18 The Use of Ultrasonography in the Management of Parathyroid Diseases

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Abstract

Ultrasound affords certain key advantages in general and specifically for parathyroid disease management. It can be readily performed in the office and even portably in the operating room, allows real-time examination that is noninvasive and comfortable for the patient, identifies co-existing thyroid pathology that may require treatment, and can be performed by a clinician who is evaluating the patient with access to all relevant clinical information. Recognizable sonographic features allow identification of abnormal parathyroid glands, can be readily learned, and make ultrasound a powerful tool especially when performed by clinicians with access to comprehensive information about the patient's parathyroid disease. Ultrasound can guide appropriate interventions to clarify challenging diagnostic scenarios, although ultimately it should not be viewed as a diagnostic test for hyperparathyroidism. It has a demonstrated history of valuable clinical use.

The following review highlights these advantages, describes the technical and anatomical findings expected with parathyroid ultrasound, relates the specific indications for its use, and presents an overview of reported performance as a localizing study in the management of hyperparathyroidism.

Keywords

Ultrasonography • Mibi scan • Parathyroid • Hyperparathyroidism • Ultrasound

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The Modern Context of Parathyroid Ultrasound

Neck ultrasound evolved into its current role as the primary imaging modality for the evaluation of thyroid diseases and thyroid cancer over the last decade [1]. During this time period, ultrasound has also become an increasingly used tool in the management of parathyroid diseases. A query of publications indexed with the US National Library of Medicine shows fewer than 80 devoted to ultrasound and parathyroid disease in the period 1990–2000, compared to nearly 900 in the decade since[2]. Viewed from the vantage point of modern-day parathyroid surgery, this application of ultrasound is not surprising and has come as part of a paradigm shift in the treatment of primary hyperparathyroidism. Although ultrasound as a technology was available in the 1980s, the philosophy of treating parathyroid disease was quite different. Symptomatic patients with obvious primary hyperparathyroidism constituted the vast majority of those with parathyroid diseases. Operative rather than medical treatment was logical and rarely questioned, and the strategy at surgery was a mandatory four-gland parathyroid exploration with removal of the gland or glands which appeared abnormal. Parathyroid localization procedures were rarely used, since surgery was successful in >95% of patients without them [3, 4].

A sequence of technological innovations occurred by the mid-1990s to change the paradigm from bilateral parathyroid examination to focused surgery targeted to a single area of suspected parathyroid disease [5]. These innovations included the use of other radiologic modalities, most notably 99-technetium Sestamibi (Mibi) scans, and the intraoperative measurement of parathyroid hormone (PTH) as a metric of disease cure [6, 7]. Additionally, the landscape of parathyroid disease broadened to include significantly more patients with incidentally discovered, asymptomatic hyperparathyroidism for whom the benefits of surgery came be viewed as controversial, prompting the development of treatment guidelines [8–11]. It is in this context and from the need for reliable, noninvasive localization methods that ultrasound was incorporated into the management of parathyroid disease.

It is also not surprising, then, that surgeons have in large part driven the use of ultrasound in parathyroid disease [12–20]. Most patients with endocrine diseases, such as primary hyperparathyroidism, have received extensive biochemical diagnostic evaluation before referral to a surgeon. Indeed, ultrasound is not a diagnostic tool for primary hyperparathyroidism, but a tool to refine intended surgical treatment. Surgeons bring unique dimensions to a parathyroid ultrasound examination: images are interpreted by those who encounter the relevant anatomy daily and directly in the operating room and can recognize subtle findings; available to them are the full history, physical exam, and laboratory findings to complete an assessment of hyperparathyroidism; and the ultrasound images can give a mental picture of expected findings in the operating room for that particular patient. Not all surgeons perform parathyroid ultrasound. That expertise may reside with other specialists as well, whose contributions are essential and enormous in providing valuable information to guide patient care, particularly in collaboration with other treating physicians [21–24].

Ultrasound affords certain key advantages in general and specifically for parathyroid disease management. It can be readily performed in the office and even portably in the operating room, allows real-time examination that is noninvasive and comfortable for the patient, identifies coexisting thyroid pathology that may require treatment, and can be performed by a clinician who is evaluating the patient with access to all relevant clinical information. The following review highlights these advantages, describes the technical and anatomical findings expected with parathyroid ultrasound, relates the specific indications for its use, and presents an overview of reported performance as a localizing study in the management of hyperparathyroidism.

Equipment and Technique of Parathyroid Ultrasound

Parathyroid ultrasound should be performed with a high-resolution, real-time ultrasound with both gray scale and color Doppler resolution. Because of the relatively superficial location of the thyroid and parathyroid glands, the anatomic imaging can be remarkably detailed. Although a variety of ultrasounds are commercially available, a key feature is the use of high-frequency transducers at 7.5–15 MHz. These can be linear or small curvilinear ("fingerprint") transducers. Other helpful features of the ultrasound equipment include the ability to adjust focal zones, the ability to evaluate the vascular pattern of the abnormal findings with the color Doppler function, and the ability to store images for documentation.

For ultrasound examination, the patient is positioned supine with a small pillow below the shoulders to achieve gentle extension of the neck, mimicking the position during surgery (Fig. 18.1a, b). This allows abnormally enlarged parathyroids that reside in deeper neck planes to be brought into more prominent view on ultrasound. Parathyroid abnormalities can be appreciated upon even further degrees of neck hyperextension achieved during surgery in an anesthetized patient, which might be impractical or uncomfortable during an office-based exam. This supports the virtue of repeating a parathyroid ultrasound in the operating room, especially if office-based ultrasound was negative, and demonstrates its versatility as a stethoscope-like tool. The sonographer usually stands on the patient's right side (as illustrated in Fig. 18.1b) and faces the ultrasound machine.

The region of the thyroid and the central neck should be examined in transverse and longitudinal planes (Fig. 18.2a, b). The lateral cervical regions, particularly along the carotid and jugular vasculature and the region adjacent to the submandibular gland, should likewise be examined, for the purpose of identifying ectopic parathyroids (Fig. 18.2c). For the same purpose, tilting the transducer toward the upper mediastinum can identify abnormal parathyroids in the upper mediastinum or cervical thymus. As with thyroid ultrasound, the sequence of examination should ideally be performed in a step-wise and systematic fashion that visualizes all anatomic regions of the thyroid and immediately adjacent soft tissue. Additionally, regions along the posterior border of the thyroid, and the paratracheal, retroesophageal, and pretracheal spaces, require careful evaluation. In these regions, graded pressure or a balloting motion applied by the

Fig. 18.1 Patient positioning for parathyroid ultrasound examination in an office-based setting (**a**) and in the operating room (**b**)

Fig. 18.2 Ultrasound examination is oriented in transverse (**a**) and longitudinal (**b**) planes in the area immediately adjacent to the thyroid. To detect abnormal parathyroid glands in ectopic cervical regions, the lateral aspects of the neck (**c**) along the carotid and jugular vasculature (*line*) and submandibular glands (*smg*) should also sonographically imaged, and the probe directed toward the upper mediastinum (*med*) as well

transducer can sometimes cause an abnormal parathyroid to "pop out" or shift with respect to surrounding structures. Swallowing by the patient may also aid in abnormal parathyroid identification. A patient with hyperparathyroidism may bring medical records of a thyroid ultrasound that fails to describe an obvious parathyroid abnormality. This may be understandable in the context that a thyroid ultrasound focuses solely on the thyroid parenchyma and potential thyroid nodular disease. Communicating a specific request to the sonographer, however, to perform dedicated ultrasound examination for parathyroid abnormalities is crucial.

