Background: Ultrasonography has become an essential tool for the evaluation and management of thyroid and parathyroid diseases. Its applications extend beyond neck endocrine conditions to a multitude of pathologies within the head and neck region.

Objectives: Our study aimed to: (1) provide a broad review of neck ultrasonography and key findings in neck endocrine diseases; (2) support skilled performance office-based diagnostic ultrasonography and its varied applications.

Materials and methods: A review of the current literature was supplemented with clinical examples of key ultrasonographic findings.

Results: Current applications and key findings of ultrasonography in the diagnosis and management of neck endocrine conditions are reviewed.

Conclusion: Ultrasonography is a fundamental component in the evaluation and management of neck endocrine diseases. The reader is encouraged to use this review to enhance office-based performance and application of ultrasonography.

Keywords: Imaging · Ultrasound · Head · Neck · Endocrine

Ultrasonography (US) has a well-established role in the diagnosis and management of conditions of the thyroid and parathyroid glands and has increasing relevance for nonendocrine neck conditions. Once under the purview of radiologists, US has become a central feature of clinical practice for many surgeons and endocrinologists. Its versatility, favorable safety profile, ability to deliver real-time imaging, and low cost compared to other radiologic modalities have contributed to its widespread adoption [1].

Background

Since the initial application of US to thyroid evaluation in the 1960s, US technology has undergone a remarkable evolution with significant improvements in imaging quality as well as the development of more compact and user-friendly equipment [2]. Modern US devices utilize a transducer that functions as both a transmitter and receiver for the production and detection of ultrasound waves. Underlying this is the piezoelectric effect, in which application of an alternating voltage to crystals embedded in the transducer causes their mechanical deformations and produces pulsed ultrasound waves. Optimized use of US technology and interpretation of US images requires a basic understanding of the underlying physics of US, including imaging artifacts produced by physical properties of US, which are outside the scope of this article.

While US has become most recognized for its role in the diagnostic evaluation and management of thyroid and parathyroid disease, US applications extend to a multitude of pathologies within the head and neck, including salivary gland disorders, adult and pediatric neck masses, and assessment of laryngeal function. Furthermore, US-guided diagnostic procedures include fine-needle aspiration and core-needle biopsy. These methods have similar diagnostic efficacy [3]; preference for one approach over the other is often re-
Thyroid ultrasonography

Familiarity with the appearance of the normal thyroid gland and its surrounding structures enables an appreciation of thyroid pathology. The normal thyroid gland in the low midline neck is readily identified by its homogeneous gray appearance (Fig. 1). The thyroid isthmus appears crescent-shaped as it courses over the trachea, whose hyperechoic cartilaginous rings contain an anechoic interior. The examiner may take note of a paramedian pyramidal lobe coursing cranially, as well as thyroglossal duct remnants most often found just superior or inferior to the hyoid bone. The overlying sternothyroid and sternohyoid muscles appear hypoechoic to the thyroid; the superficial layer of the deep cervical fascia investing the strap musculature appears as thin hyperechoic lines. The esophagus usually protrudes to the left of the trachea and appears as concentric hyperechoic rings (Fig. 1). The thymus is typically atrophic in adults but can be seen inferior to the thyroid in younger patients and appears hypoechoic with bright internal punctate reflectors, an appearance that can be mistaken for metastatic papillary thyroid carcinoma (PTC).

The thymus is typically atrophic in adults and not readily seen on US

The relatively superficial position and soft tissue composition of the thyroid make it well-suited to US examination. An US evaluation can confirm the presence of a nodule, objectively characterize a nodule's size, location, and appearance, assess for benign or suspicious features, and evaluate for the presence of other thyroid nodules or cervical lymphadenopathy [6]. Nodule characteristics that should be evaluated to assess risk of malignancy include echogenicity, composition, shape, margins, presence of calcifications, and associated lymphadenopathy.

