Response to: Letter to the Editor Regarding the Article “Thyrotropin Suppression Increases the Risk of Osteoporosis Without Decreasing Recurrence in ATA Low- and Intermediate-Risk Patients with Differentiated Thyroid Carcinoma”

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Dear Editor:

We very much appreciate the comments of Schneider *et al.* (1) and are grateful for pointing us to their study, which we inadvertently overlooked in discussing our findings. We also agree with the authors that long-term, prospective, controlled studies are the ideal methodology to identify the full extent of beneficial and adverse effects of levothyroxine therapy on cancer patients.

Within the limitations of a retrospective design, we agreed on what we thought was the most robust and clinically relevant way of defining osteoporosis in the population that we studied. Given that most of our patients were post-menopausal women (median age 57 years, range 39–84), we elected to use a postoperative bone mineral density (BMD) T-score ≥ -2.5 in the lumbar spine, femoral neck, or total hip as the definition of new osteoporosis since this methodology currently drives indication for treatment in the majority of our patients. In addition, we relayed on physician documentation of osteoporosis as a “new diagnosis” and the initiation of bisphosphonate therapy in the absence of metastases or Paget’s disease when bone density tests were unavailable. Of the 29 women adjudicated with the diagnosis of postoperative osteoporosis, 18 had bone density tests showing a T-score of -2.5 or greater in the lumbar spine, femoral neck, or total hip, and 11 women were classified as having new osteoporosis on the basis of bisphosphonate initiation. When preoperative BMD tests were available, we collected the information, and this allowed us to exclude 32 women with preoperative osteoporosis. Ten of 18 women with diagnosis of osteoporosis based on their BMD test had had BMD tests before and after thyroidectomy, always determined with the same system (Hologic, Lunar, or Norland), as it is customary practice to recommend the use of the same bone densitometry unit to avoid the need for cross-calibration. These women had a mean increase in T-score of -0.4 over 6.5 years. We agree

with Schneider *et al.* that the World Health Organization criteria are not validated for cancer patients. However, height and weight are collected in each diagnostic bone densitometry test and factored into the calculation of a T-score, so metabolic changes due to levothyroxine therapy, at least in part, are accounted for in these tests. Finally, determination of architectural parameters and bone markers was beyond the scope of our study and almost impossible to accomplish with the limitations of a retrospective design.

The differences in outcomes between the study of Schneider *et al.* (2) and our analysis (3) may be attributed to the age of the population included and the length of follow-up. Their study included premenopausal women and men, while our study was almost exclusively composed of postmenopausal women. It is quite possible that the osteoporosis risk due to treatment with levothyroxine may only occur in postmenopausal women. Bone fractures represent a more clinically relevant outcome and the ultimate reason why osteoporosis is a concern. The largest meta-analysis to date on subclinical hyperthyroidism and fracture risk conclusively shows that endogenous and exogenous subclinical hyperthyroidism are associated with an increased risk of fractures at any site (4). Long-term, prospective, randomized, controlled trials are needed to find a more definitive association between osteoporosis risk and levothyroxine suppression in thyroid cancer patients as well as risk of bone fractures and subclinical hyperthyroidism.

References

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