

# Effect of Antithyroid Therapies on Bone and Body Composition: A Prospective, Randomized, Clinical Study Comparing Antithyroid Drugs with Radioiodine Therapy

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## Abstract

**Background:** Thyrotoxicosis is associated with loss of body weight and bone mineral content (BMC). Antithyroid drugs (ATD) and radioiodine therapy (RIT) are the common options for the management of thyrotoxicosis. We evaluated the effect of ATD and RIT on BMC and body composition. **Materials and Methods:** In this prospective study, we randomized 60 patients of thyrotoxicosis (20–50 years, treatment naïve, males) to receive either ATD (Group 1) using carbimazole or RIT (Group 2). We excluded patients with significant ophthalmopathy and thyroid malignancy. The patients were followed serially for 1 year. Body composition was analyzed using the bioimpedance method and BMC by dual-energy X-ray absorptiometry technique. The data were analyzed using appropriate statistical measures. **Results:** The patients had a mean age of  $33 \pm 4.2$  years and mean symptoms duration of  $8.2 \pm 2.7$  months before the diagnosis. A total of 51 patients had Graves' disease, and the remaining 9 had toxic multinodular goiter. BMC at lumbar spine and femoral neck improved with both the therapies similarly at the end of 1 year. The body weight, protein, and fat content also increased after 1 year of observation similar between the two groups. None of the observed parameters showed a difference with regard to the mode of ATD. **Conclusion:** ATD and RIT have comparable effects on the bone and body composition in the management of thyrotoxicosis. Further long-term studies are needed to confirm the observed findings.

**Keywords:** Body composition, bone mineral density, carbimazole, radioiodine therapy, thyrotoxicosis

## INTRODUCTION

Thyrotoxicosis is seen commonly due to Graves' disease (GD), autonomously functioning toxic nodule, toxic multinodular goiter, iodine excess, and other conditions.<sup>[1]</sup> Thyrotoxicosis is reported to be more prevalent in females due to the autoimmune etiology of the condition. Thyroid hormones have profound effects on the entire body systems including cardiovascular, skeletal and intermediary metabolism.<sup>[2]</sup> Thyroid hormones play an important role in determining the body composition, bone mineral density (BMD), and bone mineral content (BMC).<sup>[3]</sup> Thyrotoxicosis is associated with reduction in lean body mass (LBM) and BMD, leading to increased fracture risk. The effect of thyroid hormones on the body composition is of particular importance in the clinical practice. Thyroid dysfunction is one of the commonly abused reasons for the changes in the body weight.<sup>[4]</sup> The basal metabolic rate is increased in thyrotoxicosis leading to loss of weight despite increased appetite. Long standing

hyperthyroidism leads to increased bone resorption, osteoporosis, and predisposes an individual to fragility fractures.<sup>[5]</sup>

Thyrotoxicosis is managed by the use of beta-blockers, antithyroid drugs (ATD), radioiodine therapy (RIT), and thyroidectomy.<sup>[6]</sup> The choice of therapy is decided based on a multitude of factors, including the availability and affordability. Conventionally, the United States physicians choose RIT and Europeans choose ATD as the preferred option of therapy.<sup>[7]</sup> Jayaraman *et al.* have shown that the use of RIT is economical over the ATD and recommends the same for every patient with

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GD.<sup>[8]</sup> The opponents of RIT argue about the harmful effects of the radiation and also a doubtful increased risk of malignancy in tissues exposed to the RIT.<sup>[9]</sup> A Cochrane review on the subject also did not give any definite conclusion regarding the best possible option for the management of GD.<sup>[10]</sup> Most of the published studies have evaluated the effects on disease remission and not on the systemic parameters.<sup>[11]</sup> A very limited data exist regarding the effects of these therapies on the BMC and body composition.<sup>[12]</sup> Hence, we conducted this study to evaluate the effects of the types of antithyroid therapies on the bone and body composition.

## MATERIALS AND METHODS

### Study population

This prospective, observational study was conducted at a tertiary level referral center of the armed forces located in Delhi. Sixty patients with newly diagnosed thyrotoxicosis (age between 20 and 50 years, treatment naïve) were included in the study. We excluded patients with a history of thyroid disease, significant ophthalmopathy (Clinical activity score more than 1), thyroid malignancy, previous exposure to RIT, known systemic disorders (chronic liver disease, chronic kidney disease, and thyroid disease), and long-term intake of drugs that could affect the body composition and skeletal mass (glucocorticoids and insulin). The patients were randomized using a computer-generated random sequence to receive either ATD (Group 1) or RIT (Group 2). The local ethics committee approved the trial protocol, and all patients provided written informed consent.

### Study measures

A detailed history regarding the thyrotoxicosis was obtained from all the participants. The general physical examination was conducted, including the exophthalmometry. Carbimazole was started with a dose of 30 mg initially for 2 months, followed by tapering or continuation as per the clinical status of the patient. RIT was given orally as a single dose of <sup>131</sup>I-labeled sodium iodide 10 mCi in capsule form along with water. The patients were followed serially at 2 monthly intervals for 1 year after entry into the study.

