalcin up to 2 weeks after surgery is noted due to stimulation of osteoblasts, thereafter a decline is noted on subsequent follow-up. Similarly, markers of bone resorption start declining after surgery due to a decrease in the osteoclastic activity (23,24).

The novel findings from this study suggest that the preoperative level of PTH may be helpful in predicting improvement following curative parathyroidectomy. We report that patients with a higher baseline PTH had a lower forearm BMD at baseline and it remained significantly low at 2 years, as compared to people who had lower PTH. In addition, following curative parathyroidectomy, there was a significant improvement in TBS at 2 years as compared to baseline. Long-term follow-up is needed to ascertain further improvement of TBS and its implications on long term bone health in individuals with PHPT.

The strength of this study is that all subjects were symptomatic at presentation and were followed up for 2 years; and the novel finding was that forearm BMD in the high PTH group remained low even at the end of 2 years, while BMD at other sites were not significantly different. The limitation of this study is that it excluded subjects with multiglandular disease or patients with multiple endocrine neoplasia type 1. Although vertebral fractures are common in PHPT, their prevalence was not assessed by a vertebral fracture assessment. This limitation is duly acknowledged.

CONCLUSION

In conclusion, patients with symptomatic PHPT had a significant improvement in bone mineral parameters 2 years after parathyroidectomy, which was reflected by an increment in the BMD, TBS, and improvement of BTMs. Although forearm BMD showed improvement following surgery, the difference between the high and low PTH group, remained significant even at the end of 2 years.

DISCLOSURE

The authors have no multiplicity of interest to disclose.

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