An abnormality detected by ultrasound to be suspicious but not convincing for parathyroid disease can further be evaluated, if appropriate, by ultrasound-guided fine needle aspiration biopsy (FNAB). This is a valuable technique for evaluation of potential intrathyroidal or other ectopic parathyroid glands, abnormalities located in a previously operated neck, and recurrent hyperparathyroidism when imaging results give discordant findings [25, 26]. Although reported by some as a routine procedure for patients with initial primary hyperparathyroidism [27, 28], parathyroid FNAB is usually reserved for challenging scenarios and is not the preferred or prevailing approach with initial localization, as it can affect tissue integrity for subsequent surgery [29]. The FNAB aspirate is examined both cytologically and for PTH measurement [25]. It is important to alert the pathologist that the source of the FNAB was a potentially abnormal parathyroid, as the cytologic appearance can mimic a thyroid follicular neoplasm [30]. It is also important to alert the laboratory that the PTH sample is a nonserum sample. A number of methods for PTH measurement have been described [25, 31]; simply drawing up 5 ml of sterile saline into the syringe used for the biopsy, then submitting this aliquot for testing usually yields enormously elevated PTH values that leave no diagnostic uncertainty; one study suggested that a PTH aspirate value of 42 or higher gave no false-negative findings [25]. The typical finding of a parathyroid cyst is the aspiration of a perfectly clear, colorless fluid, described by some to appear as water or ethyl alcohol [32, 33].

To achieve mastery of the parathyroid ultrasound technique, a number of resources exist as publications and educational venues. Several professional societies offer annual certification courses (American College of Surgeons, American Association of Clinical Endocrinology, Societies for Head and Neck Surgery) and a collaborative program has been established between radiologists and endocrinologists (Endocrine Certification in Neck Ultrasound, ECNU) to enhance expertise in clinician-performed ultrasound. Although many publications deservedly highlight the virtues of surgeon-performed ultrasound, it should be emphasized that the ability to perform highly accurate parathyroid ultrasound rests with any clinician who invests dedicated focus and practice to this application.

Survey of Normal and Abnormal Parathyroid Anatomy with Ultrasound

Parathyroid Anatomy

Ultrasonographic examination relies on knowledge of the anatomy and embryology of parathyroid glands to detect expected locations of abnormal glands. Most individuals have four parathyroid glands situated on the capsule of the thyroid, but 10% can have supranumerary glands and 5% can be ectopic (Fig. 18.3) [34]. Normal parathyroid glands are typically not seen by ultrasound. They are too tiny (6×3×2 mm oval shape or smaller). They also have a somewhat fatty consistency, may be encased in a purely fatty halo of tissue and kept flattened close to the thyroid surface under a thin adventitial veil. Thus, as ultrasound waves penetrate this region, normal parathyroid glands may not reflect waves sufficiently differently from either adjacent fat or thyroid tissue to appear as discreet entities.

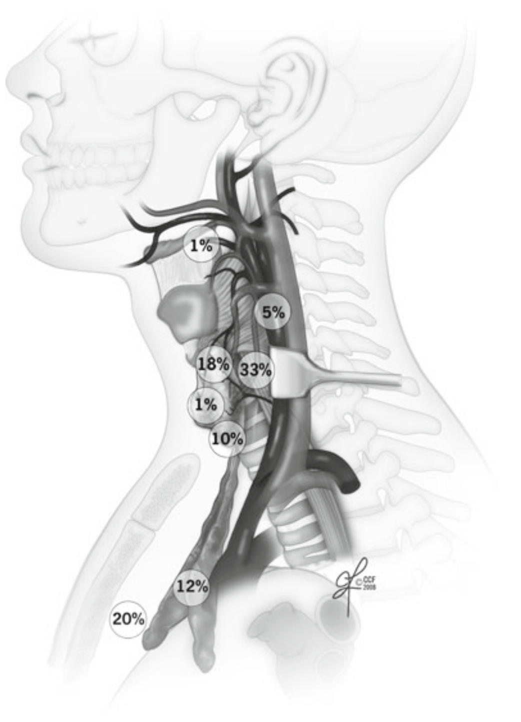

Fig. 18.3 Ectopic distribution of abnormal parathyroid glands in patients with primary hyperparathyroidism. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2008–2011. All Rights Reserved

Superior parathyroids are located on the posterior thyroid surface, generally on the medial aspect close to the tracheoesophageal groove (Fig. 18.4a). Most are within a 2 cm diameter region centered around the intersection between the recurrent laryngeal nerve (usually not seen on ultrasound) and the inferior thyroid artery and its most distal branches (typically seen clearly on ultrasound in both transverse and longitudinal views). The inferior thyroid artery usually enters the midportion of the thyroid and gives an arterial branch to the superior and inferior parathyroids. When imaged longitudinally, an enlarged parathyroid centered on the posterior midportion of the thyroid gland, or higher toward the upper pole of the thyroid, is typically an abnormal superior parathyroid. Because the normal superior parathyroid glands favor a posteromedial position, when they become enlarged, they track downward along the tracheoesophageal groove, to become situated even more posteriorly or inferiorly. In these deep positions, which can extend even to the upper mediastinum, enlarged superior parathyroids may not be discernible on ultrasound. It is here that the technical maneuvers described above (neck extension, transducer pressure, or balloting) may become helpful. Superior parathyroid glands also have ectopic locations and knowledge of these is useful for sonographic examination. Most enlarged superior parathyroid in these ectopic regions are detectable by ultrasound, particularly those where the gland is situated higher than the superior pole of the thyroid gland, among the superior thyroid vessels, or higher in the carotid sheath.

Inferior parathyroid glands are located typically on the lateral tip of the lower thyroid pole and are much more anterior in location, with respect to virtually all reference points, such as the superior parathyroid glands, the course of the recurrent laryngeal nerve and inferior thyroid artery (Fig. 18.4b). They can also be distributed

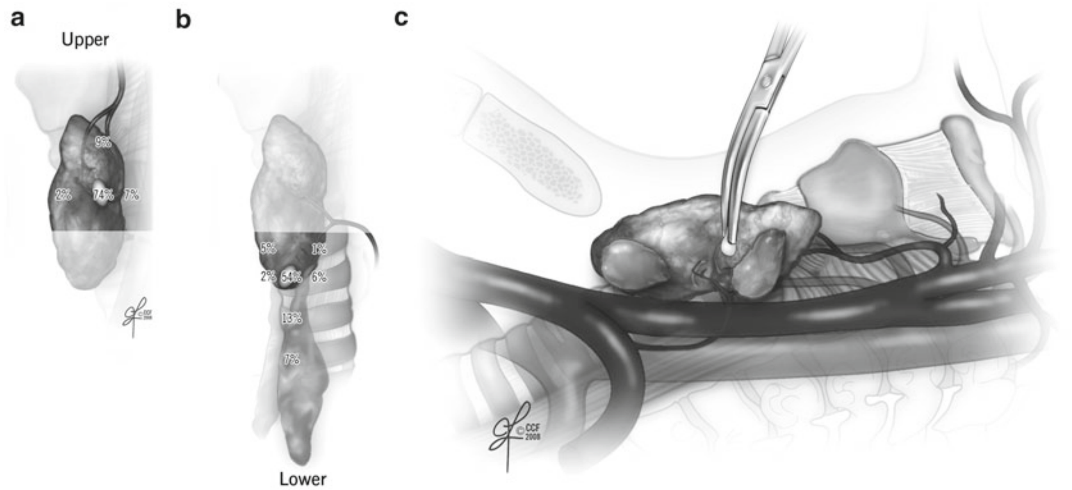

Fig. 18.4 Normal distribution of superior (**a**) and inferior (**b**) parathyroid glands. The drawing in (**b**) demonstrates the entry of the inferior thyroid artery on the posterior midportion of the thyroid gland. Enlarged inferior and superior parathyroids are illustrated in (**c**). Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2008–2011. All Rights Reserved

