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Gender differences in bone mineral density in patients with sporadic primary hyperparathyroidism

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Summary

Context: Primary hyperparathyroidism reduces bone mineral density, which increases the risk of fracture.

Objective: To investigate differences in bone mineral density and clinical characteristics after parathyroidectomy between men and women (premenopausal and postmenopausal) with sporadic primary hyperparathyroidism.

Design: This is a retrospective study of adult patients who underwent parathyroidectomy in a tertiary referral center from 1990 to 2013.

Patients: A total of 1529 patients underwent parathyroidectomy during the study period; 80 patients met the inclusion criteria. Of these, 24 were men and 56 were women (10 premenopausal and 46 postmenopausal).

Measurements: Demographics, preoperative and postoperative biochemical analysis, preoperative and postoperative T-scores, preoperative Z-scores, preoperative and postoperative absolute bone mineral density values, and percentage change in bone mineral density from baseline to 12 ± 6 months after parathyroidectomy in the lumbar spine, femoral neck, total hip and distal one-third of the nondominant radius.

Results: Preoperative 24-hour urinary calcium levels were significantly higher in men than in women overall ($P = 0.02$) and postmenopausal women ($P = 0.01$). Men had significantly lower preoperative Z-scores than women overall, premenopausal women and postmenopausal women. Men had greater percentage change of increase in bone mineral density in the femoral neck than did women overall (2.77%; $P = 0.04$) and postmenopausal women (2.98%; $P = 0.03$) 1 year after parathyroidectomy.

Conclusions: From this study, men demonstrated a greater improvement of bone mineral density in the femoral neck from baseline after parathyroidectomy compared with women.

KEYWORDS
bone density, hypercalcemia, osteoporosis, parathyroid glands, parathyroid hormone, parathyroidectomy, primary hyperparathyroidism

1 | INTRODUCTION

Primary hyperparathyroidism (PHPT) is the autonomous over-production of parathormone (PTH) owing to hyperfunction of 1 or more parathyroid glands. It can be caused by a single-gland adenoma, multigland hyperplasia or parathyroid carcinoma.[1,2] PHPT is the third most common endocrine disorder and the most common cause of hypercalcemia in outpatients.[2,3] Its prevalence is about 1 to 4 per 1000 in the United States, and it occurs in about 3 times as many women as men.[2-4] The incidence of PHPT rises with age, peaking in women between 50 and 60 years old.[2] The classic clinical presentation of PHPT is often characterized as "bones, stones, groans, and psychiatric overtones," but since the 1970s, the availability of routine calcium testing and PTH assays has improved the recognition of PHPT and allowed earlier diagnosis with little or no symptoms.[1,2,4] Parathyroidectomy (PTX) remains the only definitive curative treatment for PHPT.[1,5,6] Recent guidelines issued by the American Association of Endocrine Surgeons clearly and objectively define the indications for PTX.[1] Observation and pharmacologic therapy are less clinically effective and less cost-effective than surgical intervention, even in patients with seemingly mild disease.[1]

Primary hyperparathyroidism is a secondary cause of osteoporosis; it causes increased bone turnover, a subsequent reduction in bone mineral density (BMD), and thus a predisposition towards fractures.[7-9] The economic impact of osteoporosis on the health care system is estimated to be $50 billion by the year 2040 in the United States.[10] Men account for one-third of all patients with osteoporotic fractures worldwide and at age 60 have a lifetime fracture risk as high as 29%.[11,12] When a fracture is present, secondary osteoporosis is estimated to occur in up to 60% of men and 30% of women.[11,13-15] Men account for at least one-third of all hip fractures, and the worldwide incidence of hip fracture is estimated to increase by 310% in men vs 240% in women by 2050.[16,17] A 50-year-old man has an estimated 17% chance of experiencing a hip fracture during his lifetime, and this risk rises to 25% by age 60.[10] One year after a hip fracture, only 20% of men return to their pre-fracture level of function.[10] Although the overall prevalence of fragility fractures is higher in women, men are reported to have higher rates of fracture-related mortality after hip fracture from the in-hospital period all the way to 6 months, 1 year, 5 years and 7 years[10,11,16,18-23] These higher rates of mortality in men are thought to be attributable to men's having higher rates of comorbidity than women.[16,24]

Multiple studies have found that surgical intervention for sporadic PHPT (sPHPT) is associated with an increase in postoperative BMD,[2,3,5–8,25-35] but only a few studies have examined gender differences in BMD improvement after PTX.[8,10,25] In this retrospective study, we aimed to determine differences in laboratory data and BMD changes after PTX between men and women (both pre-menopausal [pre-MP] and postmenopausal [post-MP]) with sPHPT. We hypothesized that after surgical intervention, there would be a similar increase in BMD between genders, emphasizing the direct impact of PTX in restoration of bone mineralization in the postoperative period.