Echogenicity

The echogenicity of a nodule is characterized relative to the appearance of normal thyroid tissue and the adjacent neck muscles [7]. Hypoechoic nodules are darker than normal thyroid; most malignancies are hypoechoic but hypoechoogenicity is not specific for malignancy, as many benign nodules are hypoechoic, especially mildly so [6]. Rather, nodules that are moderately to markedly hypoechoic have an increased likelihood of being malignant [7, 8]. Isoechoic nodules have similar echogenicity to normal thyroid; hyperechoic nodules appear brighter than normal thyroid. Isoechoic and hyperechoic nodules are less likely to be malignant although when proven to be malignant are often of the follicular-type (follicular carcinoma, Hurthle cell carcinoma, follicular variant of PTC [9-11]).
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A nodule may be solid, cystic, or a combination, referred to as “predominantly solid” or “predominantly cystic.” Malignant nodules are more often solid in composition. Nodules that have an internal microcystic appearance comprising more than 50% of the volume of the nodule are termed “spongiform” and are characterized as benign, as are purely cystic nodules [12,13].

Shape

A growth pattern demonstrating a “taller-than-wide” appearance (defined as an anteroposterior [AP] diameter that exceeds the transverse [T] diameter when imaging the thyroid in the transverse plane) is predictive of malignancy [14–18]. The basis for this finding is not well understood, although it has been proposed to relate to how normal versus cancerous nodules grow along tissue planes [8]. More recent analysis of shape in the transverse plane has highlighted its susceptibility to intraobserver and inter-observer variability and proposed the use of a slightly higher AP/T ratio or a multilevel rather than binary variable to improve specificity for malignancy without losing diagnostic performance [18,19].

Margins

Evaluating the interface of a nodule with the surrounding thyroid parenchyma and thyroid capsule is important for stratifying risk of malignancy. Smooth and well-defined margins are reassuring, whereas irregular, spiculated, or infiltrative margins suggest malignancy. Importantly, nodules with irregular or infiltrative margins should be differentiated from nodules with indistinct margins that are difficult to discern from surrounding thyroid, as the latter is not associated with increased risk of malignancy [20].

Calcifications

Several types of calcifications can be seen in both benign and malignant nodules (Fig. 2). Microcalcifications are small (<1 mm) echogenic foci that are highly associated with malignancy, usually PTC, with a specificity of over 90% [21–23]. The term “punctate echogenic foci” (PEF) has recently supplanted the term “microcalcifications” owing to the fact that not all such foci are calcifications (e.g., they can represent colloid, amyloid, or other granulomatous or reflective material). Macrocollections are coarse calcifications (>1 mm) demonstrating posterior acoustic shadowing that occurs when all US waves are reflected back, unable to penetrate the calcium deposit. When coexistent with microcalcifications, coarse calcifications are highly associated with thyroid cancer, but their presence alone is not consistently associated with malignancy [22–24]. Peripheral rim calcifications, or “eggshell calcifications,” may be seen in both benign and malignant nodules; however, the presence of an “interrupted” rim calcification caused by tumor extruding through the calcification should raise concern for malignancy [25,26].

Associated lymphadenopathy

The neck compartments should be evaluated for the presence of abnormal lymph nodes, since locoregional metastatic disease is common in thyroid cancer [6]. Notably, detection of abnormal paratracheal nodes can be difficult in the presence of the thyroid gland. By contrast, the sensitivity of US for the detection of lateral neck metastasis is high, up to 93% in thyroid malignancy, with a specificity of up to 84% [4,27]. The finding of suspicious nodes may influence the decision to perform lymph node FNAB, which may be accomplished in lieu of thyroid biopsy.

The sensitivity of US in detecting lateral neck metastasis is high

The correlation of US features with risk of malignancy has led several professional groups, including the American Thyroid Association (ATA), American College of Radiology (ACR), European Thyroid Association (ETA), and Korean Society of Thyroid Radiology (KSThR), to develop tiered scoring systems for stratifying risk and establishing size cutoffs for FNAB recommendation [6,28–30]. These guidelines focus on the presence or patterns of sonographic characteristics and are similar but nonidentical in their classification systems. Malignancy risk estimates based on sonographic appearance are closely aligned between the systems but size thresholds for biopsy differ. Since no single US finding represents a sine qua non for thyroid cancer, it is the pattern or constellation of features that informs risk classification. The ACR Thyroid Imaging and Reporting Data System (TIRADS) quantifies risk by assigning points to individual features, with more suspicious features being assigned additional points; risk level is determined by summation of points for a given nodule. The ATA classification system, EU-TIRADS, and K-TIRADS do not use a point system but similarly categorize risk based on the presence of select features. These systems have enhanced the consistency and universality of thyroid ultrasound reporting, while continuing to undergo modification.
Papillary thyroid carcinoma