more widely than superior parathyroid glands and have broader extent of ectopic locations (mediastinum, carotid sheath, and intrathyroidal). They are often within the thyrothymic tract just inferior to the tip of the thyroid gland or within the cervical portion of the thymus. When imaged longitudinally, an enlarged parathyroid just below the strap muscles is typically an inferior parathyroid.

Ectopic parathyroids that can be evaluated with ultrasound include those that are intrathyroidal (3%, typically considered to be inferior parathyroids), intrathymic, located along the carotid sheath or adjacent to the submandibular gland. They tend to have similar features to abnormal parathyroid glands located in typical distributions, and lack the distinctive sonographic architecture of the central vascular hilum of lymph nodes, which may also be found in these regions. Ectopic parathyroids that are difficult to detect with ultrasound include those that are retrotracheal and/or anterior to the cervical spine, and those deep in the mediastinum. Ultrasound is technically limited to identify substernal ectopic parathyroid disease because the acoustic shadows cast by both air-filled (trachea and esophagus) and bony structures obscure surrounding soft-tissue anatomy. However, innovative applications of transesophageal ultrasound demonstrate that even these challenging locations may be amenable to sonographic visualization using an endoscope [35].

Abnormal Parathyroid Sonographic Features

The classical appearance of an abnormal parathyroid can be described as a hypoechoic, teardrop-shaped structure with a hyperechoic line of adventitia on its anterior and posterior surfaces (Figs. 18.4c, 18.5, and 18.6). The average longitudinal size of a parathyroid adenoma is 15 mm, although the teardrop shape can be appreciated with parathyroid abnormalities as small as 8 mm. The hypoechoic texture of the enlarged parathyroid is uniform, rarely heterogeneous, and rarely with hyperechoic or more knobby configurations. Although these variations can be seen (Fig. 18.7), they occur more often with the sclerotic changes and calcifications within parathyroid tissue of patients with secondary and tertiary hyperparathyroidism. The vascular pedicle, a branch of the inferior thyroid artery, can usually be identified

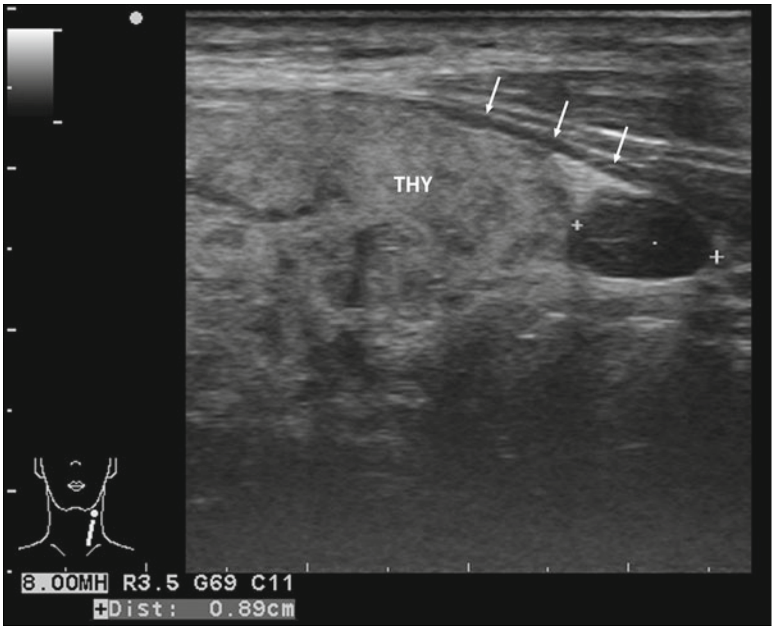

Fig. 18.5 Typical appearance of an abnormally large parathyroid gland. This example demonstrates an enlarged left inferior parathyroid gland adjacent to the lower pole of the thyroid gland (THY) and below the border of the sternothyroid muscle that appears as a hypoechoic dark stripe (below *white arrows*)

to enter the parathyroid at the narrow beginning of the teardrop shape of the abnormal parathyroid. This vascular pedicle may have a tortuous configuration outside of the parathyroid, may in some patients have multiple branching patterns within the parathyroid or just prominent Doppler signal on the parathyroid capsule. A parathyroid vascular pedicle may be difficult to image in some patients, but it rarely, if ever, has the single, clean central hilar vascular stripe that is characteristic of cervical lymph nodes (Fig. 18.8).

In addition to the clues based on anatomic distribution, there are two visual patterns that are distinctive for parathyroid sonography. The "triple circle sign," a term designated by the authors, refers to the presence of three hypoechoic circular entities lateral to the thyroid on transverse imaging: the most lateral circle is the cross section of the jugular vein, the middle circle is the cross section of the common carotid artery, and the medial circle is that of an abnormally large parathyroid (Fig. 18.9). Doppler flow examination demonstrates the distinction between the vascular and parathyroid structures clearly (Fig. 18.10). This pattern on transverse sonographic view is unique for parathyroid disease, and images with this spatial relationship are uncommon with thyroid nodules, abnormal lymph nodes, or other tissues representing the medial circle.

The other visual pattern of identification is the triangularization of the central neck, where the strap muscles (specifically sternothyroid) can be seen as the roof of the central neck space and represents one side of the triangle on a longitudinal section obtained with ultrasound transducer resting just to the side of the trachea (Fig. 18.11). Parathyroids located within this triangle are inferior parathyroid glands. Delineating this triangle helps in the methodical search for parathyroid abnormalities. The differential diagnosis of other sonographic entities in this triangular space is very limited—the only tissues that reside here are normal fibrofatty lobules, normal or abnormal lymph nodes, thymus, and occasionally accessory nodules of thyroid tissue.

