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RESTRATIFICATION OF THYROID CANCER DURING THE FIRST YEAR AFTER TREATMENT GREATLY IMPROVES PROGNOSTIC PRECISION

Castagna MG, Maino F, Cipri C, Belardini V, Theodoropoulou A, Cevenini G, Pacini F. **Delayed risk stratification, to include the response to initial treatment (surgery and radioiodine ablation), has better outcome predictivity in differentiated thyroid cancer patients.** Eur J Endocrinol 2011;165:441-6. Epub July 12, 2011; doi: 10.1530/eje-11-0466.

SUMMARY

BACKGROUND

The strategic approach to the individual treatment of differentiated thyroid cancer (DTC) has greatly evolved in recent times and continues to do so. Recently, the ATA and the ETA have produced guidelines for stratifying the risk of recurrence or persistence of DTCs (ATA: low-, intermediate-, and high-risk categories, ETA: very–low-, low-, and high-risk). This article and others recently published stress the relevance of delayed risk stratification (DRS) during the visits following the initial treatment, since this strategy can greatly change the risk category of an individual patient.

METHODS AND RESULTS

A total of 512 patients treated at the University Center of Sienna were retrospectively evaluated. Their mean (±SD) age was 46±16 years, and 89% presented with papillary and 11% with follicular thyroid cancer. Using the classification according to the AJCC/UICC system (American Joint Cancer Committee/Union Internationale Contre le Cancer), 86% of the patients were categorized as having stage I cancer, 8.4% as stage II, and 5% as stage III. All patients were treated with total thyroidectomy and radioactive iodine. Lymph-node resection in the medial central compartment was done in only 7.4%. The mean follow-up was 5.6 years. Eight patients (1.6%) died of the disease; the overall survival rate at 10 years was 98%. Five patients had recurrent disease and five had distant metastasis. Interestingly, 4 additional patients presented with elevated thyroglobulin levels but no residual lesion could be detected.

After the initial treatment, the patients were classified according to both ETA and ATA guidelines. According to ETA guidelines, tumors of >4 cm, or those extending beyond the capsule and/or with an aggressive histology and lymph-node involvement were considered high risk; all others were considered low risk. According to the ATA guidelines, some cases were classified in the intermediate-risk category (microscopic invasion, cervical lymph nodes, aggressive histology).

Six to 12 months after the initial treatment, the patients were seen again in the clinic for their first posttherapy visit. At that time, DRS was established. Clinical remission was defined as no evidence of recurrence based on either basal thyroglobulin levels or the levels after recombinant thyrotropin (TSH), ultrasound evaluation, and/or ^{131}I whole-body scans. In cases of clinical remission, substitution therapy was reduced to nonsuppressing serum TSH levels, and yearly follow-up was limited to a clinic examination and basal serum thyroglobulin levels. The other patients were considered to have persistent or recurrent disease and were treated accordingly.

The initial risk classification identified 46% (45% for ATA and 48% for ETA) low-risk patients. The ETA high-risk cases represented 55% and the ATA intermediate-risk patients 52%. Following DRS, the majority of the initially low-risk patients (87%) were considered to be in complete remission. In the higher-risk groups, as expected, only 53% were in complete remission and, thus, became low-risk cases. On the other hand, nearly 12% of initially low-risk patients moved into the high-risk category.

The recurrence rate after complete remission was extremely low (2.7%), suggesting that the DRS stratification is associated with an excellent prognosis.

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The comparison of the diagnostic value between the initial stratification and the DRS stratification is a strong argument in favor of adding an evaluation during the first posttherapy visit. For instance, the positive predictive value was very low for both the ATA and ETA classification (39%). Fortunately, however, the negative predictive value was excellent (91%), indicating that few initially severe cases are missed. DRS had a much better predictive value of 73%.

CONCLUSIONS

The data strongly suggest that even though initial stratification by the ETA and ATA guidelines are good and necessary, they need to be readjusted 6 to 12 months after the initial treatment with total thyroidectomy and radioactive iodine ablation. Many initially intermediate- or high-risk patients can be reclassified as low-risk after 1 year. However, this does not exclude an unfavorable evolution, which was observed in 12% of low risk patients.

COMMENTARY

It is worrisome that even with the updated stratification schemes of the ETA and the ATA, the positive predictive value of the initial stratification is unsatisfactory or even unacceptable. A second look is, therefore, appropriate. In practice, every endocrinologist does it spontaneously without knowing about its prognostic value. This study answers some of these questions and clearly indicates that more than 97% of the patients may be considered to be cured. However, we are missing criteria identifying those patients considered low-risk at the onset, but evolving to high-risk later on. Hopefully, molecular biology might one day be able to fill this gap; at present, several molecular markers, such as BRAF, are being evaluated with this aim in mind, but a final answer is pending.

In view of the cure rate, one may also wonder whether we are still overtreating our patients when using total thyroidectomy and radioactive iodine ablation. This open question will certainly be answered within the next decade.

— Albert G. Burger, MD