### Study intervention

Body composition and BMC were determined in the fasting state at the same time of the day in all patients. The patients did not exercise or consume caffeine or alcohol before the measurement of body fat percentage. Dual-energy X-ray absorptiometry was performed using the Hologic QDR 2000 (Hologic®, Bedford, MA 01730, USA). The BMC at the neck of femur and lumbosacral spine was included for the study purpose. Body composition analysis was done using the InBody 720 body composition analyzer (Biospace, Urbandale, Iowa, 50323 USA). The anthropometric details were entered into the panel, and the machine displays the details about the protein and fat content of the body. The machine also gives an estimate about the intracellular and extracellular fluid, which have not been included in this report. A fasting venous blood

sample after an overnight fast for more than 12 h was collected from each participant at 0800 h. The serum was analyzed for hematological and biochemical parameters including thyroid hormones and lipid profile. The intra- and inter-assay coefficient of variation for all the tests is < 6% in our laboratory.

### Statistical analysis

Data are presented as mean ± standard deviation (SD) and a comparison between the groups was done using non-parametric (Mann–Whitney U-test) and Fisher's exact tests.  $P < 0.05$  was considered statistically significant for all the tests and the statistical analysis was done using the GraphPad Prism Software, Version 6 (GraphPad Software, San Deigo, CA, USA).

## RESULTS

The study participants had a mean age of  $33 \pm 4.2$  years and mean symptoms duration of  $8.2 \pm 2.7$  months before the diagnosis. A total of 51 patients had GD and the remaining 9 had toxic multinodular goiter. Weight loss and heat intolerance were the common symptoms and tachycardia, tremor were the common signs. Thirty patients received the ATD and RIT each and the flow diagram of the study is given in Figure 1. The comparison between the baseline parameters between the two groups is shown in Table 1. Briefly, all the clinical and biochemical parameters were same in both groups except the level of thyroid stimulating hormone. At the end of 1 year, 22 patients in Group 1 had clinical and biochemical euthyroidism, 5 had subclinical hyperthyroidism and 2 patients had hypothyroidism. One patient did not report for the follow-up evaluation. A total of 24 patients in Group 2 developed hypothyroidism requiring levothyroxine replacement. Remaining 4 patients were euthyroid and not requiring any hormonal therapy. None of the patients in Group 2 showed persisting thyrotoxicosis requiring a repeat dose of RIT. The details about the biochemical and BMC

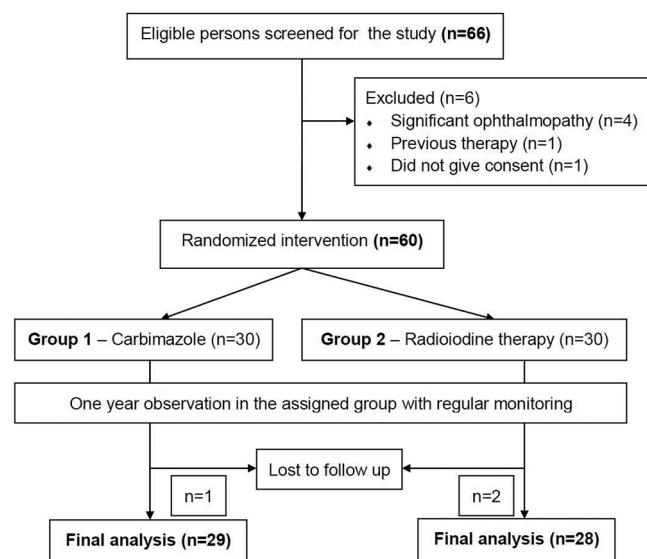


Figure 1: Flow diagram of the study

parameters after the end of 1 year observation are given in Table 2. Briefly, both the therapies have resulted in significant improvement of the BMC and body weight. All the parameters assessed after 1 year showed a significant improvement from the baseline ( $P < 0.001$ ). The body composition parameters also showed a rise in the protein and fat content of the body. Transient febrile illness was observed in 3 patients receiving carbimazole therapy. None of the patients in the RIT group had a significant adverse effect.

