Distinguishing between thyroid and parathyroid nodules by ultrasound: a potential game-changer in clinical practice?

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Thyroid nodules are highly prevalent in the general population, and the typical diagnostic approach involves a combination of palpation, neck ultrasound (US) and fine needle aspiration cytology (FNAC). US is an affordable, non-invasive method that does not expose the patient to radiation. Moreover, US can estimate the risk of malignancy in a thyroid nodule and triage cases for cytological investigation using various algorithms, such as Thyroid imaging Reporting Data System (TIRADS).[1] Similarly, patients with hyperparathyroidism may also undergo US examinations to locate an enlarged gland.[2] Given the common occurrence of thyroid nodules, it is not unusual for a patient with hyperparathyroidism to also exhibit thyroid nodules, which may result in inaccurate clinical decisions if a parathyroid gland is erroneously identified as a thyroid nodule. This misidentification is more likely to happen in nodules situated in the posterior aspect of the thyroid lobes or in intrathyroidally located parathyroid tumors. The lack of established US criteria for distinguishing a thyroid nodule from an enlarged parathyroid gland is therefore a clinical dilemma.

In *The Lancet Regional Health–Europe*, Yazgi and colleagues have detailed the ultrasound characteristics of 176 parathyroid lesions from 158 patients and 232 thyroid nodules from 204 patients attending a tertiary referral center in France, where cases were carefully matched for size, volume, age, and sex within the study groups.[3] The authors conducted US examinations to characterize all lesions, assessing nodular size, volume, morphologic patterns, content, echogenicity, and vascular features. Lesions were confirmed for their parathyroid origin through FNAC (with intranodular PTH measurements) and/or histopathological examination following surgical excision.

Striking differences in morphological patterns between parathyroid and thyroid neoplasms were noted (Fig. 1). Most thyroid nodules exhibited oval or round shapes, in sharp contrast to parathyroid neoplasms, which were often teardrop-formed (dacryoid) or displayed triangular shapes. In terms of echogenicity, parathyroid lesions were significantly more hypoechoic compared to thyroid nodules, whereas completely anechoic patterns and cystic textures were suggestive of thyroid nodules. Thyroid nodules more often exhibited peripheral vascular spots, whereas parathyroid lesions were enriched for intranodular spots. Combining findings of a non-round shape, hypoechoic (but not anechoic) patterns and intranodular vascular signals rendered a positive predictive value of 96% to safely separate a parathyroid lesion from a size- and volume matched thyroid nodule.

Notably, several of the above-mentioned US parameters found to be overrepresented in the parathyroid cohort are also high-risk US attributes suggestive of thyroid malignancy. Thus, there is a notable risk of misclassifying parathyroid lesions as high-risk thyroid nodules when applying thyroid-based risk assessment criteria—demonstrated in this study by the finding of 2 or 3 high-risk US criteria in the majority of parathyroid lesions.[3] Thus, the importance of correctly identifying a lesion as parathyroid-derived must not be overlooked, as it otherwise could lead to erroneous decisions in patient management. As many cytologists often rely solely on the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), instead of utilizing a combination of morphology and molecular panels (which frequently involve the analysis of parathyroid mRNA), there is an undeniable risk of misdiagnosing parathyroid lesions as thyroid tumors.[4] Several studies have pinpointed the difficulties in separating follicular thyroid tumors from parathyroid adenoma using FNAC only, and often advocate the use of intralesional PTH measurements, or immunocytochemistry using TTF1, GATA3 and/or PTH.[5,6]

The study has additionally identified distinct differences in US parameters among various parathyroid lesions, offering potential clues for the clinical team in reaching a final diagnosis.[3] For instance, parathyroid adenomas were characterized by larger dimensions and a higher incidence of intranodular vascular signals when contrasted with multiglandular parathyroid conditions and hyperplasia. Moreover, atypical parathyroid tumors (tumors with worrisome histological features