2 | PATIENTS AND METHODS

2.1 | Patients

From a prospectively maintained clinical database, the medical records of all adult patients who underwent PTX at The University of Texas MD Anderson Cancer Center from 27 September 1990 to 31 December 2013 were reviewed retrospectively. The population was divided by gender and MP status into 4 study groups: men, all women, pre-MP women and post-MP women. In all patients, diagnosis of PHPT had been made based on serum hypercalcemia and concomitant inappropriately elevated serum PTH levels in the absence of lithium or thiazide therapy. Patients with sPHPT presenting normal serum corrected calcium levels, but elevated serum ionized calcium and/or vitamin D deficiency was also included in the study (by definition not normocalcemic PHPT). PTX had been performed based on the principles set forth in the PTX guidelines.[1] Included patients also had available dual-energy X-ray absorptiometry (DXA) scan results at baseline (within 12 months prior to surgery) and 12 ± 6 months after surgery, with both studies performed at our institution. These strict criteria were chosen to reduce apparatus or operator differences. Exclusion criteria included: (a) prior parathyroid surgery; (b) persistent (hypercalcemia occurring within 6 months postoperatively) or recurrent (hypercalcemia occurring more than 6 months postoperatively) disease after PTX; (c) history of taking any of the following drugs: bisphosphonate, calcitonin, teriparatide, raloxifene, tamoxifen, denosumab, estrogen replacement therapy, oral contraceptive pills, aromatase inhibitors, cinacalcet, thiazide, lithium, testosterone, 5-alpha-reductase inhibitors and/or chronic corticosteroid use; (d) tertiary hyperparathyroidism (glomerular filtration rate [GFR] ≤20 mL/min); (e) bone metastasis; (f) parathyroid carcinoma/atypical adenoma; (g) multiple endocrine neoplasia syndrome; (h) normocalcemic PHPT; (i) differentiated thyroid cancer within 10 years and taking thyroid-stimulating hormone suppression therapy; and (j) thyrotoxicosis. The study was approved by the MD Anderson Institutional Review Board.

2.2 | Biochemical analysis

Total serum calcium levels (normal range, 8.4-10.2 mg/dL), serum albumin levels (normal range, 3.5-4.7 g/dL) and intact serum PTH levels (normal range, 10-65 pg/mL) were determined preoperatively and 6 months postoperatively. Preoperative samples were collected at the time of diagnosis and prior to surgery. Values determined prior to surgical intervention were used because most cases of vitamin D deficiency had already been corrected and overlapped secondary hyperparathyroidism was avoided. Values determined 6 months postoperatively were selected for consistency with the standard timing of postoperative reassessment to confirm cure.

The total serum calcium level was corrected for albumin level using the formula: total serum calcium level (mg/dL) + [(4-serum albumin level [mg/dL]) × 0.8]. Additionally, preoperative creatinine (normal range, 0.6-1.0 mg/dL), GFR (normal range, 90-120 mL/

min/1.73 m²), 25-hydroxy vitamin D (normal range, 20-52 ng/mL) and 24-hour urinary calcium levels (normal rage, 50-150 mg/dL) were gathered.

2.3 | Dual-energy X-ray absorptiometry

Dual-energy X-ray absorptiometry scans were performed using a Discovery DXA system or QDR 4500w densitometer (Hologic, Marlborough, MA). BMD was measured at the lumbar spine (LS; average L1-L4 vertebrae), total hip (TH), femoral neck (FN; average right and left) and distal one-third of the nondominant radius (D 1/3 R). BMD data were obtained as absolute values (g/cm²), as T-scores (number of standard deviations from mean bone mass compared to that of a young-adult reference population) and as Z-scores (number of standard deviations from mean bone mass adjusted for gender and age) at 2 time points: baseline (within 12 months prior to surgery) and 12 ± 6 months after surgery, with all studies performed at our institution.

2.4 | Statistical analysis

Demographic data, laboratory tests results, absolute BMD values (g/cm²), T-scores and Z-scores were collected at 2 different time points: preoperative (baseline) and 1 year after surgical intervention (12 ± 6 months). The following groups were compared: (a) men vs all women, (b) men vs pre-MP women, (c) men vs post-MP women, and (d) pre-MP women vs post-MP women. Differences between groups were analysed using Wilcoxon rank-sum tests for continuous variables and Fisher's exact test for categorical variables.

