Diagnostic Accuracy of Multiple MRI Parameters in Dealing With Incidental Thyroid Nodules

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Research Article

Keywords: incidental thyroid nodule, MRI parameters, thyroid, nodule

Posted Date: December 10th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-809922/v1

Abstract

Background: Different MRI parameters have been studied for evaluating thyroid nodules. Diffusion-weighted imaging (DWI) and T2 imaging sequences with considerable efficacy in evaluating soft tissue tumors merit further assessment for thyroid nodules investigation.

Method: In this study, patients with thyroid nodules indicative of fine-needle aspiration and cytology (FNAC) underwent MR imaging studies. The T2 signal intensity(SI), T2 signal intensity ratio (SIR), Z value, and apparent diffusion coefficient (ADC) values of the thyroid nodule were obtained for every patient. Regarding the FNAC results, the nodules were divided into malignant and benign groups. The two groups' MRI parameters were compared using a two samples independent t-test and the cut-off values estimated by analyzing the receiver operating characteristics plot.

Results: The T2 values, SIR, Z values, and ADC values were significantly higher in the benign group than malignant. The cut-off points of 230 (AUC= 0.759), 3.38 (AUC=0.754), 37(AUC=0.759), and 1.73(AUC=.690) were obtained for T2values, SIR, Z value, and ADC values, respectively.

Conclusion: T2 values, SIR, Z values, and ADC values are reliable parameters in discriminating benign from malignant thyroid nodules, and cut-off points of 230, 3.38, 37, and 1.73 could be reliable cut-off points for each parameter, respectively. However, further studies with a larger sample size are needed to confirm these findings.

Introduction

Although thyroid nodules are amongst the most common medical issues worldwide, differentiating benign nodules from malignant ones is not desirable. Fine needle aspiration and cytology (FNAC) of the nodule is the gold standard in determining these nodules' underlying pathology. However, FNAC is sometimes inconclusive in results, and surgical excisional biopsy and lobar or total thyroidectomy would be the final choice that may be a great burden of physical and psychological stress for the patient and a wastage in the medical expenses(1). The situation becomes more complicated in incidental thyroid nodules (ITNs) found in head and neck and upper mediastinum imaging studies(2). Regarding the fact that ITNs may present either a benign or malignant behavior, reporting these nodules on magnetic resonance imaging (MRI) or computed tomography (CT) studies without any particular suggestion or diagnosis may lead to overdiagnosis or underdiagnosis of the malignancies(3–5).

Therefore, the better the radiologist could distinguish the pattern and nature of ITNs, the more effective medical investigations could be applied to identify the underlying pathology, and the less the patients encounter anxiety and uncertainty(4). Although the guidelines for the management of ITNs on MRI recommend some properties to determine whether the nodules need more investigations or not, still no definite approach to discriminate malignancy from benignity on MRI of thyroid nodules is recommended(6). Moreover, research indicates that these guidelines may not be reliable as some thyroid malignancies incidentally found in MRI may be missed(3). On the other hand, many ITNs that are benign and need no further evaluation due to these guidelines have to undergo more evaluation by ultrasound study and FNAC(4). These facts highlight the need for more studies on the properties of ITNs on MRI to attain proper criteria for differentiating the malignant from the benign ones.

Recent studies in MRI of thyroid nodules have candidate T2 protocols and Diffusion-weighted imaging (DWI) for differentiating benign from malignant lesions(7–10). T2 weighted MRI has been used to assess various soft tissue pathologies, especially for estimating the probability of malignancy in lymph nodes and prostate(11). It is also suggested as a potential modality to assess thyroid nodules(8). DWI, which is reported quantitatively by apparent diffusion coefficient value (ADCV), is a functional MRI based on the Brownian movement of water molecules through the tissue. DWI can provide crucial information from the molecular profile and microarchitecture of the studied organ or pathologic tissue. Consequently, DWI is a useful tool in evaluating head and neck tumors, salivary gland tumors, and cervical lymphadenopathy(12) and is also suggested for assessing thyroid nodules(13).

In this study, we sought to define a scale for reporting thyroid nodules in MRIs and determine whether the T2 and ADC values could predict the nature of thyroid nodules. We also hypothesized that a small proportion of thyroid nodules undergo the subsequent evaluation and that certain factors related to the MRI characteristics of the nodule influence workup.

Thus, we performed an MRI in T2 and DWI sequences for patients with thyroid nodules suspicious of malignancy diagnosed by ultrasound and then compared the MRI values with the FNAC report.

Materials And Methods

Patient selection

This prospective study was conducted in a tertiary care center from 20 October 2018 to 15 December 2020. This study was approved by the committee of biomedical research ethics of our department.

