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The effect of total thyroidectomy on the recovery of bone mineral density in subjects with hyperthyroidism ☆

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ABSTRACT

Background: Although hyperthyroidism is associated with high turnover osteopenia and its recovery after treatment, the extent of recovery with different forms of therapy remains controversial. This prospective study evaluated the bone mineral density in thyrotoxic subjects undergoing total thyroidectomy and ^{131}I radioactive iodine therapy.

Methods: Newly diagnosed subjects with hyperthyroidism undergoing total thyroidectomy (group 1; $n = 127$) and ^{131}I radioactive iodine therapy (group 2; $n = 30$) were evaluated for bone mineral density by dual energy x-ray absorptiometry at the time of diagnosis (point A), on achieving euthyroidism with antithyroid drugs (point B), and 6 months after definitive treatment (point C).

Results: In group 1, bone mineral density (expressed as g/sq cm; mean ± standard deviation) in the hip (0.842 ± 0.157) and spine (0.97 ± 0.155) at point A, improved at point B (hip, 0.853 ± 0.157 and spine, 0.982 ± 0.155), and further improved at point C (hip, 0.91 ± 0.158 and spine, 1.053 ± 0.161, each $P <$ .001). In group 2, at point C, bone mineral density in the hip (0.761 ± 0.168 versus point A, 0.741 ± 0.146) and spine (0.831 ± 0.159 versus point A, 0.823 ± 0.158) were less than group 1 (each $P <$ .01).

Conclusion: Bone mineral density improved significantly after all forms of treatment of hyperthyroidism and was greatest in lumbar vertebrae (8.6%) as early as 6 months after total thyroidectomy. The delayed recovery of bone mineral density after ^{131}I radioactive iodine therapy needs long-term evaluation.

Introduction

Hyperthyroidism is a well-known cause of accelerated bone turnover resulting in decreased bone mineral density (BMD), osteoporosis, and increased risk of fracture.[1–3] Several studies have shown that treatment of thyrotoxicosis is associated with recovery of BMD and decreased risk of fracture.[1,4–6] The most common cause of hyperthyroidism is Graves' disease, followed by toxic multinodular goiter. The treatment options for both these disorders include antithyroid drugs (ATDs), ^{131}I Radioactive iodine (RAI) therapy, and operative management with near total or total thyroidectomy (TT).[7] Although treatment is associated with the improvement of BMD, the differences in the degree of recovery of BMD at different skeletal sites (trabecular versus cortical) with different forms of treatment of hyperthyroidism remains unclear. Some studies have shown failure of complete recovery of BMD loss associated with hyperthyroidism and persistence of osteopenia even beyond 1 to 4 years of treatment with either ATDs or RAI therapy, especially in postmenopausal women.[1,8,9] In contrast, complete recovery of BMD has been reported when remission is achieved after operative management of hyperthyroidism with subtotal thyroidectomy in premenopausal women.[10] Consistent with this ob-

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servation, we demonstrated previously decreased BMD at all three sites, namely hip, spine, and forearm in 40 subjects with untreated hyperthyroidism and rapid restoration of BMD as early as 6 months after operative management with TT.[11] There is paucity of data, however, with regard to the differences in the extent of recovery of BMD in subjects with hyperthyroidism after RAI therapy versus those undergoing TT.

In this study, we aimed to evaluate the effect of TT versus RAI therapy on the recovery of BMD in the hip and spine using dual energy x-ray absorptiometry (DEXA) in subjects with hyperthyroidism.

Materials and Methods

Newly diagnosed patients with overt hyperthyroidism ($n = 159$) admitted in the unit of Endocrine Surgery, Department of General Surgery, Government Mohan Kumaramangalam Medical College Hospital and SKS Hospital (both in Salem, India) from September 2014 to August 2017 were enrolled in this study. Institutional ethical clearance and informed consent were obtained.