The percentage change in BMD was calculated from absolute BMD values using the formula ([postoperative BMD - preoperative BMD]/preoperative BMD) × 100 for the LS, FN, TH, and D 1/3 R. Means and standard deviations for each value for all 4 subgroups at each anatomical site were computed. Finally, the mean values were compared between genders using Wilcoxon rank-sum tests. Differences were considered statistically significant at a P value ≤ 0.05. No adjustments for multiple testing were made. All statistical analyses were performed using R version 3.3.3.

3 | RESULTS

Eighty patients met all inclusion criteria and had both preoperative and postoperative DXA scans available for review. This represented 5.2% of the total population of 1529 patients with PHPT who underwent PTX in our institution during the study period. We excluded 1449 of these patients from the study for the reasons noted in Figure 1. Among the 80 included patients, 24 (30%) were men and 56 (70%) were women. Among the women, 10 were pre-MP and 46 were post-MP.

3.1 | Demographic comparisons

The patients' demographic data are shown in Table 1. The age at sPHPT diagnosis and age at PTX were similar in men and all women (P = 0.32 and P = 0.36, respectively). Pre-MP women were significantly younger at diagnosis and PTX than were men (P = 0.0017 and P = 0.0014, respectively), whereas post-MP women were
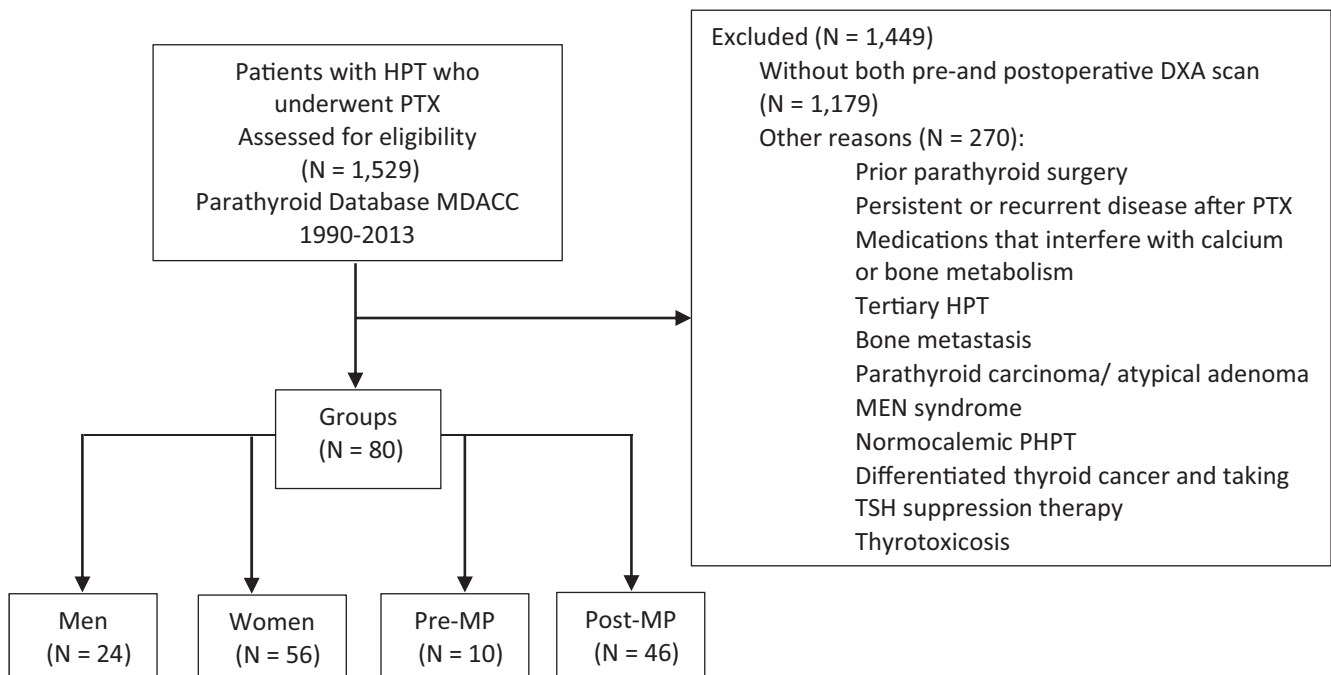
FIGURE 1 Assessed for eligibility. HPT, hyperparathyroidism; N, number of patients; MEN, multiple endocrine neoplasia; PHPT, primary hyperparathyroidism; PTX, parathyroidectomy