## DISCUSSION

Our study results suggest that the therapeutic response to either of the antithyroid therapies is similar in comparison between the ATD and RIT. Our results showed the control of the thyrotoxicosis in about two-thirds of the patients at the end of 1 year. Metso *et al.* have shown hypothyroidism in about 75% of patients after 1 year of RIT, similar to that of our study.<sup>[13]</sup> The choice of therapy did not show any difference even in the body composition and the BMD. Previous reports have shown that the BMC showed a significant change within 6 months of antithyroid therapy.<sup>[14]</sup> Previous studies have shown that either RIT or ATD have no direct skeletal actions independent of the underlying thyroid status.<sup>[15]</sup>

Epidemiological data suggest that the women are more susceptible to the autoimmune thyroid disorders including thyrotoxicosis.<sup>[16]</sup> Our hospital, being a tertiary level referral center for the armed forces receives mostly male patients. This explains the gender bias and male predominance in our study. We also have a system of captive follow-up of the patients in uniform thereby limiting our data for male patients only. The weight loss in thyrotoxicosis is predominantly due to the loss of LBM.<sup>[17]</sup> The protein content of the body corresponds to the LBM.<sup>[18]</sup> Treatment with ATD results in an increase in the body weight contributed predominantly by the LBM and a minor contribution by the fat mass.<sup>[19]</sup> Our results have shown a similar quantum rise in the protein and fat content after therapy. Previous reports have even suggested alterations in the adipocytokines such as leptin and ghrelin as the mediators of the change in the body composition.<sup>[17,20]</sup>

BMC is the amount of mineral matter per square centimeter of bones. BMD is assessed by the *T* score and *Z* score derived from the population-specific normative data. The mean age of our patients is 33 years only, who are close to achieving the peak bone mass.<sup>[21]</sup> Hence, we used the BMC instead of the BMD in assessing the change in mineral. Our data also suggest a comparable efficacy and safety profile between the

**Table 1: Comparison between two groups regarding the baseline parameters**

Feature	Units	Group 1 (n=30)		Group 2 (n=30)		P
		ATD		RIT		
Age	Years	32.9 (6.3)		34.1 (7.6)		0.5082
Graves' disease	n	27		24		0.4716
Toxic MNG	n	3		6		0.4716
Body mass index	kg/m <sup>2</sup>	20.9 (2.1)		20.7 (1.9)		0.7070
T3	ng/mL	3.4 (0.6)		3 (1.1)		0.0857
T4	µg/dL	19.2 (3.5)		18.5 (4.3)		0.4920
TSH	µIU/mL	0.08 (0.03)		0.05 (0.02)		<0.001
BMD neck of femur	g/cm <sup>2</sup>	0.74 (0.11)		0.76 (0.09)		0.4440
BMD lumbar spine	g/cm <sup>2</sup>	0.88 (0.07)		0.86 (0.09)		0.3407
Protein content	Percentage	9.7 (0.95)		9.5 (0.94)		0.4158
Fat content	Percentage	10.9 (3.5)		9.4 (2.5)		0.0611

Mean (SD). SD: Standard deviation, ATD: Antithyroid drug, RIT: Radioiodine therapy, BMD: Bone mineral density, TSH: Thyroid stimulating hormone, T4: Thyroxine, T3: Triiodothyronine, MNG: Multinodular goiter

**Table 2: Comparison between two groups at baseline and after 1 year of therapy**

Feature	Units	Group 1 (n=30)		Group 2 (n=30)	
		Before	After 1 year	Before	After 1 year
Body mass index	kg/m <sup>2</sup>	20.9 (2.1)*	22.9 (1.8)	20.7 (2)	22.6 (1.3)
T3	ng/mL	3.4 (0.6)	1.1 (0.4)	3 (1.1)	1.4 (0.9)
T4	µg/dL	19.2 (3.5)	8.4 (3.2)	18.5 (4.3)	7.7 (4.1)
TSH	µIU/mL	0.08 (0.03)	1.1 (0.6)	0.05 (0.02)	2 (2.3)
BMD neck of femur	g/cm <sup>2</sup>	0.74 (0.11)	0.79 (0.12)	0.76 (0.09)	0.82 (0.09)
BMD lumbar spine	g/cm <sup>2</sup>	0.88 (0.07)	0.92 (0.06)	0.86 (0.09)	0.91 (0.09)
Protein content	Percentage	9.7 (0.95)	11.4 (1.1)	9.5 (0.94)	11.4 (1.3)
Fat content	Percentage	10.9 (3.5)	12.1 (3.5)	9.4 (2.5)	10.5 (2.4)

\*Mean (SD). All values have been significant ( $P < 0.05$ ) using paired *t*-test. BMD: Bone mineral density, TSH: Thyroid stimulating hormone, T4: Thyroxine, T3: Triiodothyronine, SD: Standard deviation

use of carbimazole and RIT. The majority of practitioners in India uses ATD for 1 year before taking a decision about the RIT.<sup>[22]</sup> The comparable results between the groups increase the confidence of choosing either of the therapies depending on the availability and affordability. The strengths of our study include randomized design with robust follow-up at a single center. However, our study has certain limitations, including small sample size, lack of female patients, body composition assessment by an inferior method, and limited follow-up period of 1 year.

## CONCLUSION

Our study suggests that the changes in the bone and body composition were similar irrespective of the choice of antithyroid therapy. ATD and RIT have comparable outcomes at the end of 1 year observation period. Further long-term studies involving a number of patients are required to confirm the findings observed in our study.

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## Conflicts of interest

There are no conflicts of interest.

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