All the subjects had a thorough physical examination and blood investigation with a complete hemogram, thyroid profile, and liver and renal function. Serum levels of 25-hydroxy vitamin D (reference for deficiency < 25 nmol/L; insufficiency 25–75 nmol/L; sufficiency, 75–175 nmol/L; toxic > 250 nmol/L), alkaline phosphatase (32–90 IU/L), and corrected calcium (reference range: 2.12–2.62 mmol/L) were measured serially. Diagnosis of hyperthyroidism was based on the increased levels of total triiodothyronine, free tetraiodothyronine [reference range: 0.79–2.2 ng/dl], and suppressed thyroid stimulating hormone (TSH) [reference range 0.3–5.5 mIU/L]. The etiology of hyperthyroidism was based on the clinical manifestation of Graves' disease, increased levels of thyroid autoantibody, increased radiotracer activity of the thyroid gland in ^{99m}Technetium pertechnetate thyroid scintigraphy, and final histopathology.

Patients with medical causes of low BMD, such as long-term steroid therapy, immunosuppressive therapy, malignancy, chronic liver and kidney diseases, and primary hyperparathyroidism, were excluded. Subjects aged > 70 years, smokers, alcoholics, and patients on antiresorptive agents were also excluded.

Group 1 subjects (Surgery - Total Thyroidectomy)

Group 1 included subjects with hyperthyroidism with one or more of the following indications for TT: large-volume goiter, pressure symptoms, Graves' ophthalmopathy, presence of cardiovascular dysfunctions, ultrasonography/cytology suspicious for malignancy, patients planning for pregnancy, noncompliance to antithyroid drugs, patient preference for TT, and logistic reasons. These subjects were treated with the antithyroid drug carbimazole (10-60 mg/day) with or without beta adrenergic blockers (propranolol 40– 160 mg/day in 3 divided doses) and dosage titrated with thyroid profile every 4 to 6 weeks.

On achieving euthyroidism, TT was the procedure of choice by institutional protocol and was performed by the same members of the surgical team with uniform techniques. Postoperatively, a replacement dose of levothyroxine was administered.

Group 2 subjects (RAI)

Subjects with hyperthyroidism who preferred RAI therapy were included in group 2. Pregnancy, lactation, and moderate to severe Graves' orbitopathy were contraindications. The β-adrenergic blocking agent propranolol (40–160 mg/day in 3 divided doses) was given for amelioration of symptoms. An empiric fixed dose of ^{131}I radioactive iodine therapy of (15 mCi) was administered. A few subjects received ATD, carbimazole (10–60 mg/day) tailored to clinical needs, which was withdrawn on achieving euthyroidism or hypothyroidism, and an appropriate dose of levothyroxine was started.

Hypovitaminosis D in both groups was treated with an oral dose of cholecalciferol 60,000 IU weekly for 8 weeks or until sufficiency.

Densitometry

BMD measures the bone mass adjusted for the projected area of the region scanned but not its depth and is expressed in gram per square centimeter (g/cm^2). BMD was determined by DEXA with the bone densitometer model, Discovery Wi, v 4.0.2 (HOLOGIC Inc, Bedford, MA, USA). The instrument was equilibrated against a phantom daily, according to the manufacturer's instructions. The regions of interest were measured as per the manufacturer's specification. The BMD spine measured the bone density in the lumbar vertebrae L1–L4; the BMD hip was measured at the neck, trochanter, and Ward's triangle of femur on both the sides. The BMD was determined at the time of diagnosis of hyperthyroidism (point A), on achieving euthyroidism with antithyroid drugs (point B), and 6 months after definitive treatment (point C) by either TT or RAI therapy as per the case. In group 2, BMD was not determined at point B because RAI was administered early in the course of the disease, and only 4 subjects received ATDs before RAI therapy. The absolute value of BMD was used to assess the percent change in BMD at different time points.

Statistical analysis

Data were expressed as mean ± standard deviation. Statistics were analyzed with SPSS software v 20.0 (IBM Corp, Armonk, NY, USA). Independent *t* tests, Pearson tests, and Spearman tests of correlation were used where appropriate. A two-way repeated measures ANOVA, using the general linear model with a Bonferroni method, compared the mean difference between the groups and within the group at multiple time points. A P value < .05 was considered statistically significant.