TABLE 1 Patient demographics

Variables	Groups	N	Median	Min-Max
Age at diagnosis (y)	Men	24	59.5	34.0-73.0
P men vs women = 0.32	Women	56	62.0	28.0-88.0
P men vs pre-MP = 0.0017*	Pre-MP	10	44.5	28.0-55.0
P men vs post-MP = 0.03*	Post-MP	46	65.5	48.0-88.0
Age at surgery (y)	Men	24	59.5	34.0-73.0
P men vs women = 0.36	Women	56	62.0	28.0-88.0
P men vs pre-MP = 0.0014*	Pre-MP	10	44.5	28.0-55.0
P men vs post-MP = 0.03*	Post-MP	46	65.5	48.0-88.0
Time from diagnosis to surgery (mo)				
P men vs women = 0.13	Men	24	2.5	0.5-23.0
P men vs pre-MP = 0.31	Women	56	4.0	0.5-76.0
P men vs post-MP = 0.04*	Pre-MP	10	2.5	0.5-5.0
P pre-MP vs post-MP = 0.01*	Post-MP	46	4.0	0.5-76.0
BMI (Kg/m²)				
P men vs women = 0.25	Men	24	29.7	22.7-44.4
P men vs pre-MP = 0.50	Women	56	27.5	17.2-52.4
P men vs post-MP = 0.25	Pre-MP	10	28.5	22.3-52.4
P pre-MP vs post-MP = 0.81	Post-MP	46	27.5	17.2-47.3
Time between PTX and MP (y)		46	18	0-43
Women within 5 y after MP		10		

	Normal	Osteopenia	Osteoporosis	N
No. of patients with normal, osteopenic and osteoporotic preoperative *T*-score				
Men	4	14	6	24
Women	12	25	19	56
Pre-MP	5	5	0	10
Post-MP	7	20	19	46
No. of patients with normal, osteopenic and osteoporotic postoperative *T*-score				
Men	7	12	5	24
Women	15	21	20	56
Pre-MP	6	4	0	10
Post-MP	9	17	20	46

MP, Menopause; N, Number of patients; PTX, Parathyroidectomy.
*Statistically significant.

significantly older than men (*P* = 0.03 and *P* = 0.03, respectively). The time from diagnosis to surgical intervention was significantly longer in post-MP women than in men (*P* = 0.04). We found no differences in body mass index or ethnicity (White, Black, Hispanic and Asian) among the 4 study groups.

3.2 | Biochemical measurements

There were no significant differences between the 4 comparison groups in the following preoperative laboratory values: serum calcium, serum corrected calcium, serum intact PTH, 25-hydroxy vitamin D and GFR. However, preoperative serum creatinine and 24-hour urinary calcium levels were significantly higher in men than in

women overall (*P* = 0.0002 and *P* = 0.02, respectively) and post-MP women (*P* < 0.0001 and *P* = 0.01, respectively). Biochemical assessments at 6 months post-PTX showed significant differences only in corrected serum calcium levels, which were lower in men than women overall (*P* = 0.01) and post-MP women (*P* = 0.01). No differences were found in the laboratory values of pre-MP and post-MP women (Table 2).

3.3 | Preoperative Z-scores

The preoperative *Z*-scores are shown in Figure 2. Men had marginally lower preoperative *Z*-scores than women at the LS (*P* = 0.06). The FN *Z*-score was lower in men than in women overall (*P* = 0.0018),

