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Can Diffusion-Weighted Imanging Solve the Problem of Indeterminate Thyroid Nodule, Cross-Sectional Study

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ABSTRACT
Background: Indeterminate thyroid nodule that cannot be differentiated if is it benign or malignant thyroid nodule is problematic. Diffusion-weighted magnetic resonance imaging is new non-invasive imaging technique that can distinguish among benign & malignant lesions**.**

Objective: This study aimed to investigate the role of diffusion-weighted magnetic resonance picturing in distinguishing among malignant & benign thyroid nodules. Also, comparing apparent diffusion coefficient value with histopathological findings. **Patients & Methods:** A cross-sectional research that was conducted on 15 studied cases with solitary or dominant thyroid nodules based on ultrasonography examination from March 2021 to March 2022. Ten were females and five were males with 20 thyroid nodules.

Results: Fifteen cases with total of twenty thyroid nodules. There were ten females and five males. Their ages ranged from 25 to 65 years old, with mean age of 47.13 ± 0.8. Largest diameter of nodules varied from 13 mm to 55 mm, with mean of 28.15 mm. . .ROC curve's area under curve was one. We chose an ADC cut-off value of less than and equal to one, sensitivity, specificity, PPV, NPV & accuracy were 100%, 94.12, 75, 100, 95% respectively.

Conclusion: ADC values appeared to be capable of distinguishing benign from malignant thyroid problems. In addition, thyroid ultrasonography & US guided-FNAC (fine needle aspiration cytology) for tissue characterization of thyroid nodules, DWI has great value as diagnostic tool, and outcomes may even play role in selection of nodules that will undergo FNAC.

Keywords: Diffusion-weighted imaging, Indeterminate thyroid nodule, Fine needle aspiration cytology.

INTRODUCTION

Indeterminate thyroid nodule that cannot be differentiated if is it benign or malignant thyroid nodule is problematic. Diffusion-weighted magnetic resonance imaging is new non-invasive imaging technique that can distinguish among benign & malignant lesions. Although, clinical features and non-invasive imaging techniques like ultrasonography do not always provide conclusive diagnosis to control out malignancy, radionuclide scintigraphy can be used to decide which nodules should be histopathologically evaluated. United States used this technique as first stage in evaluating these nodules. But, there are overlapping criteria and no single US criterion has been found to accurately differentiate benign from malignant nodules. Radiation exposure is concern throughout radionuclide scintigraphy, and some functioning hot nodules seen in scintigraphy are malignant [(1)].

Fine needle aspiration biopsy is considered gold standard for diagnosis, and it has previously been noted that outcomes of FNAB may mimic symptoms of other illnesses [(2)].

T1- & T2-weighted MR imaging can only analyse nodules anatomically and its role in thyroid nodule assessment is limited because it cannot make distinction benign from malignant nodules and cannot evaluate thyroid nodule effectiveness [(3)].

MRI Diffusion-Weighted imaging is novel method for detecting brain tumours. DWI is vulnerable to variations in microstructure of tissue that heavily impact diffusion. It has been used to evaluate thyroid tumours. Apparent conductivity value is quantitative parameter used to make distinction among benign & malignant thyroid nodules [(4)].

PATIENTS AND METHODS

From March 2021 to march 2022, a cross-sectional research was conducted on 15 studied cases with solitary or dominant thyroid nodules based on ultrasonography examination.

Ten were females and five were males with 20 thyroid nodules. Their years old ranged from 25 to 65 years with a mean of 47 ± 13.8 years old. Clinically neck swelling was the most common presenting symptom in 80% of patients. Other symptoms included dyspnea, dysphagia, and hoarseness of voice that presented in 20% of patients, irritability, and weight loss in 12% of patients. Patients were referred from Clinical Oncology Department to Radio-Diagnosis Department for conventional non-contrast MRI and thyroid DWI examinations. Approval of our institutional study Ethics Committee & informed consent from all studied cases were obtained.

Ethical considerations:

Research was approved by Faculty's Ethics Committee, South Valley University. All the studied cases were informed about the surgery & the auto transplantation technique, value and possible complications and informed written consents were taken from all studied cases. This work has been carried out in accordance with Code of Ethics of World Medical Association (Declaration of Helsinki) for studies involving humans.