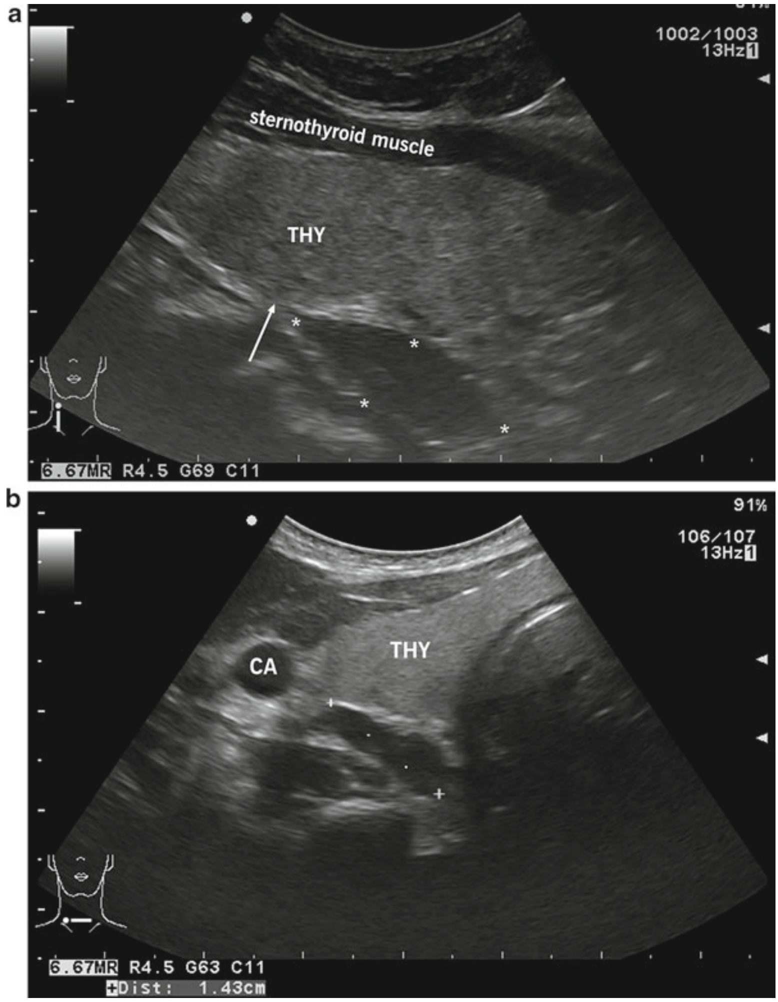

Fig. 18.6 Another illustration of a typical appearance of an abnormally large parathyroid gland, this time a right superior parathyroid in longitudinal view (**a**). The tip of its "teardrop" shape begins at the posterior midportion of the thyroid gland (*arrow*). The extent of the parathyroid is marked at four points (*asterisks*). The transverse image (**b**) measures the abnormal parathyroid as 1.4 cm, compatible with average lengths of a single adenoma. The carotid artery (CA) and right thyroid lobe (THY) are marked

Sonographic Illustrations of Abnormal Parathyroid Disease Entities

The spectrum of parathyroid abnormalities that can be identified with ultrasound is demonstrated in Figs. 18.5–18.15. Represented in this sequence are variations within the major disease manifestations of primary hyperparathyroidism. Thus, for example, a classical parathyroid adenoma is illustrated in Figs. 18.5 and 18.6, with less typical versions seen in Fig. 18.7. The multigland hyperplasia example (Fig. 18.12) is from a patient with primary hyperparathyroidism; although at surgery this patient had four-gland hyperplasia, a double adenoma might have imaged similarly on ultrasound. More subtle abnormalities suggesting parathyroid cancer are seen in Fig. 18.13. Illustrated also are more interesting examples of abnormal parathyroids in ectopic locations, such as in the carotid sheath and as implants in the sternocleidomastoid muscle (Fig. 18.14). Finally, an example of co-existing thyroid and parathyroid pathology is provided to emphasize the utility of parathyroid

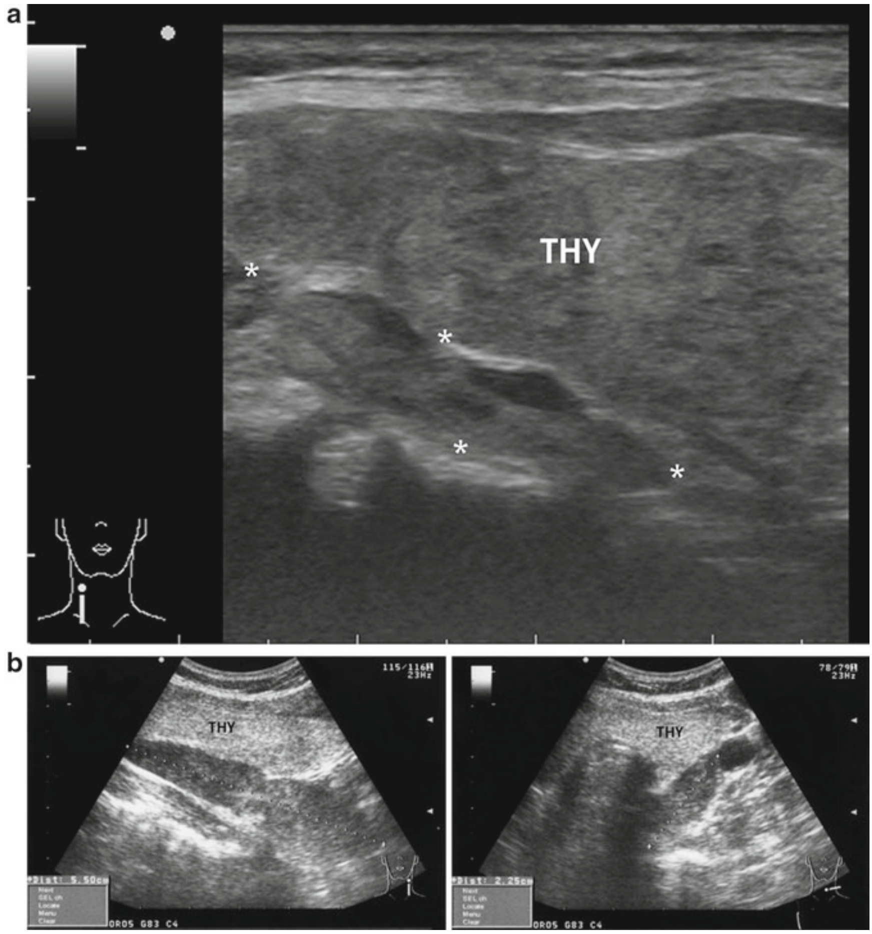

Fig. 18.7 Variations of the sonographic appearance of abnormal parathyroid glands. (**a**) Enlarged parathyroid (*asterisks*) with knobby shape, texture isoechoic with the adjacent thyroid and cystic degeneration within the parathyroid tissue (*black areas*). This was imaged with a linear transducer probe. (**b**) Left upper parathyroid imaged longitudinally to measure nearly 6 cm and be larger than the thyroid (*left panel*) and imaged transversely (*right panel*) using a "fingertip" curvilinear probe. (**c**) Right superior parathyroid (*asterisks*) is shown, imaged longitudinally and located deep to the superior pole of the thyroid gland (*lines*) and adjacent to the spine. Subtle hypoechoic densities such as this one are nevertheless indicative of abnormal parathyroid glands. (**d**) The right superior parathyroid (*asterisks*) located deep in the neck anterior to the spine does not have the typical hypoechoic sonographic texture. The protrusion of the tubercle of Zuckerkandl (tz) provides a valuable preview of an anatomic detail to expect during surgery

ultrasound in detecting adjacent pathology that might require treatment (Fig. 18.15).