TABLE 2 Biochemical measurements

Variables	Groups	N	Median	Min-Max	NA
Corrected serum calcium pre-op (normal range 8.4-10.2 mg/dL)					
P men vs women = 0.69	Men	16	10.4	9.9-12.4	8
P men vs pre-MP = 0.25	Women	33	10.5	9.5-13.0	23
P men vs post-MP = 0.90	Pre-MP	5	10.8	10.2-13.0	5
P pre-MP vs post-MP = 0.21	Post-MP	28	10.5	9.5-11.3	18
Corrected serum calcium post-op (normal range 8.4-10.2 mg/dL)					
P men vs women = 0.01*	Men	8	9.0	8.6-9.2	16
P men vs pre-MP = 0.22	Women	13	9.2	8.8-9.7	43
P men vs post-MP = 0.01*	Pre-MP	3	9.4	8.8-9.5	7
P pre-MP vs post-MP = 0.93	Post-MP	10	9.2	8.9-9.7	36
Serum PTH pre-op (normal range 10-65 pg/mL)					
P men vs women = 0.73	Men	24	106.0	56.0-586.0	0
P men vs pre-MP = 0.50	Women	56	104.0	48.0-232.0	0
P men vs post-MP = 0.86	Pre-MP	10	97.5	50.0-232.0	10
P pre-MP vs post-MP = 0.48	Post-MP	46	104.5	48.0-231.0	0
Serum PTH post-op (normal range 10-65 pg/mL)					
P men vs women = 0.56	Men	20	37.0	10.0-92.0	4
P men vs pre-MP = 0.43	Women	45	38.0	15.0-130.0	11
P men vs post-MP = 0.30	Pre-MP	10	33.0	15.0-57.0	0
P pre-MP vs post-MP = 0.06	Post-MP	35	42.0	18.0-130.0	11
Serum 25-OH Vit D pre-op (normal range 20-52 ng/mL)					
P men vs women = 0.10	Men	24	25.5	9.0-68.0	0
P men vs pre-MP = 0.26	Women	53	34.0	7.0-90.0	3
P men vs post-MP = 0.12	Pre-MP	10	34.5	15.0-90.0	0
P pre-MP vs post-MP = 0.90	Post-MP	43	34.0	7.0-57.0	3
Urinary calcium pre-op (normal range 50-150 mg/dL)					
P men vs women = 0.02*	Men	17	351.0	165.0-770.4	7
P men vs pre-MP = 0.35	Women	43	270.0	100.0-840.0	13
P men vs post-MP = 0.01*	Pre-MP	9	322.0	225.0-840.0	1
P pre-MP vs post-MP = 0.12	Post-MP	34	252.5	100.0-686.0	12
Serum creatinine pre-op (normal range 0.6-1.0 mg/dL)					
P men vs women = 0.0002*	Men	24	1.1	0.7-1.5	0
P men vs pre-MP = 0.20	Women	55	0.8	0.5-1.9	1
P men vs post-MP = <0.0001*	Pre-MP	10	1.0	0.6-1.3	0
P pre-MP vs post-MP = 0.22	Post-MP	45	0.8	0.5-1.9	1
GFR pre-op (normal range 90-120 mL/min/1.73 m²)					
P men vs women = 0.98	Men	21	73.0	48.0-122.0	3
P men vs pre-MP = 0.90	Women	55	74.0	32.0-121.0	1
P men vs post-MP = 0.99	Pre-MP	10	76.0	45.0-102.0	0
P pre-MP vs post-MP = 0.90	Post-MP	45	74.0	32.0-121.0	1

N, Number of patients; NA, Number of missing entries.
*Statistically significant.