Results

We studied a total of 159 subjects, including 63 men and 96 women with mean age of 39 ± 11 years. The clinicopathologic data of the 2 groups are included in Table 1. Group 1 (TT) consisted of 129 subjects (M:F, 59:70; age, mean ± SD, 37 ± 10 years; median, 35; mode, 27; range, 22–61 years) who underwent TT after antithyroid medication for a mean duration of 3.2 ± 1.1 month. On histopathologic examination, group 1 (TT) comprised 88 patients with Graves' disease, 39 with toxic nodular goiter, and 2 with papillary thyroid carcinoma. These 2 cases of incidental papillary thyroid carcinoma, including 1 male and 1 female, required ^{131}I RAI ablation of the remnant, followed by TSH suppressive therapy, and therefore were excluded from the study. Preoperatively, 9% of patients ($n = 12$) and postoperatively, 36% patients ($n = 46$) had symptomatic transient hypocalcemia and received oral calcium carbonate (0.5 to 2 g/day) for a mean of 21 ± 4 days. Group 2 (RAI) included 30 subjects ($n = 30$; M:F, 58:69; age, 46 ± 15 years; median, 52; mode, 56; range, 15–65 years) who received RAI therapy; none of them required a second dose of RAI therapy either for persistence of hyperthyroidism or relapse. At 6 months post-RAI therapy, 22 subjects (73%) developed hypothyroidism and were given appropriate doses of levothyroxine to maintain euthyroid state; 17% ($n = 5$; M:F = 1:4) who had hypocalcemia received calcium supplements.

Table 1
Clinicopathologic features of group 1 and 2 subjects.

Parameters	Group 1 (surgery) ($n = 127$)	Group 2 (RAI) ($n = 30$)	P value
Age (years)	37.08 ± 9.8	45.47 ± 14.8	.006
Sex M:F	58: 69	4: 26	.001
Weight (kg)	52.17 ± 2.3	60.7 ± 11.4	< .001
Duration of hyperthyroidism (months)	7.4 ± 5.7	5.63 ± 2.1	.099
Free tetraiodothyronine ng/dl	5.22 ± 2.3	4.9 ± 2.05	< .001
Thyroid stimulating hormone mIU/L	0.010 ± 0.017	0.025 ± 0.035	.033
Serum calcium mmol/L	2.28 ± 0.15	2.29 ± 0.18	.910
Serum 25-hydroxy vitamin D nmol/L	60.75 ± 26	54.2 ± 22	.207
Serum alkaline phosphatase IU/L	142.8 ± 70.8	141.96 ± 62.8	.947

Table 2
Bone mineral density (BMD) in group 1 (surgery) at multiple time points.

Bone mineral density	Point A	Point B	Point C	P value		
				A versus B	B versus C	A versus C
BMD Hip in g/sq cm	0.842 ± 0.157	0.853 ± 0.157	0.910 ± 0.158	< .001	< .001	< .001
BMD spine in g/sq cm	0.970 ± 0.155	0.982 ± 0.155	1.052 ± 0.162	< .001	< .001	< .001

Point A–At the time of diagnosis of hyperthyroidism.
Point B–At the time of achieving euthyroid state with antithyroid drugs.
Point C–At 6 months after definitive treatment either TT or RAI therapy in groups 1 and 2, respectively.

Table 3
Bone mineral density (BMD) in group 2 (RAI) before and 6 months after RAI therapy.

Parameter	Point A	Point C	P value
BMD hip in g/sq cm	0.741 ± 0.146	0.761 ± 0.168	.008
BMD spine in g/sq cm	0.823 ± 0.159	0.831 ± 0.159	.001

Point A–At the time of diagnosis of hyperthyroidism.
Point C–At 6 months after RAI therapy.