The Use of Ultrasound in the Clinical Management of Hyperparathyroidism

Parathyroid ultrasound is intended principally as a localizing rather than diagnostic tool. Thus, the main indications for its use are (1) to identify the site or sites of abnormal parathyroid glands in patients with initial diagnosis of hyperparathyroidism following biochemical confirmation of primary, secondary, or tertiary forms of this disease and (2) to aid localization of persistent or recurrent parathyroid disease. For the first indication, ultrasound can be used as the sole localizing modality or in combination with other radiologic methods, such as Mibi scans and/or computed tomography scans (CT) [16, 36–43]. For the second indication, ultrasound is typically always

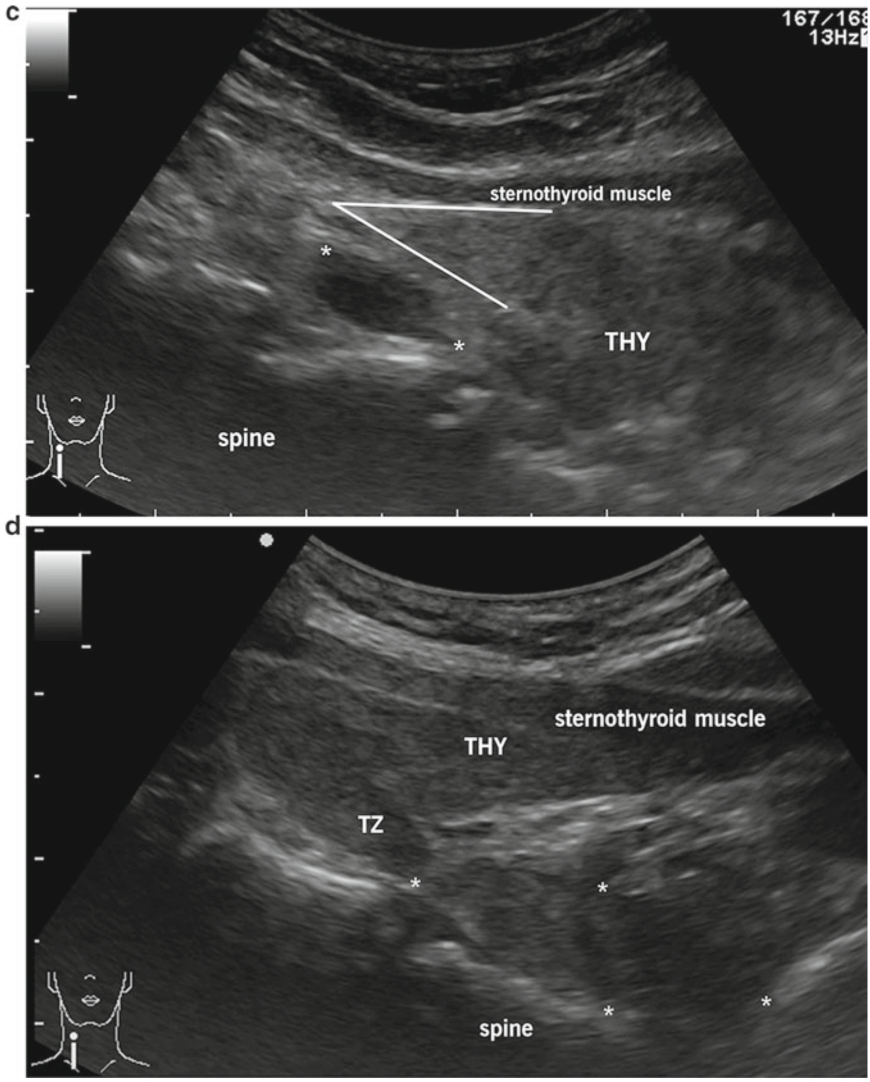

Fig. 18.7 (continued)

part of a sequence of several localizing modalities, usually within an algorithm meant to enhance the accuracy of potential re-operative surgery [44–47]. A negative ultrasound—one that does not reveal any potential sites of parathyroid disease—should not be viewed as excluding the diagnosis of hyperparathyroidism, especially if a complete biochemical work-up has not been performed. A negative ultrasound with confirmed diagnosis of hyperparathyroidism usually raises the likelihood of the presence of multigland hyperplasia (rather than a single adenoma) or the presence of ectopic disease [37, 38, 40, 48].

While principally used for these indications, ultrasound naturally confers some broader functionality and benefits. It can facilitate focal parathyroid exploration or "minimally invasive parathyroid surgery," particularly when a Mibi scan is unrevealing [29, 42]. Ultrasound identifies co-existing thyroid disease and thyroid cancer, thus refining the surgical management plan so that the patient and surgeon have clearer

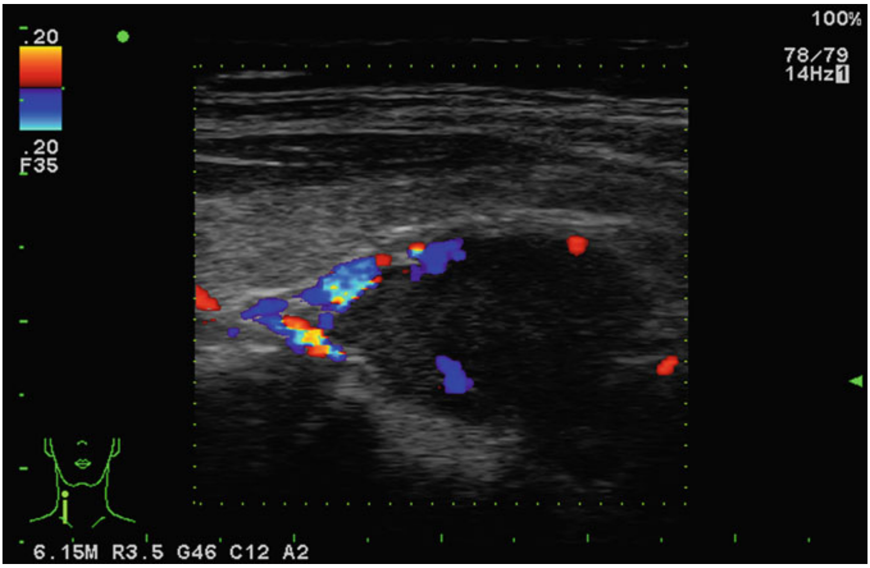

Fig. 18.8 The vascular pedicle of an abnormal parathyroid caps the superior tip of the parathyroid. Unlike the vascular hilar stripe of a lymph node which appears centrally within the lymph node, there is no central, linear vascular signal in this parathyroid, which remains uniformly hypoechoic

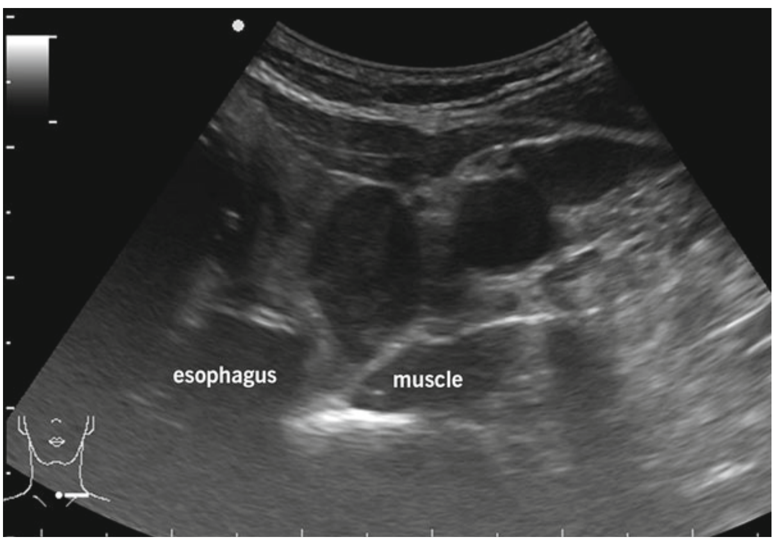

Fig. 18.9 The "triple circle sign" refers to the three dark circles imaged on transverse view during parathyroid ultrasound. These are purposefully unlabeled to be seen in contrast to the esophagus and underlying muscle. The dark circle belonging to the left superior parathyroid adenoma is in the center, the carotid artery cross section is next, and the jugular vein cross section is at far right

expectations of the necessary extent of treatment before surgery [49–51]. One study suggested that the rate of concomitant thyroid surgery during parathyroidectomy was reduced from 30 to 6% by being able to diagnose benign thyroid disease preoperatively [51]. The rate of thyroid cancer diagnosed concurrently with hyperparathyroidism when evaluations involved ultrasound has