pre-MP women ($P = 0.05$) and post-MP women ($P = 0.0023$). Men also had significantly lower preoperative Z-scores at the TH and D 1/3 R than did women overall ($P = 0.05$ and $P = 0.02$, respectively) and post-MP women ($P = 0.04$ and $P = 0.02$, respectively). The preoperative Z-scores between pre-MP women and post-MP women did not differ.
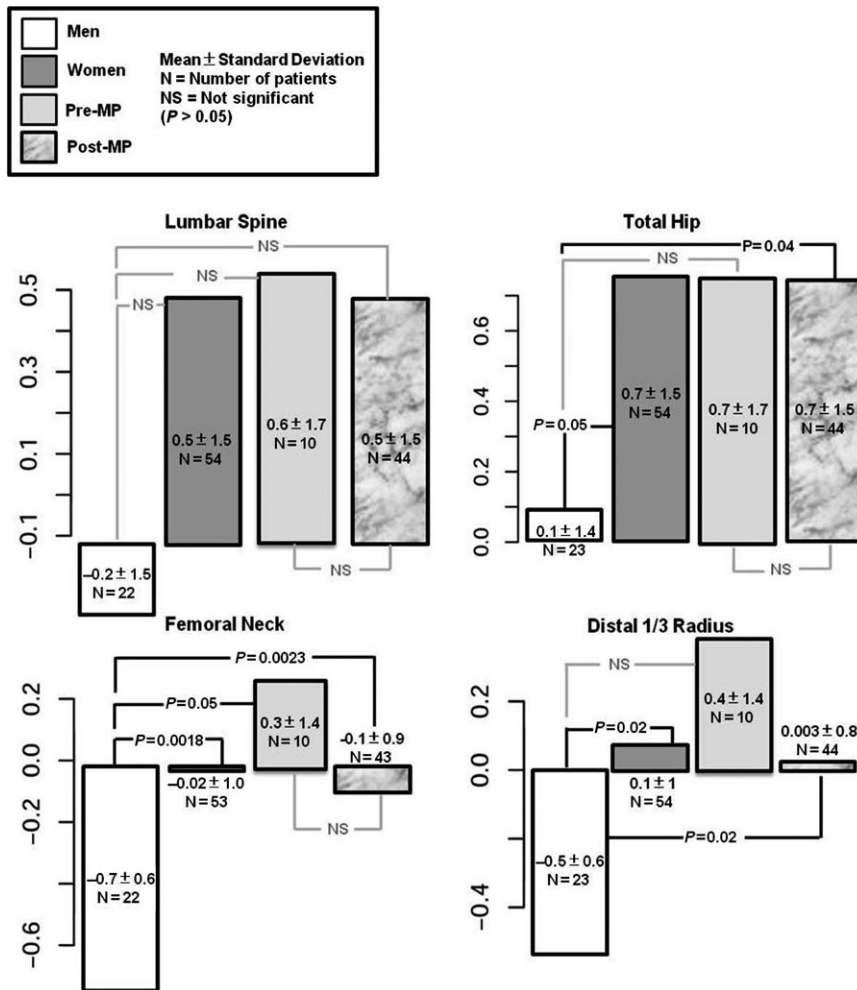
FIGURE 2 Preoperative Z-scores
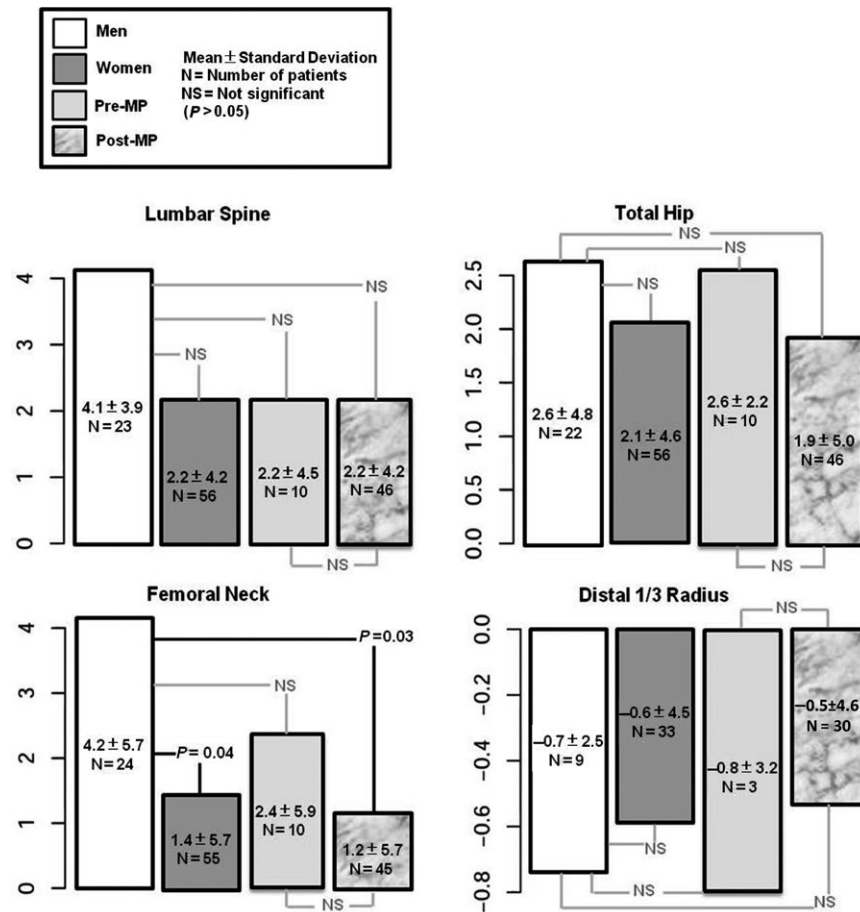
3.4 | BMD change after parathyroidectomy

The percentages of change in BMD from baseline to 12 ± 6 months after PTX are shown in Figure 3. At all sites except for the D 1/3 R, men demonstrated a larger percentage increase in BMD values than women overall, pre-MP women and post-MP women 1 year after PTX. This difference was found to be statistically significant in the FN, where men had 2.77% and 2.98% greater improvement in BMD than did women overall (P = 0.04) and post-MP women (P = 0.03), respectively. The percentage of change in BMD did not differ between pre-MP and post-MP women.

