CORRESPONDENCE

Increased Cancer Incidence After Radioiodine Treatment for Hyperthyroidism

Metso et al.[1,2] recently reported increased cancer mortality in hyperthyroid patients treated by radioiodine. Major limitations of those works, as lacking of hyperthyroid controls, were correctly discussed by the authors. However, in our opinion the evaluation of administered activity and associated mortality risk should be biased. In fact, the analysis was performed on 3 subgroups (ie, patients treated by 55–258 MBq, 259–369 MBq, and 370–2664 MBq, respectively) and increased mortality was observed only in the latter. Because 1) mean administered activity was 305 MBq, 2) only 24% of patients received more than 370 MBq, and 3) the 370–2664 MBq is a very wide range, more detailed analysis of the activity received by patients who died after radioiodine is needed. In fact, activities more than 600–740 MBq are not usually administered to treat hyperthyroidism and Metso et al.[3] themselves proposed a fixed dose approach by administration 259 MBq of radioiodine in patients with hyperthyroidism. In this instance, a focused analysis of mortality among patients treated with 370–740 MBq seems to be of pivotal importance. If no differences will be proved in this subgroup, the conclusion should be reformulated by underlining the differences between the administered activities and associated mortality risk.

REFERENCES

1. Metso S, Jaatinen P, Huthala H, Salmi J, Otsala H. Increased cancer incidence after radioiodine treatment for hyperthyroidism. *Cancer*. 2007;109:1972–1979.
2. Metso S, Auvinen A, Huthala H, et al. Increased cardiovascular and cancer mortality after radioiodine treatment for hyperthyroidism. *J Clin Endocrinol Metab*. 2007;92:2190–2196.
3. Metso S, Jaatinen P, Huhtala H, Luukkaala T, Oksala H, Salmi J. Long-term follow-up study of radioiodine treatment of hyperthyroidism. *Clin Endocrinol*. 2004;61:641–648.

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Reply to Increased Cancer Incidence After Radioiodine Treatment for Hyperthyroidism

We thank Dr. Luca Giovanella for his interest in our study[1] and for his remarks. Dr. Giovanella suggests that the evaluation of administered activity and associated cancer risk is biased in our

study because the subgroup analysis concerning the highest dose group included patients receiving more than 740 MBq of radioactive iodine (RAI).

We would like to make some additional comments. In our patients the mean *first* dose of RAI was 241 MBq while the mean *total* dose of RAI administered was 305 MBq. The maximum first dose of RAI did not exceed 740 MBq in any of the patients. We repeated the subgroup analysis excluding the 86 patients (13% of the highest dose group) who received more than 740 MBq of RAI, and this did not change the results. The cancer risk was higher in the patients who received a cumulative dose of 370–740 MBq than in the patients who received 259–369 MBq or 55–258 MBq of RAI (rate ratio, 1.73; 95% confidence interval [CI], 1.05–2.84 vs 1.32 [1.00–1.75] vs 1.11 [0.89–1.39]). Furthermore, the cancer risk increased with the cumulative dose of RAI, when the RAI dose was analyzed as a continuous variable instead of a categorical variable, the relative risk of cancer being 1.06/100 MBq (95% CI, 1.03–1.09) in the Cox regression analysis.

On the basis of the present[1] and previous[2] results, we conclude that the treatment with RAI causes a small but significant increase in cancer incidence and mortality in hyperthyroid patients. Even the exposure to the lowest doses of ionizing radiation has the potential to cause double-strand breaks in the DNA, which in the absence of a fully efficient repair system may result in long-term damage.[3] The slightly increased risk of cancer should be weighed against the low remission rates after medical therapy,[4] adverse effects of surgery,[5] and the simplicity and cost-effectiveness of RAI therapy.[6] Hyperthyroidism should be effectively treated because it increases cardiovascular mortality, as seen in the present study.

REFERENCES

1. Metso S, Jaatinen P, Huthala H, Salmi J, Otsala H. Increased cancer incidence after radioiodine treatment for hyperthyroidism. *Cancer*. 2007;109:1972–1979.
2. Holm LE, Hall P, Wiklund K, et al. Cancer risk after iodine-131 therapy for hyperthyroidism. *J Natl Cancer Inst*. 1991;83:1072–1077.
3. UNSCEAR 2000 Report. Vol. II. Available from URL: http://www.unscear.org/unscear/en/publications/2000_2.html
4. Abraham P, Avenell A, Park CM, et al. A systematic review of drug therapy for Graves' hyperthyroidism. *Eur J Endocrinol*. 2005;153:489–498.
5. Sosa JA, Bowman HM, Tielsch JM, et al. The importance of surgeon experience for clinical and economic outcomes from thyroidectomy. *Ann Surg*. 1998;228:320–330.
6. Patel NN, Abraham P, Buscombe J, et al. The cost effectiveness of treatment modalities for thyrotoxicosis in a U.K. center. *Thyroid*. 2006:16:593–598.

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