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Inclusion criteria:

Cases in different years old groups with solitary or multiple thyroid nodule(s) with dominant one, solid or mixed solid and cystic nature undergo ultrasound examination before surgery or FNAB and histopathological examination of the nodules postoperatively.

Exclusion criteria:

All contraindication of MRI e.g. pace-makers, claustrophobia, patients with a totally cystic nodule and patients with hyperthyroidism.

The studied cases were subjected to following:

Clinical assessment including full clinical history, clinical tests & laboratory tests including thyroid function examinations.

Imaging assessment:

Thyroid US and color Doppler examination was performed by the superficial linear probe (frequency 7.5-12 MHz) using an ultrasound system (GE, logic P7). Each nodule was scored for categorizing nodules on TI-RADS classification. Conventional non-contrast Magnetic Resonance (MR) imaging is preliminary to the diffusion-weighted imaging test. It was performed at a 1.5T superconducting MR imager (Achieva, Philips Medical Systems, and Netherland B.V.). Studied cases were positioned in supine position & were instructed not to move or swallow while testing. Examination was done by neck circular polarization surface coil with a small field of view & thin cuts.

MRI protocols have initially sagittal spin-echo collection of photos that is acquired to determine location of axial pictures. 2- Thin (2-4 mm) axial Tl-weighted photos with repetition time of 579 ms and echo time of 21ms, flip angle ninety and FOV 210 mm, and T2-weighted photos with intersection gap of one mm. For axial images, the field of view is generally 210 with matrix of 256 X 256. Axial TI and T2 images were acquired from hyoid bone (approximately 3rd cervical vertebra) to apex of lung. Coronal T2 pictures were obtained to assess masses that stretched underneath cervicothoracic junction.

Thyroid diffusion MRI:

DWI was acquired in axial plane with multi-section single-shot spin echoplanar sequence (TR/TE/NEX: 1.5s/68ms/l) and dispersion sensitivities of 0,500, 750, and 1000 s/mm^2. Dispersion gradients were applied in 3 directions sequentially. With average scan time of 3.5 minutes, sections of 2-5 mm thickness, inter-slice gap of 1 mm, 240 mm FOV, & 256 X 256 matrix were used. ADC maps were automatically created, and circular regions of interest ranging in size from ten to forty mm depending on nodule were positioned in center of solid nodules & on solid portion of mixed solid-cystic thyroid nodules. ADC is monitored in square millimeters each second.

Cytology and histopathological examination: Cytology and histopathological examination were considered the gold standard and all patients underwent an examination either by US-guided fine needle aspiration (FNA) cytology & post-surgical histopathological examination.

Statistical analysis

Statistical analysis was done by SPSS Version sixteen. Variables were presented as a mean and standard deviation and numbers (percentage). The comparison was done by t-test. Sensitivity and the specificity of DWI were calculated. Probability (p-value) was considered significant when $p \leq 0.05$).

RESULTS

Fifteen cases with total of twenty thyroid nodules. There were ten females and five males. Their ages ranged from 25 to 65 years old, with mean age of 47.13 ± 0.8. Largest diameter of nodules varied from 13 mm to 55 mm, with mean of 28.15 mm. There were 14 nodules in thyroid gland's left lobe, 5 nodules in right lobe, and one lesion in thyroid isthmus As shown in table (1).

Table (1): Demographic and clinical data of studied cases.

Sex Male female	 5(33.3%) 10(66.7%)
Age (years) mean ±SD	 47.13 ± 0.8
Diameter of nodules (mm) mean ±SD	 28.15 ± 2.4
Nodules in thyroid gland's **Right** **Left** **thyroid isthmus**	 14(93.3%) 5(33.3%) 1(6.7%)

All cases underwent MRI examination and thyroid nodules were identified and inspected for restricted diffusion on DWI & the ADC value of selected ROI placed in the center of solid nodules or solid parts of complex nodules was calculated. Benign thyroid nodules had ADC values ranging from 1.5 to 1.8 X 10^{-3} mm^2/s (mean: 1.65) (fig 1). Figure (2) showed that ADC values of malignant thyroid nodules ranged among 0.7 and 1.0 X 10^{-3} mm^2/s (mean: 1.0).

