

International Journal of Radiology and Diagnostic Imaging



E-ISSN: 2664-4444
P-ISSN: 2664-4436
www.radiologypaper.com
IJRDI 2020; 3(2): 91-94
Received: 20-02-2020
Accepted: 23-03-2020

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B-Mode Sonography and Doppler ultrasound in characterizing thyroid nodules and its correlation with pathological diagnosis

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DOI: <http://dx.doi.org/10.33545/26644436.2020.v3.i2b.103>

Abstract

The first diagnostic application of ultrasound occurred in 1942. In a paper entitled “Hyperphonography of the Brain,” Karl Theodore Dussic reported localization of the cerebral ventricles using ultrasound. Unlike the current reflective technique, his system relied on the transmission of sound waves, placing a sound source on one side of the head, with a receiver on the other side. A pulse was transmitted, with the detected signal purportedly able to show the location of midline structures. While the results of these studies were later discredited as predominantly artifact, this work played a significant role in stimulating research into the diagnostic capabilities of ultrasound. This was a prospective study to evaluate if nodule/s is/are benign or malignant by ultrasonography and Doppler study and pathological correlation in atleast 50 patients referred in view of clinically / incidentally (Carotid Duplex Doppler / neck ultrasound for non thyroid pathologies) detected goitre / thyroid nodule. Of the total 59 cases of thyroid nodules associated with lymphadenopathy, 1 (1.69%) lymph node with loss of central echogenic was pathologically proven to be lateral aberrant thyroid due to papillary thyroid carcinoma metastases. One (1.69%) case of thyroid malignancy associated with lymphadenopathy showed preservation of central echogenic hilum. Six (10.17%) cases of benign had associated lymphadenopathy with loss of central echogenic hilum and 51 (86.44%) benign cases had intact central hilum. The sensitivity of association of lymph node with loss of central echogenicity with thyroid malignancy was 50% and specificity was 89.5%.

Keywords: B-Mode Sonography, Doppler Ultrasound, Pathological Diagnosis, Thyroid

Introduction

The thyroid gland weighs 10 to 20 g in normal adults and is responsible for the production of two families of metabolic hormones: the thyroid hormones thyroxine (T4) and triiodothyronine (T3) and the calcium-regulating hormone calcitonin. The spherical thyroid follicular unit is the important site of thyroid hormone production. The thyroid follicle is made up of a single layer of cuboidal follicular cells that encompass a central depository of colloid filled mostly with thyroglobulin (Tg), the protein within which T4 and T3 are synthesized and stored. Each follicle is surrounded by a rich network of capillaries that interdigitate among the multiple follicular units contained within normal thyroid matrix^[1].

C cells, derived from the neural crest, migrate into the thyroid during embryologic development. These cells rest in a parafollicular position, predominantly in the upper lobe of each thyroid. C cells are responsible for production of the hormone calcitonin, which has important regulatory properties on calcium metabolism.

Ultrasound evaluation and ultrasound-guided FNA biopsy are critical for the diagnosis and treatment of patients with thyroid nodular disease. Ultrasound imaging is based on differences between the abilities of different tissues to reflect US waves (cyclic sound pressure of an elastic medium with a frequency greater than 20,000 Hz). There is no exposure to ionizing radiation in ultrasound examination^[2].

Some animal species such as dolphins, whales, and bats are capable of creating a “visual” image based on receiving reflected sound waves.

Prior to World War II, sonar, the technique of sending sound waves through water and observing the returning echoes to characterize submerged objects, inspired early ultrasound investigators to explore ways to apply the concept to medical diagnosis.

In 1880, Pierre and Jacques Curie discovered the piezoelectric effect, determining that an electric current applied across a crystal would result in a vibration that would generate sound waves, and that sound waves striking a crystal would, in turn, produce an electric voltage. Piezoelectric transducers were capable of producing sonic waves in the audible range and ultrasonic waves above the range of human hearing.