Before including patients in the study, informed consent was obtained. The study aims, procedures, and risks were completely defined for the patients. It is essential to mention that this study had no interference with standard care for patients diagnosed with thyroid nodules

In this study, patients were already suspected or diagnosed with thyroid nodules by expert endocrinologists and referred to the radiology department for the thyroid nodule's ultrasound study. According to the American College of Radiology (ACR) Thyroid Imaging Reporting and Data System (TI-RADS), based on the size and structure of the nodules in ultrasound study, the TI-RADS score is indicative for either fallow-up or FNA of the nodule. In this study, we needed to determine the nature of the nodules by FNA and pathologic studies. Therefore, we only included (Fig. 1) patients with TI-RADS scores indicative of FNA, which is shown in Table1.

Table 1
Indication of FNA considering TI-RADS score.

TI-RADS score indicative for FNA
1) score 3, size ≥ 2.5 cm
2) score 4 to 6, size ≥ 1.5 cm
3) score 7 or more, size ≥ 1 cm

Ultrasonography protocol

The ultrasound study was performed by an expert radiologist with 10 years of experience in thyroid US using the same ultrasound scanner (siemens-healthineers, ACUSON NX) for all patients with a 15MHZ linear transducer. The examination was performed in transverse and longitudinal views to investigate any thyroid nodule, abnormal lymph node, tumor infiltration, metastasis, and other soft tissue pathologies differentially diagnosed thyroid nodule. The ultrasound study was reported according to the American College of radiologists' TIRAD system.

MRI protocol

MRI was performed by a 1.5T scanner (Philips medical system, Ingenia ambition 1.5TX, the Netherlands) using a neck coil. All patients were studied by the same mentioned machine and coil.

The MRI protocol included Axial T2-weighted (T2WI) (repetition time/ echo time (TR/TE): 2904 ms/80 ms, slice thickness, 3 mm; gap, 0.5 mm; (number of excitation) NEX, 4; field of view (FOV), 16 cm; matrix,320 × 224) and DWI on axial plane on diffusion gradient b factor = 800 (TR/TE: 5000 ms/minimum; FOV, 16 cm; NEX, 4; matrix, 128 × 128; slice thickness, 4 mm; and gap = 0.5 mm.

Quantitative image analysis

Two radiologists with 10 and 8 years of experience in head and neck imaging who were blinded to the patients' ultrasound reports measured signal intensities of thyroid nodules and paraspinal muscles on T2-weighted imaging by placing a circular ROI cursor. In thyroid nodules, circular ROI covered the entire nodule at the largest cross-section area without including artifacts or cystic portions of the nodule. Signal intensity ratio(SIR) on T2-weighted was measured as a ratio of signal intensity of the thyroid nodule on T2-weighted to that of paraspinal muscle.

Also, signal intensities of background noise on T2-weighted were measured.

The Z value is calculated as following:

$$\frac{\text{signal intensity of thyroid nodule} - \text{mean signal intensity of noise (T2-wieghted)}}{\text{SD signal intensity of noise (T2-wieghted)}}$$

The DWI sequence was performed to obtain the ADC values of each patient's thyroid nodule by analyzing the ADC map for every individual (Fig. 2,3).

Ultrasound-guided FNA and cytology study

Under sterile conditions after ultrasound-guided localization of the nodule and local anesthesia, a 21-gauge or 22-gauge was used to perform aspiration biopsy. The specimen was fixed and stained for histopathology study. An expert interventional radiologist performed the FNA of the thyroid nodule for each patient in the intervention section of the AL-Zahra hospital's radiology department, Isfahan, Iran, and the samples were transported to the pathology department. The cytological study was performed independently by a pathologist, an expert in thyroid cytology. The pathologist was blinded to the patients' MRI and ultrasound results.

Statistical analysis

Quantitative variables were reported as mean, median, standard deviation, and interquartile ranges. Qualitative variables were reported as numbers and percentages. The quantitative data were assessed for being normal by the Kolmogorov-Smirnov test and Q-Q plot. The comparison of quantitative variables between the malignant and benign groups was made by two samples independent t-test. The diagnostic values of thyroid nodule signal intensity on T2-weighted, T2 SIR, Z value, ADC value of thyroid nodule, and the cut-off points of each parameter in the malignant and benign group were determined by analyzing the receiver operating characteristics (ROC). Sensitivity, specificity, positive likelihood ratio (LR+), and accuracy of the cut-off points were also determined. The area under the curve was reported with a 95% confidence interval.

Results

A total of 37 solid thyroid nodules were identified in 33 patients.22 nodules were benign, and 15 nodules were malignant. Mean, median, standard deviation, and interquartile ranges of patients' age, signal intensity on T2-weighted, T2 SIR, Z value, ADC value of thyroid nodule in benign and malignant nodules were summarized in Table2.