DWI and ADC mapping revealed that sixteen nodules were benign and four nodules were malignant. One of the 4 malignant nodules proved to be benign (false positive) with histopathological examination.

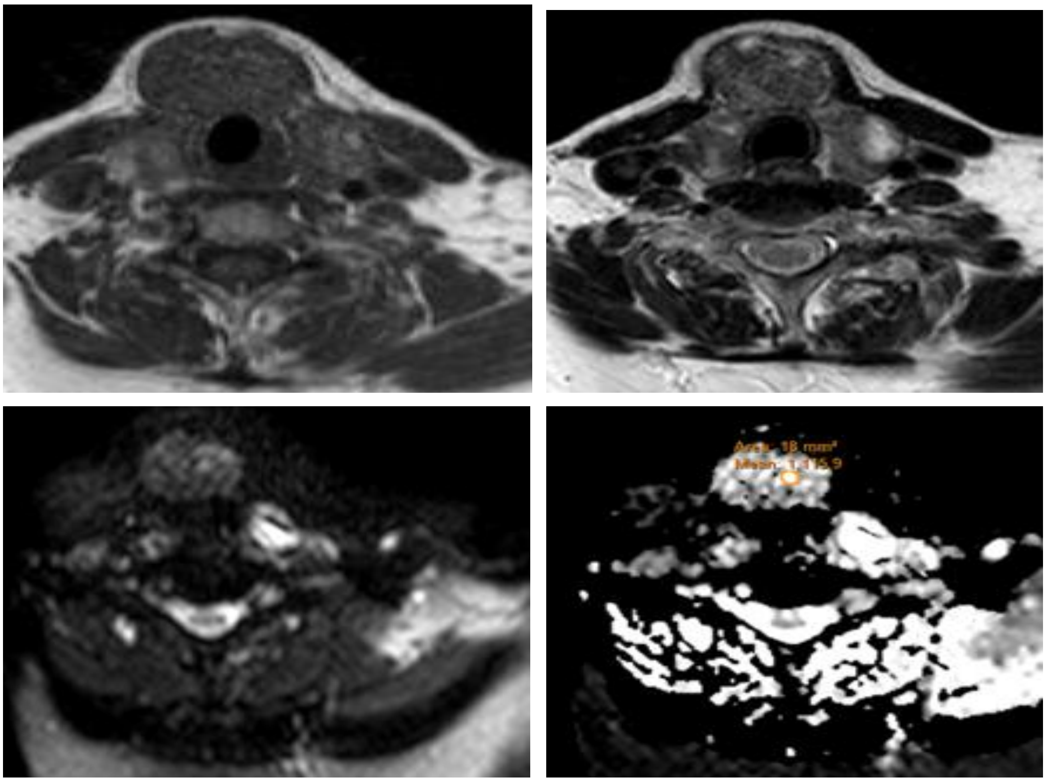

Figure 1: Female patient 33 years old complaining of midline thyroid swelling, T1WI showed well defined isthmic nodule 2 x 3 cm with hyperintense dot inside that represent hemorrhage, T2WI the nodule was isointense, DWI showed facilitated diffusion and ADC value was about 1.15 mm^{2-}/s……histopathologically proved benign follicular adenoma.