The US features typical of PTC include a solid, hypoechoic lesion with microcalcifications or PEF (Figs. 2a and 3a). Microcalcifications are highly specific for PTC, and are favored to represent psammoma bodies [32] (tiny laminated, spherical collections of calcium which appear as tiny bright foci)—a histopathologic feature considered pathognomonic for PTC—or, less often, crystalline colloid. Cystic components may be present within a solid lesion. Margins are irregular or lobulated and taller-than-wide morphology is often present. Doppler examination is inconsistent but may reveal disorganized hypervascularity.

Follicular carcinoma

Follicular neoplasms, both benign and malignant, are typically solid, and can be hyperechoic, isoechoic, or hypoechoic lesions (Fig. 3b), the latter sometimes with a halo—a rim of decreased echoes around the nodule. Cystic components and calcifications are rare. Hypervascularity is common and FNAB samples are often bloody.

Hürthle cell carcinoma

The US characteristics of Hürthle cell carcinomas are similar to follicular neoplasms. These tumors tend to be solid with hyperechoic and hyperechoic components. An irregular border may sometimes be seen. Neither calcifications nor a halo is typically present.

Medullary thyroid carcinoma

The US appearance of medullary thyroid carcinoma (MTC) shares some features of PTC. Medullary thyroid carcinoma appears solid and hypoechoic and frequently has PEF representing both amyloid deposition and calcification (Fig. 3c). These foci may also appear within affected lymph nodes. Doppler examination may reveal disorganized hypervascularity.

Anaplastic thyroid carcinoma

The US findings of anaplastic thyroid carcinoma include a markedly hypoechoic lesion infiltrating the entire thyroid lobe with areas of necrosis or ill-defined calcifications (Fig. 3d). Involved lymph nodes may also exhibit necrotic changes. Invasion into surrounding vessels or soft tissue is often seen.
Lymphoma

The US appearance of lymphoma varies and may include a focal lesion within a lobe or diffuse abnormality involving the entire gland. The involved tissue is usually heterogeneous and hypoechoic and may be mistaken for anaplastic carcinoma. Posterior enhancement of the gland may be seen, owing to differences in acoustic impedance with the surrounding soft tissues. Associated lymph nodes appear large, round, hypoechoic, and hypervascular.

The thyroid is prone to developing multiple, often coalescent nodules

Thyroid US can aid in the diagnosis of benign thyroid diseases through evaluation of glandular size, echotexture, nodularity, and vascularity. Characteristic features may be seen in some conditions described in the following sections.

Chronic lymphocytic thyroiditis

The US findings of chronic lymphocytic thyroiditis, or Hashimoto’s thyroiditis, include patchy poorly defined hypoechoic areas resulting from accumulation of lymphoid tissue. Inflammatory changes alter thyroid architecture and generate heterogeneity and the appearance of “pseudonodules,” or hyperechoic and poorly demarcated regions sometimes separated by hyperechoic septations. Vascularity may be increased early and decreased late in the disease course. In later stages, the atrophied gland appears shrunken and imparts a “honeycomb” appearance. Central neck adenopathy may be prominent as a result of increased local immune activity and may be difficult to distinguish from small malignant lymphadenopathy.

Graves’ disease

The US features of Graves’ disease include diffuse thyroid enlargement, a thickened thyroid isthmus, heterogeneous hypoechogenicity, and hypervascularity. The hypoechoic appearance corresponds with increased vascular flow, increased cellularity, and lymphocytic infiltration [33]. Increased flow is also noted through the inferior thyroid artery.