In group 1 (TT), the BMD in the hip and spine were 0.842 ± 0.157 g/cm^2 and 0.97 ± 0.155 g/cm^2, respectively at point A. At point B, BMD in the hip (0.85 ± 0.16 g/cm^2) and spine (0.98 ± 0.16 g/cm^2) improved and further improved at point C (hip, 0.91 ± 0.16 g/cm^2 and spine, 1.05 ± 0.16 g/cm^2, each $P < .001$). In group 2 (RAI), BMD at point A were 0.74 ± 0.15 g/cm^2 (versus point C, 0.76 ± 0.17 g/cm^2, $P = .008$) in the hip and 0.82 ± 0.16 g/cm^2 (versus point C, 0.83 ± 0.16 g/cm^2, $P = .001$) in the spine, respectively. At point C, BMD in the hip and spine was greater in group 1 than in group 2 subjects (each $P < .001$). The improvement in the BMD at different time points during treatment of hyperthyroidism in group 1 and 2 are presented in Tables 2 and 3, respectively. At point C, the percent increment in the BMD hip was 8.4% after TT versus 2.3% post-RAI and was 8.6% post-TT versus 0.9% post-RAI therapy in the spine. The differences in age and sex were statistically significant between the two groups, based on an independent t test. Moreover, the study design was unbalanced with unequal numbers in each arm (ie, 127 subjects) in group 1 (TT) versus 30 subjects in group 2 (RAI). Therefore, the general linear model was used to correct the unbalanced study design. Also, age and sex adjustments were included in this model. The results are tabulated in Table 4. The two-way repeated measures ANOVA with a Greenhouse-Geisser correction revealed that the mean BMD in the hip and spine increased from point A to point C in both groups (each $P < .001$) and more pronounced in group 1 (TT), as shown in Figs 1 and 2. Post hoc tests, using the Bonferroni correction, revealed that the two groups were different ($P < .001$). The use of a two-way or two-factor repeated measures ANOVA was useful when we measured a dependent variable (BMD in our study) over two or more time points, or when subjects had undergone two or more conditions (ie, TT versus RAI therapy). The two factors are "time" and "conditions." Thus, we can conclude that TT elicited a greater increment in BMD than in RAI therapy as early as 6 months after definitive treatment of hyperthyroidism, both in the hip and spine.

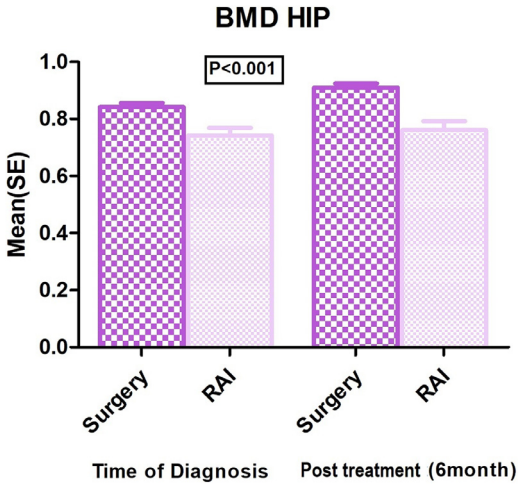

Fig 1. The mean bone mineral density (expressed as g/sq cm) in the hip increased significantly after treatment of hyperthyroidism with surgery compared with RAI therapy.

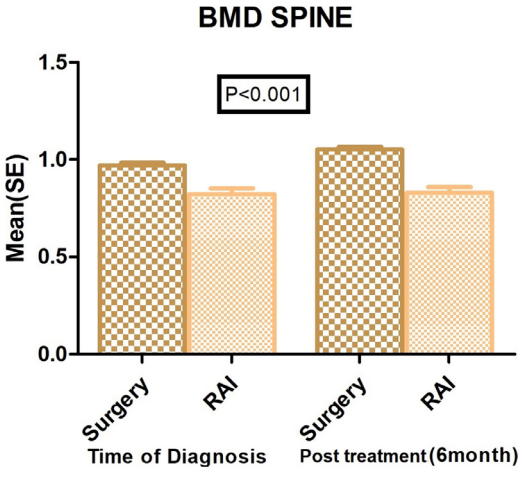

Fig 2. The increase in mean bone mineral density ([BMD] expressed as g/sq cm) in the spine from the time of diagnosis of hyperthyroidism to 6 months posttreatment was higher in subjects undergoing surgery compared with RAI therapy.

Table 4
The two-way repeated measures ANOVA*.