Table 2
Mean, median, standard deviation, and interquartile ranges of patients' age, thyroid nodule signal intensity on T2-wighted, T2 SIR, Z value, and ADC value of thyroid nodule in benign and malignant nodules

variable	Mean (SD)	Median	interquartile	P value
Age				
Benign	50.18(10.9)	51	15	0.943
Malignant	49.87 (14.1)	57	28	
T2 SI of thyroid nodule				
Benign	314.64(127.4)	281	205.2	0.001
Malignant	203.67(52)	207	155	
T2SIR				
Benign	4.21(1.3)	3.5	3.3	0.002
Malignant	2.96(0.9)	2.8	2.1	
Z value of T2				
Benign	51.19(21.2)	45.5	32.9	0.001
Malignant	32.66(8.7)	33.2	24.5	
ADC value				
Benign	1.63(0.7)	1.8	1	0.08
Malignant	1.26(0.4)	1.3	0.9	

The mean age was 50.05 years, and in the malignant and benign group was 50.18 and 49.87 years, respectively, without any significant differences between the groups (p = 0.943). The sex distribution was not significantly different between the groups as well.

The T2-weighted signal intensity of Thyroid nodule, T2 SIR, ADC value of thyroid nodule, and Z value was compared between the malignant and benign group. The mean T2-weighted signal intensity of thyroid nodule, SIR, and Z values were 314 ± 127, 4.21 ± 1.3, and 51 ± 21.2, which were significantly higher in the benign group. P- values were 0.001,0.002 and 0.001 respectively. The ADC value in the benign group was 1.63 ± 0.7 and in the malignant group was 1.26 ± 0.4, which was marginally higher in the benign group (P value:0.08).

Based on ROC analysis, optimal thresholds of T2-weighted signal intensity of thyroid nodule for differentiating benign and malignant groups was 230, which was the most accurate (68%), cut off point with a sensitivity of 68.18%, specificity of 67%, and positive likelihood ratio(LR+) of 2. The area under the curve for this cut-off point was 0.759 ($p < 0.01$) (Fig. 4a)

Also, the diagnostic value of T2 SIR and Z value was evaluated by ROC, and the results indicated that 3.38 with AUC = 0.754($p = 0.01$) (Fig. 4b) and cut off point of 37 with AUC = 0.759($p = 0.01$) (Fig. 4c) were the most accurate, specific, and sensitive cut off point with the highest positive likelihood ratio.

The evaluation of ADC values by ROC indicated that the 1.73 with AUC = 0.690 ($p < 0.05$) has the greatest accuracy, specificity, and sensitivity with the highest positive likelihood ratio(LR+) discriminating benign from malignant nodules. (Fig. 4d).

Cut-off points of theT2 values, SIR, Z value, and ADC values with specificity, sensitivity, and positive likelihood ratio, are summarized in Table 3.

Table 3
Cut off points of theT2 values, SIR, Z value, and ADC values between benign and malignant nodules with sensitivity, specificity and positive likelihood ratio.

Variable	AUC (95% conf. interval)	Cut off point	sensitivity	Specificity	Positive likelihood ratio	accuracy	P value
T2 SI	0.759 (0.605–0.913)	230	68.18%	67%	2	67%	< 0.01
SIR	0.754 (0.594–0.914)	3.38	77%	66%	2.3	72%	< 0.01
Z value of T2	0.759 (0.605–0.913)	37	68%	66%	2	67.5%	< 0.01
ADC value	0.690 (0.490–0.890)	1.73	66%	92%	9	78%	< 0.05

Discussion

Studies evaluating MRI parameters in reporting benign and malignant thyroid lesions have been controversial. T2 weighted MRI always has been a subject of interest for distinguishing malignant from benign lesions, especially in soft tissue tumors(7, 14). To our best knowledge, there is no study particularly reporting T2 imaging protocol as a reliable method to evaluate thyroid nodules. However, in a study of 181 patients with thyroid nodules, *Wang et al.*(10) reported that among T1, T2, and ADC protocols, only ADC values of thyroid nodules have diagnostic values. On the other hand, *Shi et al.*(7) indicated that T2* values of thyroid nodules could be diagnostic and had reported the cut-off point of 25.00 msec. Herein we assessed the diagnostic value of T2 imaging protocol in thyroid nodules of 37 patients (15 malignant and 22 benign nodules). The results were indicative of a reliable diagnostic value of T2 protocol in ITNs with a cut-off point of 230 (AUC of 0.759, sensitivity of 68.18, specificity of 66.67, and LR + of 2.0455).