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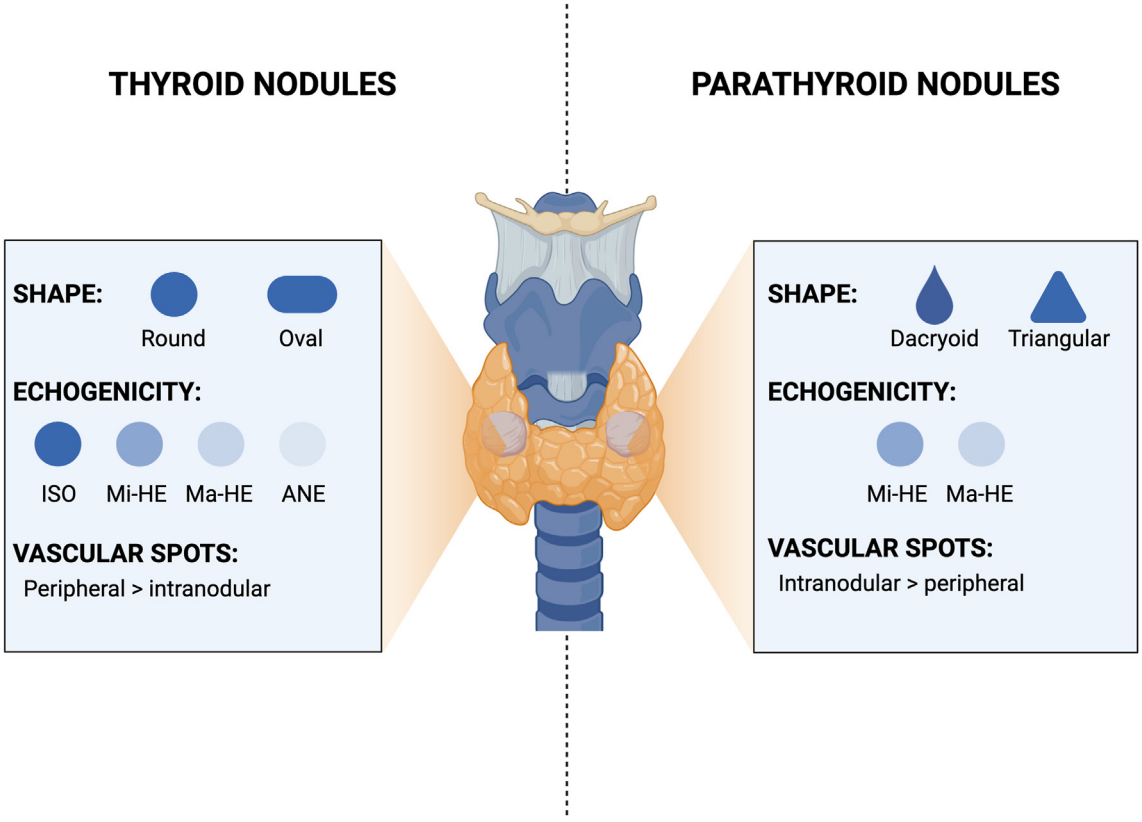

Fig. 1: Differences in ultrasound characteristics of size- and volume-matched parathyroid and thyroid nodules from age- and sex-adjusted patient cohorts. Parathyroid lesions were significantly more often non-oval in shape, which was in contrast to thyroid nodules. Moreover, parathyroid nodules often displayed mild or marked hypoechoic (Mi-HE/Ma-HE) patterns as opposed to thyroid lesions that in addition exhibited isoechoic (ISO) and anechoic (ANE) features. Finally, intramodular vascular spots were significantly associated to parathyroid nodules. Created using BioRender.com.

but not fulfilling criteria for malignancy) were consistently larger than conventional adenomas.[7]

An interesting question is whether the application of the herein described diagnostic nuances of thyroid and parathyroid nodular disease can be expected to be adopted also by all non-radiologists who perform neck ultrasound on a nearly daily basis. Can we expect the endocrinologists and surgeons to reach the same accuracy as would be expected by the expert radiologist? This may have implications for responsibility discussions: must all these patients be investigated by a radiologist, with possible overuse of limited resources? Is there a minimum level of education and numbers of investigations required before decision-making for or against surgery should be allowed?

The study of Yazgi et al. holds several clinical implications.[3] Most notably, the findings offer the potential for ultrasound operators to more accurately distinguish between thyroid and parathyroid nodules based on parameters like shape, echogenicity, and vascularity. Furthermore, the idea that parathyroid lesions not correctly identified during the assessment of a neck nodule might display ultrasound features indicating a high risk of malignancy through the TIRADS algorithm, can contribute significantly to our comprehension of misdiagnosis, emphasizing the need to rule out the possibility of a parathyroid origin.

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Declaration of interests
The authors have no conflicts of interest to disclose.

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