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The clinical impact of a new highly sensitive thyroglobulin assay in low-risk patients treated for differentiated thyroid cancer

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Measurement of Thyroglobulin (Tg) in serum represents a high specific biomarker for the detection of residual functioning thyroid tissue and/or recurrence/metastases in following-up patients previously treated for differentiated thyroid cancer (DTC). Recently, several highly sensitive Tg assays have been developed but their real clinical benefit still remains largely undetermined.

Aim of the study was to evaluate the clinical impact of Tg values determined by a highly sensitive, rapid and practicable assay (Access) during L-T4 suppressive therapy in a group of 106 consecutive low-risk DTC-treated patients, submitted to routinely follow-up which included neck ultrasonography, \textsuperscript{131}I assay (Access) during L-T4 suppressive therapy in a group of 106 consecutive low-risk DTC-treated patients, submitted to routinely follow-up which included neck ultrasonography, \textsuperscript{131}I whole-body scanning and conventional Tg measurement (Immulite) before and after recombinant human TSH stimulation (rhTSH).

Undetectable (i.e. < 0.1 µg/l) Tg measured with Access assay has a very high negative predictive value (99%) of a Tg negative response (i.e. < 2 µg/l) to rhTSH test, similar to that of the classical assay Immulite which satisfies the parameters of functional sensitivity requested for Tg assays. At the same time, the presence of minimal amounts of measurable Tg, (i.e. > 0.1 but < 1 µg/l) during thyroid hormone (TH) suppressive therapy correctly identifies the majority of patients (90% of total) with a positive (> 2 µg/l) response to rhTSH; this at variance with the results obtained with the Immulite assay where only 40% of patients were correctly identified. In 18.7% of patients undetectable (i.e. < 0.1 µg/l) values of Tg Access during TH suppressive therapy were associated to a measurable response of Tg after rhTSH (i.e. > 0.5 µg/l) that still remains between the limit of a negative response (< 2 µg/l); this finding indicates that measurement of Tg by a highly-sensitive technique is not able to ameliorate the resolution of the clinical/analytical issue represented by minimal Tg response after rhTSH.

In conclusion, a highly-sensitive Tg assay may represent a useful diagnostic tool to better interpret Tg results during post-operative monitoring of low risk DTC patients on TH suppressive therapy and to optimize the execution of the expensive rhTSH test.

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Role of 18F-FDG PET and PET/CT imaging in thyroid cancer

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In patients affected by differentiated thyroid carcinoma (DTC), the lacking of \textsuperscript{131}Iodine trapping by metastatic tissue does not allow \textsuperscript{131}Iodine whole body scintigraphy to visualize metastatic spread as well as the use of \textsuperscript{131}Iodine therapy to cure such metastatic spread. Prognosis of \textsuperscript{131}Iodine-negative DTC metastasis, so-called non-functioning metastasis, is significantly worst. In these patients an early diagnosis of non-functioning metastasis and their surgical extirpation remains the optimal therapeutic approach. In this view, a high sensitive localizing imaging different form \textsuperscript{131}Iodine whole body scintigraphy is required. Ultrasonography is characterized by a relatively high sensitivity in these patients but it is highly operator-dependent and, moreover, it can be used to explore neck alone. CT scan and MR imaging are characterized by a relatively low sensitivity even if they are useful to provide the surgeon with anatomical information of the operating basin. Various tumor-seeking radiotracers have been proposed, mainly using SPECT as \textsuperscript{201}Thallium, \textsuperscript{99m}Tc-Sestamibi and \textsuperscript{99m}Tc-Tetrofosmin with good results. Even more favorable results have been reported with some positron radiotracers, mainly the \textsuperscript{18}F-FDG with PET and more recently with PET/CT tomographs. The typical indication to performing with examination is the DTC patient previously treated by total thyroidectomy and \textsuperscript{131}Iodine ablative therapy, with increased serum Thyroglobulin or anti-Thyroglobulin antibodies during follow-up but with negative \textsuperscript{131}Iodine whole body scintigraphy even obtained after high, therapeutic \textsuperscript{131}Iodine doses.

Several studies in literature have reported high sensitivity (up to 85%) and specificity (up to 95%) of FDG PET in metastatic DTC patients. The integrated PET/CT fusion imaging systems, seem able to provide some additional advantages over PET alone, mainly related to a better anatomical localization of the hypermetabolic metastatic lesions. A change in the management of DTC patients affected by non-functioning metastatic spread not visualized by other imaging techniques has been reported in 30% of patients. Lastly, the role of PET and PET/CT fusion imaging systems seem to be promising also in patients affected by medullary thyroid carcinoma, especially for the detection of neck and mediastinal lesions, with a sensitivity superior to the other currently available imaging methods, however the data reported on medullary cancer are little and further studies are needed to elucidate the preliminary promising results.

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What have we learned after 25 years of mibg use in neuroendocrine tumors?

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