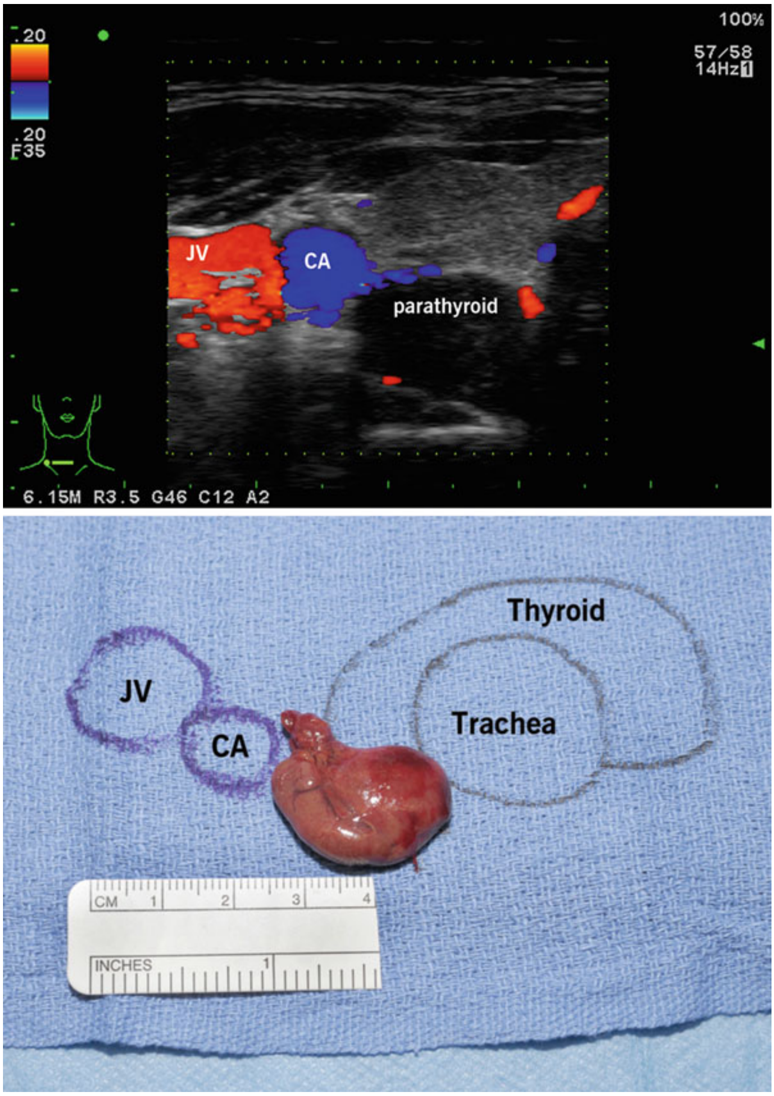

Fig. 18.10 Illustrated is the "triple circle sign" of a right-sided parathyroid adenoma, with marked cross sections of the jugular vein (JV), carotid artery (CA), and enlarged parathyroid gland in the sonographic image (*top*). The specimen photo (*bottom*) orients the large 3-cm right parathyroid adenoma in the anatomical context of these structures

been reported as 5–15% [49–51]. Among other benefits, the awareness of additional concerns improves the informed consent process between patient and surgeon, and reduces the anxiety to the patient and their family of unanticipated findings and duration of surgery. Ultrasound poses no radiation risks and is therefore the main imaging modality in the rare event hyperparathyroidism is diagnosed in pregnant women or in patients with other contraindications for usage of radioisotopes or radiologic dyes. For recurrent hyperparathyroidism, and for unusual and ectopic lesions even with initially diagnosed hyperparathyroidism, ultrasound can help confirm the parathyroid origin of a suspected abnormality by guiding FNAB for cytologic and PTH evaluation. Some authors have even used it to guide aspiration of bilateral jugular vein blood samples for PTH measurement during an office-based visit, helping lateralize the abnormality to the right or left side of the

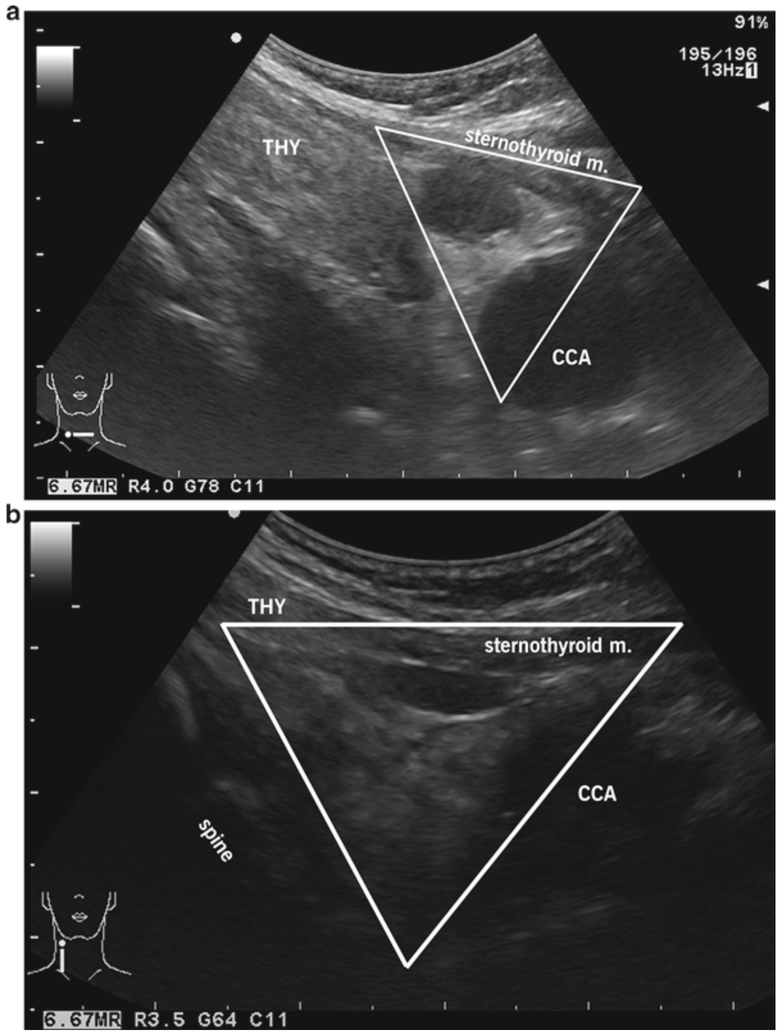

Fig. 18.11 The "triangularization" of the central neck is a view in the longitudinal ultrasound plane that helps define a space where abnormal inferior parathyroids reside. The outlines of the triangle are the sternothyroid muscle, a line paralleling the spine to reach the lower pole of the thyroid gland, and a line across the sternal notch, or in example A, the cross section of the common carotid artery (CCA). The hypoechoic density contained within this triangle is an inferior parathyroid adenoma. Note also that the orientation icon, which requires manual change by the operator, has remained incorrectly designated in a transverse orientation—a reminder that these icons are often not as reliable as what the ultrasound image itself conveys. The anatomy of the sternothyroid muscle clearly establishes a longitudinal view. In example B, the lower parathyroid has classical sonographic features and the icon also indicates a longitudinal view

