LETTER TO THE EDITOR

Thyroid nodules with indeterminate cytology: is it safe to say ‘thyroidectomy can be excluded if ¹⁸F-FDG-PET suggests benignity’?

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Dear Editor,

We read with interest the article by Rosario *et al.*, published in the January 2021 issue of *Endocrine-Related Cancer* pages R1–R9, which summarized the practical applicability of accessible imaging method in the management of thyroid nodules with indeterminate cytology (TNIC) (Rosario *et al.* 2021). For ¹⁸F-FDG-PET, it was stated that ‘a nodule characterized by low or absent ¹⁸F-FDG uptake is considered at a very low risk of malignance’, and ‘thyroidectomy can be excluded if these tests suggest benignity’. We respectfully want to share a different opinion based on our previous work.

Hybrid ¹⁸F-FDG PET/CT is the current state of the art and represents a more objective and accurate technique compared to ¹⁸F-FDG PET alone. However, in our most recent meta-analysis, we found that the rule out performance of PET alone is significantly better than PET/CT (sensitivity, 0.95 vs 0.73; negative likelihood ratio, 0.20 vs 0.53; and negative predictive value, 0.99 vs 0.91) for TNIC (Qichang *et al.* 2020). This led us to the conclusion that ¹⁸F-FDG PET alone is overvalued in the literature and future studies should be performed with ¹⁸F-FDG PET/CT. At the same time, we hypothesize that the lack of precise localization of suspicious FDG uptake in the neck region (physiological or pathological tracer uptakes from the tonsils, pharynx, cervical lymph nodes, and other thyroid nodules mistaken as being attributed to a malignant TNIC which in fact had no FDG accumulation) might have largely contributed to this overvaluation for PET alone studies.

For ¹⁸F-FDG PET/CT, it is still not safe to say thyroidectomy can be excluded if it suggests benignity.

Our Fagan’s nomogram indicated that when the pretest probability (prevalence of malignancy) was assumed to be 24%, which is the median value of our included studies, the negative post-test probability decreased to 12% for a negative PET/CT scan. This is well above the risk of malignancy criteria for a cytology report to indicate benignity (<5%) (Haugen *et al.* 2016).

Nevertheless, we hope that ¹⁸F-FDG PET/CT will be progressively gaining space in the management of patients with TNIC. Integrating PET features into existing individualized risk prediction models might help to spare a patient with benign TNIC from thyroidectomy. However, such studies have not been published as far as we know.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this article.

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