Benign thyroid nodules

Most nodules are nonneoplastic, hyperplastic, or adenomatous nodules, consisting of follicular cells and colloid. Aggregates of colloid have a characteristic US appearance as bright echogenic foci with reverberation artifact in which echogenic lines of decreasing width appear posterior to the reflector. This so-called comet-tail sign distinguishes colloid from microcalcifications or other PEF. Spongiform appearance, as discussed earlier, is characteristic of benign nodules (Fig. 4). Follicular adenomas are benign neoplasms that present as homogeneous hyper-, iso-, or hypoechoic well-encapsulated round lesions, often with a halo sign distinguishing them from normal surrounding thyroid tissue. Nodules that are purely cystic are nearly uniformly benign and FNAB is not indicated, as nondiagnostic rates are high. Cystic lesions with a solid component requiring biopsy should undergo US guidance for any FNAB to ensure sampling of the solid component.

Multinodular goiter

The thyroid is highly prone to developing multiple, often coalescent nodules, and the primary goal in the evaluation of multinodular goiter is to identify whether there are any suspicious outliers within a gland full of otherwise benign change (Video 5). With increasing gland size comes decreasing accuracy of measurement. One should consider complementary cross-sectional imaging to more fully evaluate thyroid extent and impact, especially if substernal extension is suspected.

Parathyroid ultrasonography

High-resolution US is extremely useful for localizing abnormal parathyroid glands in patients with hyperparathyroidism. The success of US localization depends on the experience (and arguably, the motivation) of the examiner, with sensitivities for correct side and quadrant localization that exceed the performance of sestamibi scanning [34, 35]. In addition to its lower cost and ease of use, office-based US offers greater anatomic detail for preoperative planning, facilitating performance of focused parathyroidectomy. Furthermore, it allows for identification of coexistent thyroid pathology that may be managed concurrently.

Normal parathyroid glands are difficult to identify on US, owing to their small size and subtle US characteristics [36]. A recent investigation suggests that normal parathyroid glands can in fact sometimes be seen on US as small oval homogeneously hyperechoic structures ([37]; Fig. 5a). By contrast, abnormal hypercellular parathyroid glands characteristically appear as hypoechoic well-circumscribed ovoid structures (Fig. 5b), although a variety of shapes may be seen and the degree of hypoechogenicity may be variable. Parathyroid adenomas typically have a polarc blood vessel that terminates near the capsule in the gland; its identification can be useful in differentiating a parathyroid adenoma from reactive lymphadenopathy, which is characterized by the presence of a hyperechoic fatty hilum [38]. Hyperplastic parathyroid glands similarly appear as hypoechoic ovoid structures; hyperplastic glands identified in the setting of longstanding secondary or tertiary hyperparathyroidism may demonstrate nodularity that gives the appearance of irregular borders. Calcifications within the gland may also be seen [38].

Skilled localization of abnormal parathyroid glands is predicated on knowledge...
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Normal parathyroid glands are sometimes detectable, appearing as small oval homogeneous hyperechoic structures (left inferior parathyroid gland, transverse and sagittal views, open arrows). Trachea, CCA common carotid artery. Hypercellular parathyroids (both adenomas and hyperplastic glands) usually appear as hypoechoic well-circumscribed ovoid structures (left inferior parathyroid adenoma, transverse and sagittal view). LN adjacent benign lymph node of parathyroid embryologic development. The superior parathyroid glands develop from the fourth branchial pouch and are usually located on the posterior aspect of the thyroid gland near the cricothyroid joint, dorsal to the recurrent laryngeal nerve (RLN). By contrast, the inferior parathyroid glands develop from the third branchial pouch, travel with the thymus, and have a relatively longer and more variable path of migration inferiorly. The inferior parathyroid glands may be located at the level of the inferior thyroid lobe on the anterior or posterolateral surface, along the thyrothymic ligament or within the thymic tongue at the thoracic inlet. The inferior parathyroid glands are situated ventral to the RLN. Notably, because the inferior and superior glands cross paths during embryologic migration, the inferior gland may be located cranial to the superior gland or the two glands may be found in close proximity.

