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Perspective

Thyroglobulin an Informative Marker with Adjunctive FDG PET/CT in Management of Differentiated Thyroid Carcinoma

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Perspective

The aim of this review is to highlight the final situation of F-18 (florodeoxyglucose Positron Emission Tomography/Computed Tomography) FDG PET/CT examination and blood thyroglobulin (Tg) level in the management of the Differentiated Thyroid Carcinoma (DTC). The follow up algorithms of DTC are completely based on Tg examinations. Blood Tg levels reflect any tiny recurrences and/or metastasis related to DTC. Thus in the management of the patients with DTC Tg is the cornerstone marker in case of negative anti-Tg status. In case of high or increasing Tg levels without iodine accumulation the patients are referred to FDG PET/CT examination. However what kind of approach would be appropriate for the patients after definition of FDG positive focus is still not certain. Additionally there is still a debate about the FDG PET/CT indications in DTC patients; the cut-off values in stimulated or unstimulated states of Tg and lastly whether to perform empiric radioiodine treatment to iodine negative and FDG positive tumors or not.

The first issue is to determine the indications and interpretation of F-18 FDG PET/CT results in the patients with DTC. F-18 FDG accumulation in DTC reflects dedifferentiation, iodine negativity thus challenge in the treatment. Additionally it is clearly known that intensity of the FDG accumulation is directly related to the worse prognosis [1,2]. Usually it is accepted that there is a reverse relationship between FDG and iodine accumulation. However there may be lesions that concentrate both tracers. In a previous study the ratio of the patients with iodine and FDG positive lesions was 9% [3]. In a recent study including a selected patient population with positive doubling time of Tg this ratio was 25% [4]. In that study the researchers strictly recommend using doubling time of Tg as an important marker [4]. The most important therapeutic agent for DTC is I-131 and the treatment method is highly effective and curative. Since iodine negativity and FDG positivity points out the lesions that will not be able to take up iodine and previous studies have shown that these lesions has limited response to iodine treatment [5]; these patients will have unfavorable disease course. Most of the researchers however suggest performing therapy with guidance of dosimetry if it is considered [4,6,7].

Secondly the place of empirical radioiodine treatment or any focus in morphological analysis in patients without iodine accumulation in patients with DTC has to be determined. In a certain part of the patients with Tg elevation no intervention shows the focus including ultrasonography, iodine scan or F-18 FDG PET/CT. For these kinds of patients empiric treatment is an optional approach. Rosario et al. have performed empirical iodine treatment in patients without a documented focus in any diagnostic modality but who has elevating Tg levels in the long term follow up [8]. However neither Rosario et al. nor other researchers performing treatment in these patients could achieve significant iodine uptake in post treatment scan [8,9]. Although the clinical relevance is not known a drop in Tg levels might be achieved in these patients. In our small patient group also slight Tg decrease was obtained as well but it increased after a few moths follow up.

The cut-off limit for the Tg levels that has to be evaluated by F-18 FDG PET/CT is the third concern. There have been no accepted cut-off Tg levels previously in decision of indication of PET/CT. Most of the researchers have found positive association between Tg levels and FDG positivity [10,11]. However the relationship between FDG positivity and Tg levels is not documented clearly. Recently Vural et al. have suggested performing PET/CT in patients with Tg levels higher than 1.9 ng/mL in suppressive state and 38.2 ng/mL in stimulated state [12]. In their selected patient population they have reported sensitivity, specificity and accuracy of 94%, 100% and 93% respectively [12]. They additionally have analyzed prognostic factors related to FDG positive recurrences and concluded that extra thyroidal invasion was the most important factor [12]. Vural et al. additionally have determined that in case of presence of negative F-18 FDG PET/CT scan and Tg elevation with TSH stimulation; the likelihood for recurrence is low [12]. This important suggestion needs further evaluation and future prospective studies are warranted about this topic. We also performed PET/CT in low patients with low Tg levels in the follow up but did not reveal significant findings. However in the elevating Tg group there was significant findings in PET/CT. This observation was in accordance with previous studies [12].

Additional to these approaches some researchers have investigated the impact of FDG PET/CT in the management of patients with thyroid carcinoma and they did not select only Tg positive and iodine negative patients [13]. They have concluded that PET/CT might add information that cannot be obtained by other methods like ultrasonography or fine needle aspiration biopsy in detection of recurrent disease [13]. In their study the PET/CT results changed patient management in 24% of the patients while other previous reports have showed change in 14-57% of the patients [13-15]. They have suggested performing PET/CT as a follow up modality

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in patients with thyroid carcinoma whether the Tg is elevated or not [13].

In our department recently we prefer to perform PET/CT in just patients with significantly elevated Tg levels or elevating Tg levels. In fact we did perform PET/CT in patients with slightly elevated Tg levels and observed no remnant tissue previously. On the other hand increasing Tg levels is completely problematic because these metastasis or recurrences generally do accumulate FDG but not iodine and efficiency of empiric treatment is questionable thus it may be performed for once. Other treatment types like Sorafenib are not safe treatment methods as radioiodine and they have plenty of side effects thus they are generally recommended only in progressive and symptomatic patients.

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