neck [52]. In rare cases, ultrasound can also guide nontraditional therapy for hyperparathyroidism, such as ethanol injection of parathyroid glands, a procedure that may have limited role in patients with recurrent, inoperable, or challenging parathyroid disease scenarios [53–56]. For an experienced sonographer, ultrasound can function also to preview the anatomy expected at surgery, with nuances that alert to more complex or simple technical details about how to surgically approach the parathyroid. As mentioned previously as well, ultrasound can be performed within the operating room as a procedure prior to start of surgery; if needed, the transducer can also be placed in a

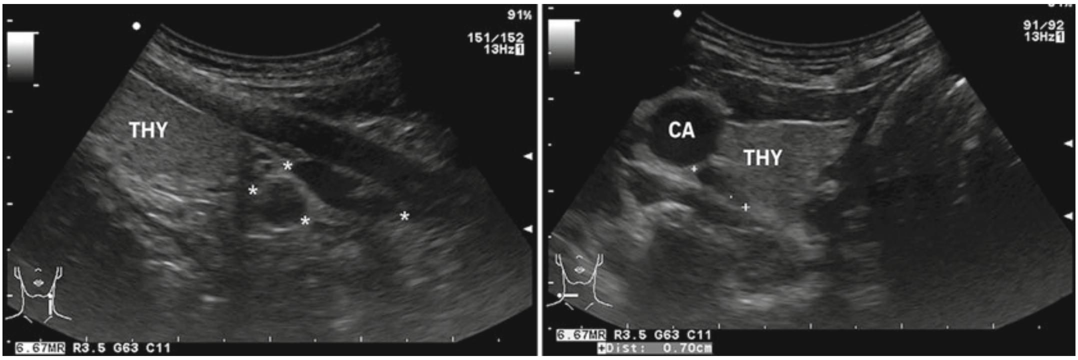

Fig. 18.12 Multigland parathyroid hyperplasia in hyperparathyroidism is more likely to be the underlying etiology when small (0.7–1.0 cm) hypoechoic densities are imaged bilaterally (*asterisks*). In the *left panel*, the left inferior parathyroid was found at surgery to be lobulated, as suggested in the ultrasound image. Similar bilateral distribution but usually with much greater parathyroid enlargement occurs in secondary hyperparathyroidism

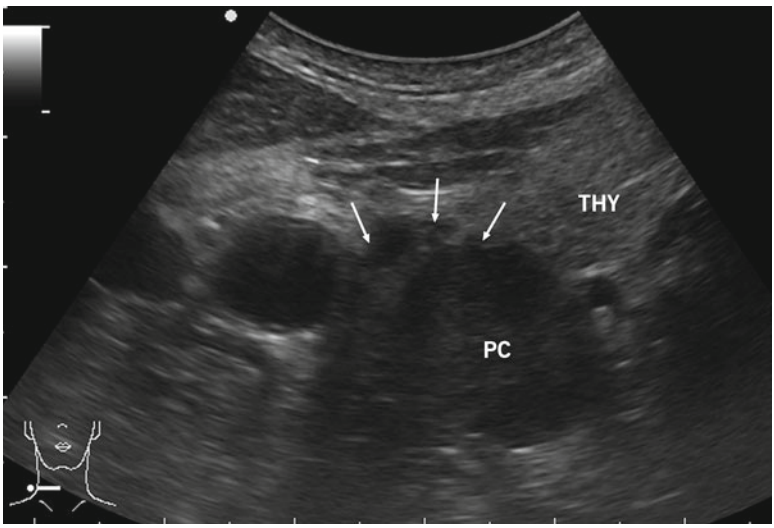

Fig. 18.13 Parathyroid cancer (PC) suspected from a large 3-cm parathyroid with irregular border (*arrows*) adjacent to the thyroid gland, in a patient with primary hyperparathyroidism and preoperative calcium values of 14 mg/dL and PTH 1,200 pg/ml

sterile sheath and used to search for parathyroid densities within the surgically exposed neck space after the incision has been made. These benefits are highlighted in Table 18.1.

An evidence-based review of the literature shows that accuracy of ultrasound varies with the manner used for localization of abnormal parathyroid glands [16, 19–24, 36–38, 42]. It appears from these studies that, on average, 75–80% of abnormal parathyroid glands are correctly detected by ultrasound. However, this performance varies depending on clinical circumstances, type of underlying parathyroid disease, the definition used for successful localization and accuracy, and the specialist conducting the ultrasound exam. When performed by experienced surgeon—sonographers, parathyroid ultrasound was found to be superior to Mibi in all clinical subgroups: single adenomas, double adenomas, hyperplasia, familial hyperparathyroidism, and secondary/tertiary forms of hyperparathyroidism [57]. Ultrasound sensitivity was greater for single

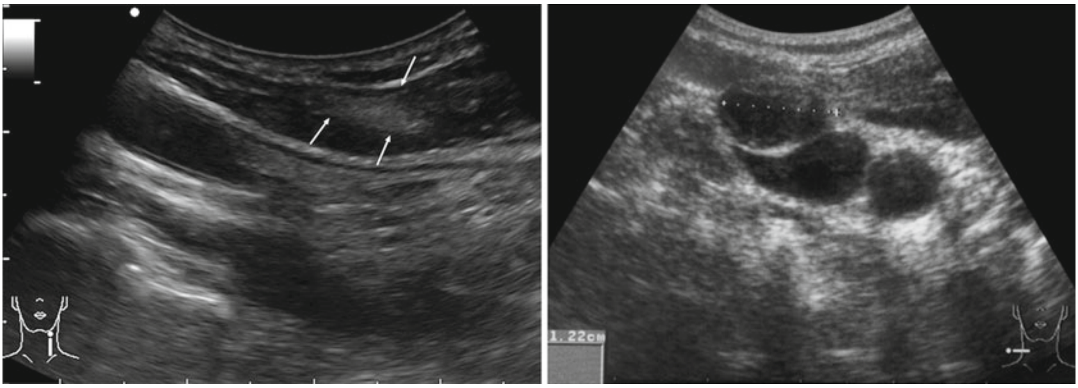

Fig. 18.14 Images of ectopically located abnormal parathyroids in the neck. A hyperechoic and vague density (*arrows*) in the left sternocleidomastoid muscle represents an adenoma that developed at the site of a parathyroid autotransplant performed 20 years previously during thyroid surgery (*left panel*). An ectopic parathyroid adenoma measuring 1.2 cm is situated adjacent to the jugular vein and carotid artery (*right panel*). In both instances, ultrasound-guided FNA was used to confirm parathyroid tissue