Ectopic parathyroid glands result from abnormalities of embryologic migration. Failure of the inferior gland to descend may result in a location within the submandibular triangle or carotid sheath. On the other hand, failure of the inferior parathyroid gland to separate from the thymus may result in a location within the chest, often within the retrosternal thymus. Ectopic superior parathyroid glands may be found above the superior pole of the thyroid, near the carotid artery, in the retropharyngeal/retroesophageal space, or even within the pyriform sinus. Both inferior and superior parathyroid glands may be intrathyroidal in their location. Enlarged superior parathyroid glands may descend into the upper mediastinum through a combination of gravity, favorable tissue planes, and swallowing movements thought to contribute to downward displacement. Importantly, these overly descended superior glands retain their dorsal relationship to the RLN, which may lead to inadvertent RLN injury if the surgeon fails to recognize the superior origin of the gland. The inferior thyroid artery or posterior surface of the carotid artery approximate the plane of the RLN; taking notice of the depth of the adenoma candidate relative to these structures on US examination can alert the surgeon to this possibility.

When localizing enlarged parathyroid glands, the examiner initially directs attention to the regions posterior and inferior to the thyroid gland between the carotid artery and the trachea; the transducer should be tilted at the sternal notch to examine the superior mediastinum. Scanning should be undertaken in a transverse plane (Video 6); longitudinal imaging should be used to interrogate structures of interest and assess craniocaudal position (Video 7). Depth, frequency, and focal adjustments may be made on the US system to optimize imaging of deeper planes. When an enlarged gland is not identified in an expected location, ectopia should be considered. However, ectopic glands located within the retropharyngeal or retroesophageal space may be difficult to visualize, as US waves do not pass through the air-filled structures that lie anterior to these spaces. Similarly, ectopic glands located behind bone within the chest cannot be visualized with neck US.

**Neck ultrasonography**

As noted in the previous section, US may be applied to the evaluation and management of many conditions that extend beyond the endocrine glands of the neck. The full scope of US applications cannot be covered here; instead, some additional applications beyond the thyroid and parathyroid glands related to the management of neck endocrine disease are discussed.

**Lymph node evaluation**

For patients with known or suspected thyroid cancer, US remains the most important imaging modality; its application should include assessment of the cervical lymph nodes to guide the need for compartment-based nodal dissection (Videos 8, 9). The sensitivity of ultrasound for detecting metastatic disease varies in the literature, and is highly operator-dependent, but is generally higher in the lateral neck (53–100%) than in the central neck...
Benign ovoid level 2 lymph node with central hyperechoic linear hilum (left panel, transverse view) and minimal superimposed hilar flow on power Doppler (right panel, sagittal view). By contrast, rounded lymph node with metastatic papillary thyroid carcinoma, lacking visible hilum, with irregular margins and internal echogenic material (arrow). Despite the presence or absence of a visible hilum, the fatty hilum carries the blood supply of the node and appears as a central hyperechoic linear structure within a benign hypoechoic node. Use of color or power Doppler reveals a hilar vascular pattern, or no flow at all, in benign nodes. When nodal architecture is disrupted and angiogenesis occurs due to tumor, the hilum may be destroyed and vascularity becomes disordered and diffuse. As such, the presence of a clear echogenic hilum is highly sensitive in predicting benign cytology upon FNAB ([47]; Video 10).

Salivary gland ultrasonography

The superficial anatomic location of the major salivary glands is well-suited for US evaluation ([48]; experienced clinicians can frequently examine and interpret findings without the need for more costly cross-sectional imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI)). Moreover, US may be used to evaluate the full spectrum of salivary gland pathology, including infectious, inflammatory, neoplastic, and calculous disease.

Normal salivary glands have a homogeneous echotexture that is similar to the normal thyroid gland. The parotid gland lies anterior to the ear and sternocleidomastoid muscle, overlying the mandible and masseter muscle. It is divided into
Artificially induced sialadenitis [50, 51]. Initial pain and swelling associated with salivary duct constriction may occur; later development of chronic sialadenitis is marked by parenchymal destruction and fibrosis as well as fatty degeneration and atrophy [51, 52]. Ultrasonographic features of RAI-induced sialadenitis include decreased glandular size, coarse echotexture with decreased echogenicity, and lobulated margins [52]. Notably, these changes may not correlate with the degree of xerostomia experienced [53].