Parameters	Time points	Group 1 (surgery) ($n = 30$)	Group 2 (RAI) ($n = 30$)	P value
BMD hip in g/sq cm	Point A	0.875 ± 0.146	0.741 ± 0.146	< .001
BMD hip in g/sq cm	Point C	0.941 ± 0.140	0.761 ± 0.168	< .001
BMD spine in g/sq cm	Point A	1.011 ± 0.165	0.823 ± 0.158	< .001
BMD spine in g/sq cm	Point C	1.094 ± 0.167	0.830 ± 0.159	< .001

Point A–At the time of diagnosis.
Point C–At 6 months after definitive treatment for hyperthyroidism.
* Using the general linear model. The Bonferroni method measured the dependent variable bone mineral density (BMD) between groups 1 and 2 over 2 time points

Age correlated inversely with BMD in the hip (r = –0.459, $P = .001$) and spine (r = –0.497, $P = .001$). TSH (r = 0.238; $P = .002$) and weight of the patient (r = –0.32; P=0.001) correlated with preoperative BMD. Sex, duration of hyperthyroidism, and 25-OH vitamin D levels did not correlate with BMD.

Discussion

The present study demonstrated that the BMD was decreased in subjects with untreated hyperthyroidism and all forms of treatment, including ATDs, RAI therapy, and TT, were associated with significant recovery of BMD in the hip and spine. The extent of recovery of BMD was greater after operative treatment with TT compared with RAI therapy for hyperthyroidism. At 6 months after TT, the percent increment of BMD was greatest in the lumbar vertebrae at 8.6%, followed by the femur at 8.4%. This improvement is consistent with our previous report,[11] which demonstrated the greatest recovery of BMD in the lumbar vertebrae (8.3%), followed by hip (7.6%) and forearm (3%) in subjects with overt hyperthyroidism within 6 months after TT. In contrast, group 2 subjects at 6 months post-RAI therapy displayed smaller increases in the BMD at the hip (2.3%) and a marginal increment of 0.9% in the lumbar vertebrae. Vestergaard et al[9] and others [3,12–14] had demonstrated persistence of an increased risk of fracture in subjects who received RAI therapy alone for hyperthyroidism, which agrees with our observation; however, there is a paucity of evidence regarding improvement of BMD after RAI therapy among Indian subjects with hyperthyroidism. In the present study, there was a greater incidence of thyroid dysfunction after RAI therapy and 77% developed subsequent hypothyroidism. Evidence supports a temporal decrease in BMD in hypothyroidism,[3] and a lag time of 5 years or more is required for return of normal bone turnover and full restoration of BMD.

The rapid and near complete recovery of BMD after TT may be explained by the fact that complete remission is achieved within a few days after surgery. With the return of the euthyroid milieu, normal bone turnover resumes, and bone remodeling space expands with subsequent increases in BMD to normal levels. In contrast, remission is delayed by several months after RAI therapy. The release of preformed thyroid hormone after RAI therapy from the damaged thyroid follicles for a variable duration of time results in the persistence of the thyrotoxic milieu, and subsequently hypothyroidism. In addition, calcium and vitamin D supplementation in 36.2% of group 1 subjects postoperatively may be a reason for improved BMD.

The lumbar vertebra, being a trabecular bone, has a greater activation frequency and a larger number of bone remodeling units and, therefore, reflects the changes in the bone turnover.[15] This could be a plausible explanation for the observed differences between the groups (ie, rapid and full restoration of lumbar BMD after TT and a smaller increment post-RAI therapy).

Mosekilde et al[12] and others[3] showed that hyperthyroidism aggravated age-related bone loss. The decrease in BMD with increasing age may be attributed to the irreversible bone loss attributable to a net negative bone balance per remodeling cycle in elderly subjects with smaller anabolic reserve (estrogen and, perhaps, growth hormone). Thus, inclusion of older subjects, especially postmenopausal women, could have contributed to the lesser BMD values observed in group 2 at all the time points compared with group 1, which comprised young men and premenopausal women. In support of this observation, many investigators[16,17] have reported greater bone loss with advancing age in postmenopausal women than in premenopausal women.