The first operational sonar system was produced two years after the sinking of the Titanic in 1912. This system was capable of detecting an iceberg located two miles distant from a ship. A low-frequency audible pulse was generated, and a human operator listened for a change in the return echo. This system was able to detect, but not localize, objects within range of the sonar. Over the next 30 years navigational sonar improved, and imaging progressed from passive sonar, with an operator listening for reflected sounds, to display of returned sounds as a one-dimensional oscilloscope pattern, to two-dimensional images capable of showing the shape of the object being detected [3].

The first medical application of ultrasound occurred in the 1940s. Following the observation that very high intensity sound waves had the ability to damage tissues, lower intensities were tried for therapeutic uses. Focused sound waves were used to mildly heat tissue for therapy of rheumatoid arthritis, and early attempts were made to destroy the basal ganglia to treat Parkinson’s disease.

The first diagnostic application of ultrasound occurred in 1942. In a paper entitled “Hyperphonography of the Brain,” Karl Theodore Dussic reported localization of the cerebral ventricles using ultrasound. Unlike the current reflective technique, his system relied on the transmission of sound waves, placing a sound source on one side of the head, with a receiver on the other side. A pulse was transmitted, with the detected signal purportedly able to show the location of midline structures. While the results of these studies were later discredited as predominantly artifact, this work played a significant role in stimulating research into the diagnostic capabilities of ultrasound [4].

Methodology:

Inclusion Criteria: This was a prospective study to evaluate if nodule/s is/are benign or malignant by ultrasonography and Doppler study and pathological correlation in atleast 50 patients referred in view of clinically / incidentally (Carotid Duplex Doppler / neck ultrasound for non thyroid pathologies) detected goitre / thyroid nodule.

Procedure and Equipment: USG and Doppler study of thyroid nodule was performed on Philips iU22(Philips Medical Systems, Bothell, WA, USA) using linear transducer of 5MHz To 17MHz.

US options utilized for the diagnosis of thyroid diseases include the following:

1. Grayscale
2. Color Doppler Imaging
3. Power Doppler Imaging
4. Panoramic scan

The patient was positioned supine, with the head thrown back and a bolster under the shoulders.

USG and color flow in each nodule will be characterized

under the guidance of consultant radiologists.

Further, above patients were subjected to US Guided FNAC using 23 – 27 G needle as per the consensus recommendation of the Society of Radiologists in Ultrasound for confirmation of benign and malignant lesions.

Results:

Table 1: Vascularity patterns in cases with malignant and benign thyroid nodules

Vascularity	Nature		Grand Total
	Malignant	Benign	
1	0.00%	78.57%	78.57%
		55	55
2	1.43%	14.29%	15.71%
	1	10	11
3	1.43%	4.29%	5.71%
	1	3	4
Grand Total	2.86%	97.14%	100.00%
	2	68	70

Out of all the 70 cases with thyroid nodules, none of the cases with malignant nodules (2) showed type I or absent peripheral or intranodular vascularity. One (1.43%) case with malignant nodule showed type 2 of perinodular vascularity and one (1.43%) showed type 3 or intranodular as well as perinodular vascularity. Type 1 vascularity was seen in 55 (78.57%) cases with benign nodules, type 2 vascularity in 10 (14.29%) benign cases and type 3 vascularity in 3 (4.29%) benign cases.

Table 2: Consistency of malignant and benign thyroid nodules

Consistency	Nature		Grand Total
	Malignant	Benign	
Solid	2	29	31
	2.86%	41.43%	44.29%
Cystic	0	39	39
	0.00%	55.71%	55.71%
Grand Total	2	68	70
	2.86%	97.14%	100.00%

Out of the total 70 cases with thyroid nodules, all (2) cases of malignant nodules had solid with no cystic component. Twenty nine (41.43%) cases with benign nodules were found to be solid and 39 (55.71%) to be predominantly cystic.

The sensitivity of solid consistency of a nodule as a predictor of malignancy was found to be 100% and specificity, 57.4%.