Assessment of vocal fold mobility

Perioperative assessment of vocal fold function is regarded as an essential component of care in thyroid and parathyroid surgery [6, 54–57]. The US assessment of vocal fold mobility, when compared with the gold standard of fiberoptic laryngoscopy, has a reported sensitivity and specificity for detecting motion abnormalities ranging of 53.8–93.3% and 50.5–97.8%, respectively [58–60]. Adequate assessment of vocal fold mobility may be obtained in patients with favorable anatomy; gender and age impact successful visualization such that older men are often more difficult to image due to the shape and calcification of the thyroid cartilage [55, 60]. Further, US assessment may have special utility in resource-limited settings where laryngoscopy is not available. Its use has also become relevant during the COVID-19 pandemic where aerosol-generating procedures such as laryngoscopy pose potential infectious risk to clinicians [61].

» US assessment may have special utility in resource-limited settings

The technique for laryngeal evaluation involves placement of a linear transducer with ample gel at the vertical midpoint of the thyroid cartilage or inferior to it in the cricothyroid region with the transducer angled superiorly. Reducing frequency to the 7–8-MHz range improves sound penetration. Vocal fold abduction and adduction are best visualized during respiration (Video 11). Assessment during phonation is difficult due to laryngeal movement, but maneuvers such as breath-holding and whistling may facilitate evaluation. The true vocal folds appear as hypoechoic muscle with a fine hyperechoic line at the free mucosal edge. The false vocal folds contain fatty connective tissue and appear hyperechoic; similarly, the arytenoid cartilages are hyperechoic and may be assessed for symmetry and movement.

Practical conclusion

- Ultrasound (US) has an essential role in the management of thyroid and parathyroid disease with applications that extend to a multitude of pathologies within the neck.
- Expertise in the use of US is gained through repetitious practice in the clinical setting; familiarity with normal anatomy is imperative for thorough and accurate performance of diagnostic US.
- Recently, there has been growing interest in interventional US procedures, including ablation procedures to treat conditions of the thyroid.
- It is important to recognize that safe and successful execution of these procedures is predicated on skilled performance of diagnostic US and familiarity with normal sonographic head and neck anatomy.
- The clinician who builds a strong foundation of diagnostic US in all of its varied applications will be well-positioned to incorporate interventional procedures into practice.
Zusammenfassung

Sonographie der Schilddrüse, der Nebenschilddrüsen und darüber hinaus

Hintergrund: Die Sonographie ist zu einem wesentlichen Instrument für die Beurteilung und Behandlung von Schilddrüsen- und Nebenschilddrüserkrankungen geworden. Ihre Anwendung geht über den Bereich endokriner Erkrankungen des Halses hinaus bis hin zu einer Vielzahl pathologischer Veränderungen in der Kopf-Hals-Region.

Ziel: Die vorliegende Studie zielte darauf ab, (1) einen umfassenden Überblick über die Halssonographie und die wesentlichen Befunde bei endokrinen Erkrankungen im Halsbereich zu geben; (2) die qualifizierte Durchführung der diagnostischen Sonographie in der Praxis und ihrer verschiedenen Anwendungen zu unterstützen.

Material und Methoden: Dazu wurde ein Überblick über die aktuelle Literatur ergänzt durch klinische Beispiele wesentlicher sonographischer Befunde.

Ergebnisse: Aktuelle Anwendungsbereiche und wesentliche sonographische Befunde in der Diagnose und Behandlung endokriner Erkrankungen werden besprochen.

Schlussfolgerung: Die Sonographie ist ein grundlegender Bestandteil bei der Beurteilung und Behandlung von endokrinen Erkrankungen im Halsbereich. Die vorliegende Übersicht soll dem Leser dazu dienen, die Durchführung und Anwendung der Sonographie in der Praxis zu verbessern.

Schlüsselwörter
Bildgebung · Ultraschall · Kopf · Hals · Endokrin
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