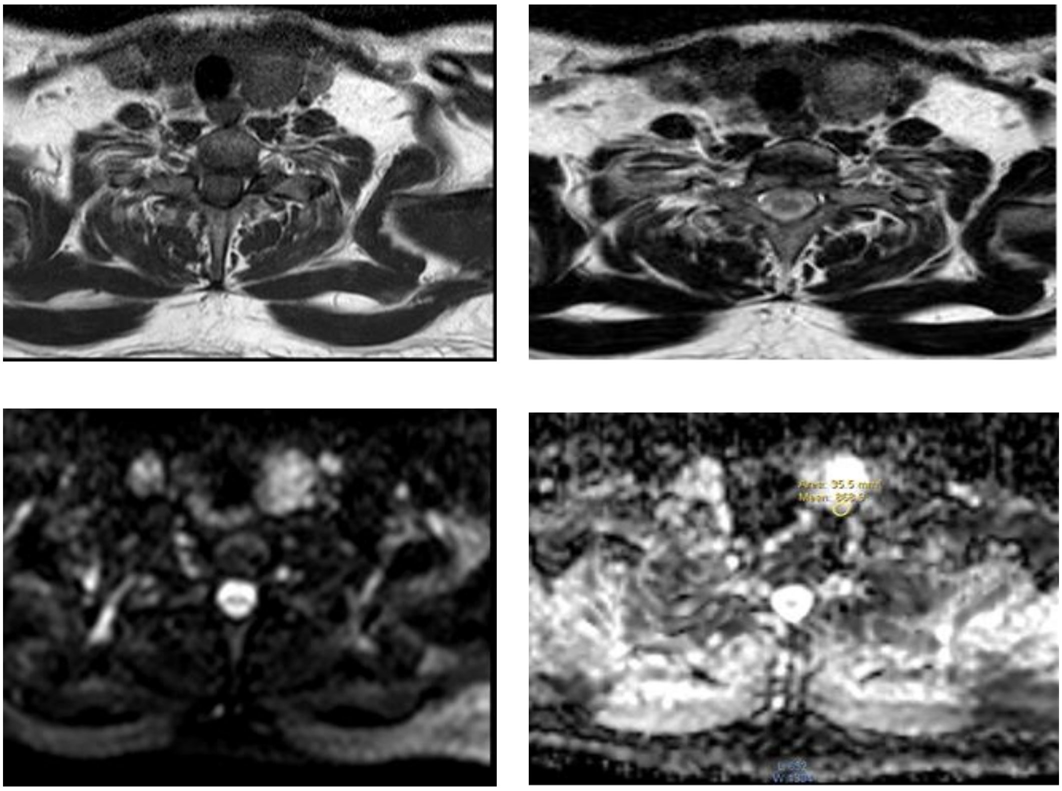

Figure (2): Female patient 45 years old complaining of thyroid swelling, T1WI showed well defined left lobe nodule 2 x 1.5 cm and T2WI the nodule was isointense, DWI showed restricted diffusion and ADC map showed hyperintense signal intensity apart from posterior hypointense signal area that had a value about 0.86 mm^{2-}/s……histopathologically proved malignant follicular changes within a follicular adenoma.

Moreover, for ADC values, Receiver Operator Characteristic curve was computed Fig. (3).

ROC curve's area under curve was one. We chose an ADC cut-off value of less than and equal to one, sensitivity, specificity, PPV, NPV & accuracy were 100%, 94.12, 75, 100, 95% respectively as shown in table (2).

Table (2): Roc curve analysis of diagnosis based upon ADC value according to histopathological results

Sensitivity	Specificity	PPV	NPV	Accuracy
100.00	94.12	75.0	100.00	95.0

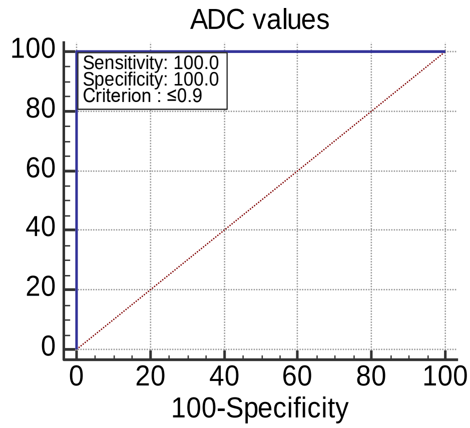

Figure 3: Receiver Operator Characteristic curve was computed for ADC values.

DISCUSSION

Thyroid nodule evaluation should differentiate among benign and malignant nodules in order to accomplish early diagnosis and subsequent extremely early therapies while ensuring minimal surgery in benign nodule cases studied [(5)].

In diagnosis of thyroid swelling, high-resolution real-time ultrasound is commonly used as 1st modality. Even so, because it is simple, quick, real-time, and inexpensive, it has limited utility in making distinction benign from malignant lesions. Use of FNAB to make distinction among malignant and benign thyroid nodules is common & very effective. Even so, 28% of studied cases had inconclusive results. New non-invasive pre-surgical diagnostic examination is required to reduce risk of unnecessary surgery. Thyroid nodule FNAC is inconclusive in cases of inadequate specimens, sampling errors, indeterminate cytology, most common limitations of FNAC are possibility of hematoma formation, pain, & inability to differentiate benign from malignant follicular lesions, in those nodules, confirmatory post-surgical histopathological examination is needed [(3)].