Our study has some limitations. Our study design was unbalanced, with unequal numbers in each arm. Wide availability of surgical expertise (free of cost in government health schemes), less frequent visits and testing for thyroid profile monitoring, and limited availability of RAI therapy (except in a few designated centers) combine to make TT a cost-effective and logistically appealing option for young economically productive patients. In contrast, elderly subjects who have comorbidities often preferred nonoperative management with RAI. Differences in the age and sex of the study subjects could have contributed to the observed variations between the groups; however, adjustments for age and sex were made in the general linear model of statistical analyses. Our study was short-term, with a follow-up of 6 months only. A long-term prospective follow-up of 4 years or more after remission may reveal more recovery of bone indices after RAI therapy. The study examined only the hip and spine. Inclusion of the forearm radius, a cortical bone, would bring out the difference in the recovery between cancellous and cortical bone. A large-scale, randomized controlled trial with three arms, including hyperthyroid subjects on either ATDs alone, RAI therapy, and TT with long-term follow up of 1 to 4 years would uncover the true differences in the rate and extent of BMD recovery with each form of treatment. Differences in the ethnicity, vitamin D status, and patient's preference for TT versus RAI therapy may be specific to our population and could have contributed to some of the observation. Therefore, a similar validation in other worldwide populations may be required. Evaluation of BMD Z scores, which is units of standard deviation from age-, sex-, height-, and weight- adjusted means may produce more accurate results and may help decrease bias.

In conclusion, our study demonstrated that BMD improved significantly after all forms of treatment of hyperthyroidism. The recovery of BMD was greatest in subjects undergoing TT, especially in the lumbar vertebrae. Rapid and near complete recovery of BMD as early as 6 months after TT supports TT as the definitive treatment of choice for hyperthyroidism. Incomplete recovery of BMD post-RAI therapy needs further long-term evaluation.

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References

1. Fraser SA, Smith DA, Anderson JB, Wilson GM. Osteoporosis and fractures following thyrotoxicosis. *Lancet*. 1971;297:981–983.
2. Wakasugi M, Wakao R, Tawata M, Gan N, Koizumi K, Onaya T. Bone mineral density in patients with hyperthyroidism measured by dual energy X-ray absorptiometry. *Clin Endocrinol (Oxf)*. 1993;38:283–286.
3. Vestergaard P, Mosekilde L. Hyperthyroidism, bone mineral, and fracture risk—A meta-analysis. *Thyroid*. 2003;13:585–593.
4. Langdahl BL, Loft AG, Eriksen EF, Mosekilde L, Charles P, Gitte A. Bone mass, bone turnover, calcium homeostasis, and body composition in surgically and radioiodine-treated former hyperthyroid patients. *Thyroid*. 1996;6:169–175.
5. Karunakaran P, Maharajan C, Ramalingam S, Rachmadugu SV. Is hungry bone syndrome a cause of postoperative hypocalcemia after total thyroidectomy in thyrotoxicosis? A prospective study with bone mineral density correlation. *Surgery*. 2018;163:362–372.
6. Mora S, Weber G, Marenzi K, Signorini E, Rovelli R, Proverbio MC, et al. Longitudinal changes of bone density and bone resorption in hyperthyroid girls during treatment. *J Bone Miner Res*. 1999;14:19971–19977.
7. De Leo S, Lee SY, Braverman LE. Hyperthyroidism. *Lancet*. 2016;388:906–918.
8. Toh SH, Claunch BC, Brown PH. Effect of hyperthyroidism and its treatment on bone mineral content. *Arch Intern Med*. 1985;145:883–886.
9. Vestergaard P, Rejnmark L, Weeke J, Mosekilde L. Fracture risk in patients treated for hyperthyroidism. *Thyroid*. 2000;10:341–348.
10. Arata N, Momotani N, Maruyama H, Saruta T, Tsukatani K, Kubo A, et al. Bone mineral density after surgical treatment for graves' disease. *Thyroid*. 1997;7:547–554.
11. Karunakaran P, Maharajan C, Mohamed KN, Rachamadugu SV. Rapid restoration of bone mass after surgical management of hyperthyroidism: A prospective case control study in Southern India. *Surgery*. 2016;159:771–776.
12. Mosekilde L, Eriksen EF, Charles P. Effects of thyroid hormones on bone and mineral metabolism. *Endocrinol Metab Clin North Am*. 1990;19:35–63.
13. Mosekilde L, Melsen F. Effect of antithyroid treatment on calcium-phosphorus metabolism in hyperthyroidism. II: Bone histomorphometry. *Acta Endocrinol (Copenh)*. 1978;87:751–758.
14. Langdahl BL, Loft AG, Eriksen EF, Mosekilde L, Charles P. Bone mass, bone turnover, body composition, and calcium homeostasis in former hyperthyroid patients treated by combined medical therapy. *Thyroid*. 1996;6:161–168.
15. Deng HW, Xu FH, Davies KM, Heaney R, Recker RR. Differences in bone mineral density, bone mineral content, and bone areal size in fracturing and non-fracturing women, and their interrelationships at the spine and hip. *J Bone Miner Metab*. 2002;20:358–366.
16. Serraclara A, Jódar E, Sarabia F, Hawkins F. Bone mass after long-term euthyroidism in former hyperthyroid women treated with ^{131}I: Influence of menopausal status. *J Clin Densitom*. 2001;4:249–255.
17. Campos-Pastor MM, Muñoz-Torres M, Escobar-Jimenez F, Ruiz de Almodóvar M, Gimeno EJ. Bone mass in females with different thyroid disorders: Influence of menopausal status. *Bone Miner*. 1993;21:1–8.