Table 3: Association of solitary and multiple thyroid nodules with malignancy and benignity

Number	Nature		Grand Total
	Malignant	Benign	
Solitary	1	9	10
	1.43%	12.86%	14.29%
Multiple	1	59	60
	1.43%	84.29%	85.71%
Grand Total	2	68	70
	2.86%	97.14%	100.00%

Of all the 70 cases with thyroid nodules, 1 (1.43%) case with malignancy was found to have solitary thyroid nodule

and 1 (1.43%) case with malignancy was found to multiple thyroid nodules. There were 9 (12.86%) cases of solitary thyroid nodules which were found to be benign and 59 (84.29%) cases of multinodular goitre were benign as well. The sensitivity of a solitary nodule being malignant was 50% with a specificity of 86.8%.

Table 4: Association margin characteristics with malignant and benign thyroid nodules

Margin	Nature		Grand Total
	Malignant	Benign	
Sharp	1	62	63
	1.43%	88.57%	90.00%
Ill defined	1	6	7
	1.43%	8.57%	10.00%
Grand total	2	68	70
	2.86%	97.14%	100.00%

Of the total 70 cases with thyroid nodules, 1 (1.43%) case with malignant nodule had illdefined margin and 1 (1.43%) malignant case was found to have sharp margin. Six (8.57%) cases of benign nodules were found to have illdefined margins and 66 (88.57%) had sharp margins. The sensitivity of illdefined margins as a risk factor for malignancy was found to be 50% and specificity was 91.2%.

Table 5: Distribution of lymphadenopathy in cases with thyroid nodular disease

Regional lymph nodes	Total
Present	61
Absent	11
Grand Total	72

Lymphadenopathy was associated with 61 (85%) cases of thyroid nodules and absent in 11 (15%) of cases with thyroid nodules.

Table 6: Association of lymph node hilar pattern with malignant and benign thyroid nodules

Hilum	Nature		Grand Total
	Malignant	Benign	
Lost	1.69%	86.44%	88.14%
	1	6	7
Intact	1.69%	10.17%	11.86%
	1	51	52
Grand Total	3.39%	96.61%	100.00%
	2	57	59

Of the total 59 cases of thyroid nodules associated with lymphadenopathy, 1 (1.69%) lymph node with loss of central echogenic was pathologically proven to be lateral aberrant thyroid due to papillary thyroid carcinoma metastases. One (1.69%) case of thyroid malignancy associated with lymphadenopathy showed preservation of central echogenic hilum. Six (10.17%) cases of benign had associated lymphadenopathy with loss of central echogenic hilum and 51 (86.44%) benign cases had intact central hilum.

The sensitivity of association of lymph node with loss of central echogenicity with thyroid malignancy was 50% and specificity was 89.5%.

Discussion

The sensitivity of illdefined margins as a risk factor for

malignancy was found to be 50% and specificity was 91.2%.

Loss of central echogenic hilum was noted in 50% of lymph nodes associated with thyroid malignancy and this marker of malignancy, was found to be 89.5% specific.

Three types of Doppler flow patterns in imaging thyroid nodules (33): type 1, no vascularity—defined as no Doppler flow in the periphery or within the nodule; type 2, peripheral vascularity — defined as Doppler flow only in the periphery of the nodule; and type 3, intranodular vascularity — defined as Doppler flow within the nodule regardless of Doppler flow in the periphery of the nodule. In our study none of the malignant showed absent (type I) flow. Type II and type III flow patterns, each, were found in 50% of malignant nodules.

Thus in our study, various ultrasound characteristics of thyroid malignancy were evaluated. However, none of the ultrasound characteristics, singly, showed statistically significant association with thyroid malignancy, possibly related to small sample that was evaluated. Furthermore, more than one positive ultrasound characteristic of malignancy increases the confidence in characterizing a thyroid nodule as malignant or benign. Thus, ultrasound appears to have its limitations in characterizing thyroid nodules as benign or malignant, at present and pathological diagnosis continues to remain the gold standard in differentiating malignant from benign nodule [5, 6].

