Association of Radioactive Iodine Treatment with cancer Mortality in Patients with Hyperthyroidism

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Summary of paper:

The aim of this study was to determine if organ-absorbed doses from radioactive iodine treatment (RAI) in patients with hyperthyroidism were associated with overall and organ-specific cancer mortality. The study was an extension of the Multicenter Cooperative Thyrotoxicosis Follow-up Study (1), where the original cohort consisted of UK and US patients diagnosed with hyperthyroidism between the years of 1946 and 1965. A sub-cohort of 18 805 patients (78% women and 93,7% with Graves´disease), extracted from the earlier cohort, who all received RAI and were either alive or could be traced in National records for death cause were included in this study. An iodine mathematical biokinetic model (2) was applied to estimate the organ-specific radioactive iodine exposure. The excess relative risk per 100mGy radioactive dose per organ was calculated, and converted to relative risks. Positive dose-response relationships were observed for all solid cancer mortality (RR 1,06; 95% CI 1,01-1,10; p=0,002) and for breast cancer mortality (RR 1,12; 95% CI 1,003-1,32; p=0,04). The authors conclude that there is a modest positive association between organ-absorbed doses of RAI and risk of solid cancer death, especially death in breast cancer.

Commentary:

This is an interesting but also controversial paper as RAI treatment to this point has been considered as a safe treatment of hyperthyroidism. The last follow-up study of the Multicenter Cooperative Thyrotoxicosis cohort, published in 1998, concluded the opposite- that there was no increased risk of cancer mortality with RAI (1). The current study differs from it precursor, not only in the addition of follow-up time but also in applying a new computer model of estimating the I-131 dose-response to site-specific organs. The computer model, described in detail in a former publication by some of the current authors (2), is taking into account the specific I-131 metabolism in hyperthyroid patients, as opposed to the commonly used model which is based on estimated I-131 uptake in euthyroid patients.

The authors themselves flag for uncertainties in the new computer model as well as possible confounders that they have not controlled for such as being overweight, drinking alcohol and smoking. Some of the patients in the study were also treated with anti-thyroid drugs, some of which back in the 1940-60s were more toxic than the current treatment and could have contributed to the increased risk of death in breast cancer. The most obvious confounder though, that the authors do not discuss, is the hyperthyroidism itself. Indeed, there are several papers associating Graves´ disease and elevated thyroid hormones with increased risk of cancer, especially breast cancer (3-5).

If the computer model is correct and if the association is causative ie RAI contributes to increased cancer mortality, this would most likely influence the current management of Graves´ disease. Especially for younger patients, and for those with other risk factors for cancer, surgery should then be favoured as definite treatment in place of RAI.

It is however difficult to determine, without a control group of hyperthyroid patients that did not receive RAI, if the increased cancer deaths are related to the RAI treatment or the hyperthyroidism itself. The future impact of this paper is hard to predict at this point, but it will most likely open up for discussion within the society of Endocrinologists and Endocrine surgeons and amongst patients. More studies are warranted to verify the accuracy of the dose-

response computer model and to establish if there is a causative relationship between radioactive iodine treatment and risk of solid cancer morbidity and mortality.

References:

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Reviewers

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