Cut off value of our result was 1, while another study reported that when DWI with b500, ADC of 1.7 X 10^{-3}mm^2/s was used as cut-off value for distinguishing benign from malignant thyroid nodules, accuracy was 87.1% and specificity 90.79% [(5)].

Our results were not in the same line as another study with sensitivity, specificity, PPV, NPV, When using a cutoff value of 1.0 X 10^{-3}mm^2/s, accuracy rates for ADC values in differentiating among benign & malignant thyroid nodules were calculated as eighty percent, ninety seven percent, eighty percent, ninety seven percent, and 96 percent, for b-values fifty, four hundred, and one thousand s/mm^2.

ROC curve's area below curve was 0.995. Sensitivity and specificity were found to be 100 percent and 95.83 percent, respectively, when we chose cut-off ADC value of 1 X 10-3mm2/s [(6)].

Another study disagreed with this research & proved that mean ADC of malignant nodule (n=11) was 0.81 ± 0.166 and that of benign (n=9) was 1.39 ± 0.113 with a significant p-value [(7)]. Others, showed that mean ADC (×10^{-3}mm^2/s) of the benign nodule was 1.72 ± 0.39 and that of malignant was 1.28 ± 0.41 with a statistically significant p-value of 0.001 [(8)]. Higher results were reported with another result that revealed 38 benign & 23 malignant thyroid nodules, respectively. With important (p 0.001) difference, benign nodules had higher ADC values (2.32 ± 0.44 10^{-3} mm^2/s) than malignant nodules (1.40 ± 0.40 10^{-3} mm^2/s) [(9)]. Another finding stated that seventeen cases (56.7%) were positive for cancer, while thirteen cases were negative (43.3%). Statistical examination disclosed that ADC values in malignant lesions were significantly (P-value 0.001) lower. ADC cutoff value for distinguishing benign from malignant lesions was 1.15, with sensitivity & specificity of 88.2% & 92.3% respectively [(10)].

Histologically, there were twenty carcinomas and five adenomas with minimum size of 8 mm. Mean ADC values (in 10^{-3} mm^2/s) differed significantly (P < .05) between carcinoma, adenoma, & normal parenchyma. There was no overlap in ADC variations (95% confidence interval) for carcinoma (2.43-3.037), adenoma (1.626-2.233), & normal parenchyma (1.253-1.602). When ADC value of 2.25 and higher was used to predict malignancy, highest accuracy of eighty eight percent was obtained, along with 85% sensitivity and 100% specificity [(11)].

Another study where Chi-square examinations were used to compare sensitivity, specificity, and accuracy of DWI & ultrasound. ADC value differed significantly. Maximum area below curve was 0.944 when threshold value was 1.12 x 10^{-3} mm^2/s. Sensitivity, specificity, & accuracy were 84.9%, 92.2%, & 87.6% respectively. Corresponding ultrasound diagnosis values were 90.1, 80.4, and 86.9 percent [(12)].

ADC cut-off point for differentiating malignant from benign thyroid lesions is 1.7 x 10^{-3} mm^2/s with high accuracy (87.1%, 95% confidence interval: 79.59-92.07%). According to findings, quantitative diffusion-weighted MRI with ADC measurement can quantitatively distinguish among benign & malignant thyroid nodules [13].

CONCLUSION

Because of its high sensitivity and specificity, quantitative DWI may be reliable, non-radiative, & non-invasive picturing modality for detection of thyroid nodules. ADC values appear to be capable of distinguishing benign from malignant thyroid problems. So, in addition to thyroid ultrasonography & US guided-FNAC for tissue characterization of thyroid nodules, DWI has great value as diagnostic tool, and outcomes may even play role in selection of nodules that will undergo FNAC. More research is necessary to confirm if what diffusion-weighted MR scanning should be added to standard picturing methods used to make distinction between malignant and benign thyroid nodule.

DECLARATIONS

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