

# How Far Should We Go in the Search and Treatment of Recurrent or Persistent Lymph Node Metastases during Follow-Up of Thyroid Cancer Patients?

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'In the sub-categories of both primary intraglandular (thyroid) carcinoma... and primary extraglandular carcinoma... the presence of pathologically defined lymph nodes ameliorated the prognosis. Furthermore, the greater the number of lymph node metastases, the lesser the mortality.' This statement was reported by Cady et al. [1] (and confirmed by other authors) upon review of a series of differentiated thyroid cancer patients treated at the Lاهی Clinic in 1976. Such a statement suggests two considerations: first, the indolent biological course of lymph node metastases, and, second, the low detection rate of lymph node metastases in the 1970s. At that time, neither neck ultrasound (US) nor serum thyroglobulin (Tg) measurements were available in clinical practice and, thus, microscopic lymph nodes were rarely detected and the patients were considered cured. With the introduction of serum Tg measurement, as a sensitive marker of even minimal disease, and of routine exploration of the neck by US, more and more patients show persistent disease in the neck nodes. Do we have to be concerned with these lymph nodes? Do we have to force their search and treatment? These are the questions that we are facing.

In this issue of *European Thyroid Journal*, the 'European Thyroid Association Guidelines for Cervical Ultrasound Scan and Ultrasound-Guided Techniques' report

the consensus of a panel of experts in the postoperative management of patients with thyroid cancer [2]. Based on the current literature and expert opinion, the Guidelines come out with several recommendations dealing with standardization of the US scanning procedure, techniques and indications for US-guided fine-needle aspiration (US-FNA), classification of malignancy risk based on cervical US, proposal of an algorithm for follow-up of thyroid cancer patients based on histopathological and cervical US findings, and potential use of US-guided ablation techniques for locoregional metastases.

Some of the recommendations pertain to methodological issues, such as the need for an experienced US operator, careful inspection of all lymph node chains (from level II to level VI), standardization of the method for US-FNA of suspicious nodes for both cytology and Tg measurement (or calcitonin in the case of medullary thyroid cancer). Other recommendations are devoted to provide indications and timing for neck US and US-FNA. In the past literature, it was advocated that follow-up of thyroid cancer patients should go on for their entire lives, based on the possibility that recurrences may develop even 20–30 years from diagnosis. Nowadays, with more stringent criteria for complete remission of papillary thyroid cancer, the critical timing for follow-up is soon after

thyroidectomy and thyroid ablation (if performed), but mainly at 6–12 months after initial treatment. At that moment, if serum Tg is undetectable and neck US is negative, there is no need for aggressive subsequent follow-up and the patient can be seen annually for the first 5 years or so in specialized centers. Thereafter, the chance of recurrence is so low that the patient can be seen by his/her general practitioner.

The other fundamental issue is how to approach the patient with suspicious nodes at neck US after initial treatment. There is no doubt that in general, large volume recurrences are associated with higher mortality. What it is unclear is the clinical benefit of diagnosing and treating small-volume recurrent or persistent disease in the neck detected by sensitive imaging modalities such as neck US. The first question is whether a few microscopic, suspicious, lymph nodes should be submitted to FNA. We know that such small lymph nodes can remain unchanged for years, and probably forever, and, so, are we sure that we must push to have a definite diagnosis by FNA? Is not just simple observation the best option? Once a cytological diagnosis has been made, it is difficult to tell the patient that observation is sufficiently safe. The guidelines address this issue and advocate caution in exploring microscopic lymph nodes.

The next step, whenever FNA has proven the metastatic nature of a lymph node, is the therapeutic approach. Apart from observation, the therapeutic approach includes surgery, radioiodine, ethanol injection or, in perspective, new techniques such as interstitial laser photocoagulation or radiofrequency ablation. No guideline can give a robust indication in favor of one or the other option. Radioiodine therapy has been the preferred choice in past years, before the concept of nonfunctioning lymph node metastases was defined and demonstrated to occur

in nearly 50% of the patients. Nowadays, most centers advocate surgery as the first-line therapy. However, we have to balance the possibility of surgical complications with the evidence that a second operation rarely results in permanent cure of the neck. Local treatment options are very attractive. Good results have been reported with ethanol injection, but the above-mentioned new techniques seem even more promising and deserve confirmation with large prospective studies in the near future.

In conclusion, the European Thyroid Association guidelines for the use of cervical neck US provide a comprehensive framework for endocrinologists and radiologists taking care of thyroid cancer patients. In my opinion, the main message to be derived is the need to manage each patient according to his/her specific risk, thus modulating both diagnostic and therapeutic interventions according to proven clinical benefit.

### Disclosure Statement

The author has no conflicts of interest to disclose.

### References

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