4 | DISCUSSION

The current study reveals that men have greater bone mineral density increase after PTX than women and that this increase cannot be attributed to hormonal variations between genders, as gains in BMD after PTX did not significantly differ between the pre-MP and post-MP women. Significant bone recovery in men should be regarded as a potential benefit of surgical cure of PHPT in a population that is usually considered less susceptible to clinically significant bone loss.

Multiple studies have reported increases in BMD after PTX,[2,3,5-8,10,25-35] but only 3 have categorized results by gender while focusing on bone disease[8,10,25] Of these three, Sharma et al[8] and Ballem et al[10] found a greater post-PTX improvement in BMD in men than in women, while Dy et al[25] determined that the extent of bone recovery after PTX was not affected by gender or menopausal status. The use of bisphosphonate, longer time for postoperative DXA scan (within 3 years of surgical intervention), and exclusive analysis at the most affected anatomical site were unique characteristics to the study by Dy et al[25] that differed from our study which might explain the different results. There are other publications that evaluated gender differences, but focused on clinical presentation[2,36] or incidence of disease[37] which were not the purpose of our study.

In our cohort, men had lower preoperative Z-scores than did women at all 4 anatomical sites, suggesting that men were more affected by bone disease before PTX. This difference could be attributable to a delay in seeking medical care or in diagnosis. It is thought that women see primary care providers more often than men.[37] Therefore, PHPT may be underdiagnosed in men. Unfortunately, we cannot currently estimate the magnitude of such an effect, if any exists. Ballem et al[10] found that bone disease in PHPT is underappreciated, underdiagnosed and consequently undertreated in men. They determined that as DXA screening in men with PHPT became more

FIGURE 3 Percent bone mineral density change 1-y after parathyroidectomy

common, rates of bone disease detection rose to levels approaching those of women. Ballem et al[10] also found that women had significantly higher rates of follow-up BMD screening than men ($P < 0.001$) and that men were 4 times less likely than women to continue experiencing bone loss after PTX.

The greater bone density increase observed in men after PTX cannot be attributed to variations in estrogen levels. We found no difference in the percentage of change in BMD values after PTX in pre-MP and post-MP women, suggesting that differences in estrogen levels do not explain the observed patterns of BMD recovery after PTX. Increased body mass index (BMI) can lead to higher estrogen levels in both men and women. As our study groups had similar BMIs (between men, all women, pre-MP and post-MP), there was no additional reason for the lower preoperative Z-scores appreciated in men, or the greater increases of BMD after PTX noticed in men. Taken together, studies suggest that PTX itself has a direct impact on the restoration of bone mineralization. Moreover, the beneficial effect of PTX in pre-MP women with reduced BMD indicates that surgical cure of PHPT has an additive effect on BMD even when abundant estrogen is present.[25] Patterns of degeneration of the cancellous bone vary according to gender. In women, rapid accelerated bone loss takes place 5 years after menopause, which then slows but continues throughout the postmenopausal years. In men, cancellous

bone loss occurs gradually and much later in life, especially after the age of 70 years.[38] Statistical analysis was run again after removing the 10 women that underwent PTX within 5 years after menopause to ensure that the greater BMD increase appreciated in men was not caused by the presence of these specific women population. New analysis showed no change compared to prior results (data not shown).

Androgens help to form the skeleton of young men and prevent bone loss in elderly men. As bioavailable testosterone levels decrease later in life, the incidence of osteoporotic fractures in men increases exponentially. Both androgens and estrogen enhance bone formation by stimulating proliferation of preosteoblasts and differentiation of osteoblasts to enhance bone formation, but only estrogen acts in suppressing bone resorption. This is when aromatization of testosterone to estradiol becomes crucial for bone health in men.[38] Interestingly, Almqvist et al[39] found that higher free testosterone levels after PTX are associated with higher hip and lumbar spine BMD in post-MP women. The authors suggested that PHPT causes relative androgen deficiency mediated by an increase in circulating sex hormone binding globulin.