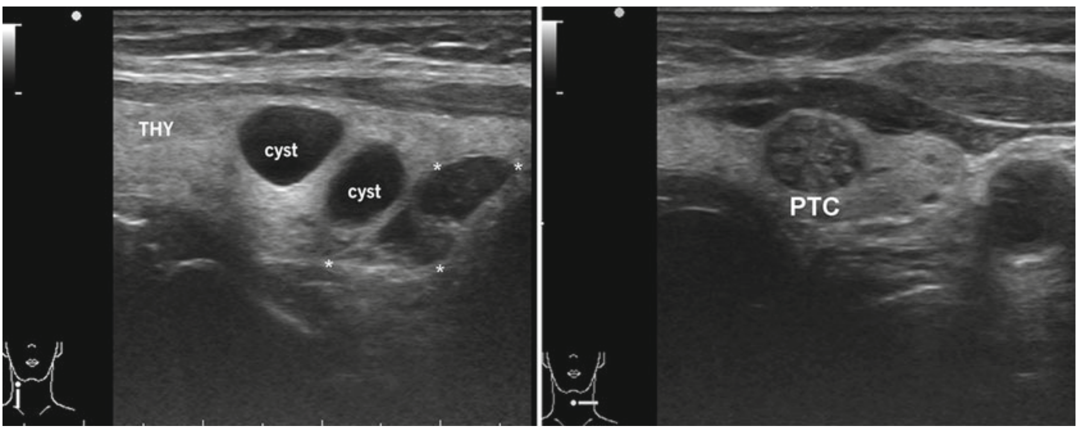

Fig. 18.15 Co-existing thyroid disease with primary hyperparathyroidism. The sonographic image depicts two intrathyroidal cysts and an enlarged right inferior parathyroid gland (*asterisks*). A small papillary thyroid cancer (PTC) was diagnosed in the contralateral thyroid lobe

adenomas than for multigland disease, whereas these rates were more comparable for Mibi scans [57]. When surgeon-performed ultrasound was used as the first localizing test and intended potentially as the only test, it was found to have equal accuracy as Mibi, but was easier to perform, identified concomitant thyroid disease, and was more cost-effective [37]. These authors suggested an algorithm that uses ultrasound as the principal localizing modality for hyperparathyroidism, with application of other interventions only in the setting of equivocal or negative ultrasound [37]. In these circumstances of surgeon-performed ultrasound, especially with stringent and selective criteria applied to operate on patients with clear sonographic findings, a true positive rate as high as 89% was achieved [14, 16, 37]. Taking into considerations that study design and definitions were not necessarily comparable, others have reported higher positive predictive values, such as 99% in a study where ultrasound was performed by interventional radiologists [23].

Table 18.1 The spectrum of advantages seen with the use of parathyroid ultrasound for evaluation of patients with hyperparathyroidism

• Localization of parathyroid disease prior to initial surgery for hyperparathyroidism
• Localization of persistent and recurrent parathyroid disease
• Ability to direct focal or limited parathyroid surgery
• Guidance of diagnostic parathyroid interventions (FNAB, jugular vein PTH sampling)
• Guidance of therapeutic parathyroid interventions (alcohol ablation)
• Identification of concomitant thyroid disease and thyroid cancer
• Reduction in concomitant thyroid surgery during operation for hyperparathyroidism
• Facilitation of surgical planning for patient and surgeon
• Preview of precise anatomical details valuable for surgery
• Convenience of use in office-based practice
• Use in the operating room
• Lack of radiation exposure
• Cost-effectiveness

Ultrasound appears to be particularly helpful following negative Mibi scans, as ultrasound was able to localize an abnormal parathyroid suggestively or conclusively in 56% of patients and surgery confirmed this prediction was correct in 84% of patients [58]. Another study found that ultrasound detected abnormal parathyroid glands in 83% of patients with negative Mibi scans [36]. In this same study, when Mibi scans were found to perform slightly better than ultrasound, this was attributed to Mibi's advantage in detecting mediastinal and multigland disease [36].

The performance of US in re-operative parathyroid surgery has been examined by a number of investigators [25, 26, 36, 44–47]. In this setting, US and Mibi should be viewed as complementary studies and both ideally need to be performed. As alluded to already, ultrasound provides the ability to have tissue or hormonal confirmation of parathyroid disease by guiding FNA of suspected lesions. In the re-operative setting, the sensitivity of ultrasound was 56% and a combined multimodality algorithm allowed a successful focal approach in 60% [44].

The use of parathyroid ultrasound in the evaluation of patients with secondary and tertiary hyperparathyroidism has likewise been described [59, 60]. As with hyperplasia in general, neither ultrasound nor Mibi scans reliably detect parathyroid hyperplasia or visualize all of the involved glands in hyperplasia, an observation consistently reported by several investigators both in the 1990s [12, 48] and more recently [36, 38, 40]. The rate of accurate diagnosis with secondary hyperparathyroidism has been reported as 64%, certainly more modest than seen with primary hyperparathyroidism [59]. In the secondary/tertiary hyperparathyroidism scenario, given that the underlying biology affects all parathyroid glands, bilateral neck exploration is essential; hence, high ultrasound accuracy does not have the same purpose of allowing focal (limited or unilateral) exploration.

A number of factors have been identified to impact detection of abnormal parathyroid glands by ultrasound. These include younger patients [37], body mass index (BMI) [57], parathyroid gland size and gland volume [57], and the skill and experience of the examiner [21, 22, 36]. What determines whether ultrasound should be chosen for initial or exclusive preoperative localization depends on the availability of skilled and experienced examiners perhaps more so than any set of benefits posed by each imaging modality. As summarized by Inabnet et al. and others [36, 37, 61], ultrasound is favored by low cost, convenience, lack of radiation exposure, precise anatomical detail, and detection of concomitant thyroid nodules and thyroid cancer. By contrast, Mibi scans seem to be favored for imaging of ectopic, especially mediastinal disease, and thus may be preferred as the initial test for patients with failed prior parathyroid surgery and suspected ectopic disease. Other imaging modalities, such as computed tomography, pose significantly higher radiation exposures to weigh against unique benefits. The data from the studies presented above seems to point out clearly that, if at all possible, ultrasound should be part of the clinical management of hyperparathyroidism.

Conclusion

Ultrasound is a readily applicable, noninvasive and versatile tool for the evaluation of patients with parathyroid diseases. It aids in the localization of parathyroid abnormalities to direct appropriate parathyroid surgery. It also offers the opportunity to identify and address co-existing thyroid disease, including thyroid cancer. Whether used as the only technique by experienced sonographers for initial localization in first-time hyperparathyroid patients, or as part of a multi-imaging algorithm, ultrasound provides valuable clinical information. Recognizable sonographic features allow identification of abnormal parathyroid glands, can be readily learned, and make ultrasound a powerful tool especially when performed by clinicians with access to comprehensive information about the patient's parathyroid disease. Ultrasound can guide appropriate interventions to clarify challenging diagnostic scenarios, although ultimately it should not be viewed as a diagnostic test for hyperparathyroidism. It has a demonstrated history of valuable clinical use [3, 13, 15, 62]. As it has in the past, ultrasound will continue to have an important role in the management of patients with parathyroid disease.

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