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Italian Association of Clinical Endocrinologists
ITALIAN CHAPTER
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Endocrine News
11-2018

Limited benefit of second radioiodine treatment in differentiated thyroid cancer

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A recent study (1) provides a retrospective evaluation of the efficacy of a second treatment with radioactive iodine (RAI) in 164 patients with differentiated thyroid cancer (DTC). Participants were in stage I/II at diagnosis (AJCC/UICC), had incomplete response to initial treatment (surgery + RAI) and did not have distant metastases.
After a median follow-up of 10 years from the diagnosis, and 7.4 years from the second RAI, the data show:

- Biochemical incomplete response (BIR, group A) in 61 of 164 patients (37%)
- Structural incomplete response (SIR) in 103 of 164 patients (63%). These patients were divided into two groups (group B and group C) according to whether or not they had further surgery before the second RAI:
  - Group B: 50 patients undergoing second surgery, FNAB positive for cervical lymph nodal metastases
  - Group C: 53 patients not undergoing further surgery, with FNAB results available in 36/53.

After about 2 years from the second RAI:

- 9/58 (15.5%) of group A patients had imaging positive for cervical lymph nodal metastases
- 21/44 (47.7%) of group B patients had positive loco-regional imaging
- 44/47 (93.6%) of group C patients with available data did not present significant reduction of serum thyroglobulin and the average diameter of the cervical lesions was mildly superior in comparison to pre-treatment. A noteworthy feature was that in this group the average diameter of the lesions at baseline was significantly inferior in comparison to group B.

38.4% of the patients have received further treatments after second RAI.

At last follow-up:

- There was no evidence of disease in 56/164 patients (34.1%)
- Imaging for loco-regional disease was positive in 74 patients (45.1%)
- Thyroglobulin was raised in 89 patients (54.3%) with no evidence of structural disease in 32 patients (21 in group A, 8 in group B, 3 in group C)
- 22/50 of the patients in group B (44%) had no biochemical or structural evidence of disease, whereas only 12/58 of the patients in group C (20.8%) were disease-free (despite further treatment in 43% of patients)
- 17/61 of the patients in group A (27.9%) had structural disease.

According to these data, patients with DTC and loco-regional disease with limited response to initial treatment, have little to gain from a second course of RAI. Patients with SIR seem to benefit from surgery rather than from RAI. Further treatments may achieve a cure in 21% of patients. It is important to point out that some BIR patients received a second RAI empirically: in these patients it cannot be ruled out that the disease could have had a favorable outcome even without a second RAI, since in many cases the post-dose scintigraphy did not show areas of hyper-capture. Besides, not all group C patients underwent cytology confirmation, with many patients diagnosed as affected by loco-regional disease only by imaging, albeit highly suspicious. As expected, the risk of persistent disease and mortality was bigger in patients with SIR than in those with BIR, and within the SIR group patients not receiving a second operation were at larger risk than patients undergoing further surgery. This study encourages further prospective research aimed at defining the role of alternative therapies in patients with incomplete response to initial treatment. It must also be remembered that the role of RAI after initial thyroidectomy has been reduced in recent guidelines. It is important to emphasize the importance of a thorough initial ultrasound evaluation of loco-regional lymph nodes, as a key to implementation of an adequate surgical approach, nowadays more conservative than in the past.

Reference

1. Hirsch D, et al. Second radioiodine treatment: limited benefit for differentiated thyroid cancer with locoregional persistent disease. J Clin Endocrinol Metab 2018, 103: 469-76.

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