Ultrasonography is the modality of choice for guiding thyroid nodule FNAC and gives more satisfactory samples than freehand FNACs. In a study by P. Mehrotra *et al.*, ultrasound-guided core samples for cytology were unsatisfactory in 19/121 (15.6%) of the cases, compared with 66/141 (46.8%) of freehand FNACs (p value < 0.0001). Ten out of eleven patients (91%) had a satisfactory US-guided core after an unsatisfactory freehand FNA; 7/15 patients (46.77%) had satisfactory repeat freehand FNACs following an initial unsatisfactory freehand FNAC (p value=0.0191) (64). The ATA guidelines state ‘‘US guidance for fine needle aspiration (FNA) is recommended for those nodules that are nonpalpable, predominantly cystic, or located posteriorly in the thyroid lobe’’. A key recommendation of The American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association (AAACE/AMA/ETA) guidelines is that ‘‘cytologic diagnosis is more reliable and the nondiagnostic rate is lower when FNA biopsy is performed with US guidance’’. Recommendation 6 of the ATA guidelines states that ‘‘US guidance should be used when repeating the FNA procedure for a nodule with an initial nondiagnostic cytology result’’ [7].

US has greatly improved the sensitivity of detection of thyroid nodules. By palpation alone, the prevalence of thyroid nodules in the general population is ~ 5%. Examination with US, however, reveals that thyroid nodules increase linearly with age, such that 10% of 25-year olds have them with the rate escalating to involve nearly 55% of women over the age of 70.

Role of US in preoperative staging. Differentiated thyroid carcinoma (particularly papillary carcinoma) involves cervical lymph nodes in 20–50% of patients in most series using standard pathologic techniques and may be present even when the primary tumor is small and intrathyroidal. Preoperative US identifies suspicious cervical adenopathy in 20–31% of cases, potentially altering the surgical approach

in as many as 20% of patients [8].

US as tool for surveillance post thyroid cancer surgery. Historically, surveillance for recurrent or persistent differentiated thyroid carcinoma included measurement of serum Tg and diagnostic whole body scans (DxWBS). Careful study has revealed, however, that the DxWBS by itself has a very poor sensitivity (21%). Instead, serum Tg in combination with a thorough cervical US has the highest sensitivity (96.3%) and negative predictive value (99.5%) of the available tests for detecting recurrent disease in low-risk patients. As a result, it is currently recommended that patients with low-risk differentiated thyroid cancer undergo US monitoring at 6–12 months after surgery and then periodically, depending on the patient's risk for recurrent disease and Tg status. In addition, serum Tg should be measured every 6–12 months at the same laboratory. Further, DxWBS does not need to be performed in low-risk patients with undetectable Tg, negative Tg antibodies, and negative US. When suspicious LNs are identified by US, consensus guidelines recommend that FNA be performed under US guidance for lesions greater than 5–8mm in the smallest diameter, if a positive result would change the management of the patient. Lymph nodes less than 5 – 8mm in the largest diameter may be followed without biopsy, with the intention of intervention if there is lesion growth or impingement on vital structures [9, 10].

Patients with recurrent disease in the neck who are not amenable to repeat treatment with radioiodine, surgery, or external beam radiotherapy may be candidates for percutaneous ethanol injection (PEI). By injecting 95% ethanol under US guidance, this procedure causes ischemic necrosis and subsequent reduction of tumor volume. US guided electrode into an area of recurrence for radiofrequency ablation (RFA) has been tried with some success for control of local disease. Thus, US may prove an invaluable resource for some patients with a small burden of recurrent disease that is not amenable to the traditional treatment protocols through utilization of PEI or RFA [11].

US elastography is a new technique to measure the elasticity of tissue. The tissue of carcinoma is harder and firmer than that of the normal thyroid parenchyma or a benign nodule. Rago *et al.*, found US elastography to be highly sensitive and specific in predicting malignancy ($P < 0.0001$), especially in cytologically indeterminate nodules. US elastography, thus, has great potential as an adjunctive tool for the diagnosis of thyroid cancer [12].

Conclusion

Thus, it can be concluded that, though ultrasonography is a very sensitive in detecting thyroid nodules it is not efficient in characterizing thyroid nodules as benign or malignant, at present, and pathological diagnosis continues to remain the gold standard in differentiating malignant from benign nodule.

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