Discussion

Dr David Schneider (Madison, WI): I was surprised that you saw a difference in the bone density as early as 6 months.

How did you handle patients that had either transient or permanent hypoparathyroidism? And would your results have been even more dramatic if you had excluded anyone that had even just transient hypocalcemia?

Dr Poongkodi Karunakaran: Yes. Our study showed that bone mineral density improved significantly within 6 months after total thyroidectomy compared with RAI therapy, in subjects with hyperthyroidism.

We found that 18.5% of the subjects who underwent total thyroidectomy developed transient hypoparathyroidism and were treated with calcium supplements and calcitriol for 2 to 3 weeks. Among subjects who underwent radioactive iodine therapy, 10% had hypocalcemia and were also treated with calcium supplements. All of them were included. In addition, the level of 25-hydroxy vitamin D was in the insufficient range, among 80% of the subjects in both the groups. We had corrected vitamin D deficiency with weekly doses of 60,000 IU of cholecalciferol for 8 weeks in both the groups in the early phase of the study. Therefore, that should not have contributed to the observed variation.

Dr David Schneider (Madison, WI): For those patients, there was no difference in the bone density response? You excluded those?

Dr Poongkodi Karunakaran: Almost 80% of the subjects enrolled in our study had vitamin D deficiency and we had corrected that with vitamin D in the early part of the treatment. They were not excluded.

Dr Mark Cohen (Ann Arbor, MI): Very nice talk and very interesting study. Did you look at whether you had a complete ablation in the patients that had radioactive iodine? If you didn't have complete ablation, maybe that could be contributing to why your BMD improvement was not as robust as with total thyroidectomy. Did you measure any thyroglobulin levels postablation?

Also, the elderly nature of the patients receiving the radioactive iodine could have contributed to their lag in BMD recovery compared to the younger cohort.

Dr Poongkodi Karunakaran:

Yes, I agree with you. Subjects included in group 2, who underwent RAI therapy, were often elderly female subjects. This is one of our limitations. Advancing age could have definitely contributed to this lag in BMD recovery, although we included age adjustments in our statistical analysis.

Dr Mark Cohen (Ann Arbor, MI): Are you sure you had complete ablation with radioactive iodine?

Dr Poongkodi Karunakaran: Yes. Our Indian subjects are relatively thinner and smaller when compared with the Western population. We used high-dose radioiodine ablation, and 22% of our subjects developed hypothyroidism within 3 months' time. None of them had a relapse of hyperthyroidism nor they did they require a second dose. However, many subjects still required antithyroid drugs for 3 to 6 months after RAI therapy.

Dr Christina Maser (Fresno, CA): Was there a difference in the time to euthyroidism between the two groups?

Dr Poongkodi Karunakaran: The subjects who underwent thyroidectomy were started on a replacement dose of thyroxine on the second postoperative day. So, they achieved euthyroidism quickly. On the other hand, the time to achieve euthyroidism was relatively prolonged in those undergoing radioactive iodine therapy. Many of them required antithyroid drugs for 3 to 6 months even after RAI therapy, thus the duration of hyperthyroidism was more prolonged in these cases. That could be a reason for the lag in BMD recovery after RAI therapy.