Given that the kidneys are susceptible to end organ damage in patients with PHPT, we assessed renal-related differences among our patient groups. Preoperative 24-hour urinary calcium excretion levels

were higher in men than in women, including post-MP women. Ballem et al[10] and Mazeh et al[2] documented similar results, with preoperative 24-hour urinary calcium levels being higher in men. Interestingly, both of these studies, which focused on gender differences in clinical presentation, noted that nephrolithiasis was more frequent in men than in women. These findings are compatible with rates found in the general population, in which the incidence and prevalence of nephrolithiasis are between 2 and 4 times higher in men than in women.[2,36] This difference is also observed in patients with PHPT, and it may be increased in the setting of hypercalciuria. Dy et al[25] noted that preoperative urinary calcium levels were higher in patients who experienced significant improvement after PTX. We suggest that the excess urinary calcium in these patients comes primarily from the bone, causing more severe bone disease but, as supported by Dy et al,[25] leads to greater improvements in BMD after PTX.

We attribute the better BMD recovery in men to their more severe bone disease at presentation (lower preoperative Z-scores) and higher preoperative urinary calcium levels than women; and thus, our data support previous suggestion by Sharma et al[8] and Dy et al[25] that more advanced bone loss and higher urinary calcium excretion create a greater opportunity for improved BMD after PTX.

Our study was unique in several respects. First, we divided the population of women by MP status. Second, we used preoperative Z-scores instead of T-scores to avoid age bias. Third, all patients in our study cohort were free of medications that interfere with calcium and/or bone metabolism. Finally, all patients' preoperative and postoperative DXA scans were performed at our institution, reducing the effect of apparatus or operator differences. Our work has the limitations expected of a retrospective study. Despite the large initial cohort, only 80 patients met our inclusion criteria, which were made strict in an effort to minimize the number of confounders. Unfortunately, the use of such stringent inclusion criteria, along with the single-institution study design, may have introduced selection bias. In addition, the statistical power to detect differences among subgroups is reduced in a small sample. Another limitation of this study is that complete laboratory analyses were not available for all patients. In addition, data on other factors that affect bone metabolism, such as physical activity, diet, smoking history and alcohol intake history, were not assessed. In light of these limitations, further studies are needed, including a multicentre prospective study comparing BMD gender differences in BMD using the Fracture Risk Assessment Tool (FRAX-score), which was not utilized in this study. It is an interesting point to consider that the FRAX risk for men in our study could have potentially been lower than that of women despite the lower preoperative Z-scores noted in men.

Because the decision to undergo PTX is ultimately made by the patient, physicians have the responsibility to deliver the most complete information to patients. Although some patients may not be concerned by hypercalcemia, the risk of sustaining a spontaneous hip fracture is likely to cause concern. Patients with PHPT should be informed about the benefit of PTX in improving bone density, as evidenced in the present study. DXA screening is crucial for identifying patients who need additional treatment for their bone disease (eg bisphosphonate, denosumab) even after undergoing PTX. Furthermore, for those asymptomatic patients a documented BMD improvement could encourage routine follow-up medical evaluation.

In conclusion, our study showed that men had a greater significant BMD increase at the femoral neck compared with women after PTX. Beyond treatment of hypercalcemia and reduction of nephrolithiasis incidence, this amount of improved BMD could translate to reduction of risk for fracture in the male population.

CONFLICT OF INTERESTS

The author reports no conflict of interests in this work.

AUTHOR CONTRIBUTION

Danica M. Vodopivec: Conception and design; development of methodology; acquisition of data, analysis and interpretation of data; writing, review and/or revision of manuscript; administrative, technical or material support (ie reporting or organizing data, constructing databases). Angelica M. Silva: Development of methodology; acquisition of data, analysis and interpretation of data; review and/or revision of manuscript; administrative, technical or material support (ie reporting or organizing data, constructing databases). Dinamarie C. Garcia-Banigan: Development of methodology; analysis and interpretation of data; review and/or revision of manuscript; study supervision. Ioannis Christakis: Acquisition of data, analysis and interpretation of data; review and/or revision of manuscript; administrative, technical or material support (ie reporting or organizing data, constructing databases). Ashley Stewart: Acquisition of data, analysis and interpretation of data; review and/or revision of manuscript; administrative, technical or material support (ie reporting or organizing data, constructing databases). Kelly Schwarz: Acquisition of data; administrative, technical or material support (ie reporting or organizing data, constructing databases). Caroline S. Hussey: Acquisition of data; administrative, technical or material support (ie reporting or organizing data, constructing databases). Roland Bassett: Statistical analysis, biostatistics, computational analysis, analysis and interpretation of data. Mimi I. Hu: Conception and design; development of methodology; analysis and interpretation of data; review and/or revision of manuscript; study supervision. Nancy D. Perrier: Conception and design; development of methodology; analysis and interpretation of data; review and/or revision of manuscript; study supervision.

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