Moreover, to better assess the competency of T2 weighted MRI in discriminating thyroid nodules, the signal intensity ratio (SIR) was calculated for every nodule, and the cut-off point of 3.38 (AUC of 0.754, Sensitivity of 77.27, Specificity of 66.67, and LR + of 2.1382) was obtained. This method with higher sensitivity may guarantee the reliability of T2 imaging protocol in the discrimination of thyroid nodules. In addition to a SIR of the nodules to diminish the background noise effect on interpreting T2 values, we corrected the T2 values of every nodule with noise in the background by calculating the Z-values. The results were conclusive for T2 values of thyroid nodules with the cut-off point of 37 (with AUC of 0.759, Sensitivity of 68.18, Specificity of 66.67, and LR + of 2.0455). These results indicated that the background noise does not significantly affect the estimated cut-off point for T2 values.

DWI protocol is better studied in the field of thyroid malignancies. Although the number of studies purposing DWI as a diagnostic method is far more than the T2 protocol, heterogeneous results and cut-off points increase the need for more investigations to establish these methods (13). A systematic review and meta-analysis by Chen et al. (13) evaluated studies assessing thyroid nodules by DWI. They concluded that although this imaging method is an accurate way to distinguish malignant and benign nodules, still more investigations are needed to determine a reliable cut-off point and b-value for this method. They also explained that the heterogeneous cut-off points reported in different studies are due to different b-values utilized in the imaging process. A brief review of studies determining cut-off points for ADC values is listed in Table 4.

Table 4
The reported cutoff points with different b-values in the studies evaluating thyroid nodules by DWI protocol.

Authors	b-value	Cutoff value	AUC
Bozgeyik et al.(15)	100	1.45×10^{-3} mm^2/s	0.997
Bozgeyik et al.	200	0.65×10^{-3} mm^2/s	1.00
Bozgeyik et al.	300	0.36×10^{-3} mm^2/s	0.884
Wu et al.(16)	300	2.17×10^{-3} mm^2/s	0.876
Wu et al.	500	1.74×10^{-3} mm^2/s	0.63
Wu et al.	800	1.65×10^{-3} mm^2/s	0.63
Linh et al.(17)	800	1.53×10^{-3} mm^2/s	
Shi et al.(18)	500	1.704×10^{-3} mm^2/s	0.942
Turan ilica et al.(19)	1500	905×10^{-3} mm^2/s.0	0.972
Nakahira et al.(20)	1000	1.60×10^{-3} mm2/s	N/A
Mutlu et al.(21)	1000	0.56×10^{-3} mm2/s	1.00
El-Hariri et al.(22)	500	1.5×10^{-3} mm^2/s	0.96–1.00
Razek et al.(23)	250–500	0.98×10^{-3} mm^2/s	0.97
Aghaghazvini et al.(9)	500–1000	1×10^{-3} mm^2/s	0.93
Wang Q et al.(24)	2000	1.46×10^{-3} mm^2/s	.975

As demonstrated, the different b- values ranging from 100 to 2000 are co-existent with heterogeneous cut-off points ranging from 0/36 to 2/17. Moreover, the literature's current state suggests the highest possible b-values in DW imaging would better discriminate malignant and benign thyroid nodules(13). Thus, in the present study, the relatively high b-value of 800 was applied, and the cut-off point for ADC values was 1.73 (AUC of 0.690, Sensitivity of 66.67, Specificity of 92.86, and LR + of 9.33). Compared to other studies, ADC values of 1.73 with the AUC of 0.69 indicated a lower accuracy than some studies. However, compared to *Wu et al.*(16) with a b-value of 800 and cut-off point of 1.65 (AUC of 0.63, Sensitivity of 53%, and Specificity of 71%), our study indicated better accuracy for the cut-off point of 1.73. *Linh et al.* (17)also reported the AUC of 0.94 with the cut-off point of 1.53, Sensitivity of 84%, and Specificity of 92%, which shows a considerably higher accuracy that could be explained by a bigger study population than us.

Study strengths and limitations

This study used two new equations to better identify the thyroid tumors' malignancy or benignity. These equations (Z and T2 values) could help the radiologists interpret thyroid nodules, especially in doubtful results by single T2 or ADC values. Regarding the covid-19 pandemic and limitations in resources, we decided to cut the number of participants in half to be able to prepare the best protective equipment and avoid any dangerous contacts for both patients and the research team; thus, due to the limited number of studied patients the risk for accidentally meaningful results is considerable, and we suggest further studies with greater study populations.

Conclusion

Our results showed that T2 and ADC values are appropriate for differentiating malignant from benign thyroid nodules. Therefore, we suggest that thyroid nodules' T2 and ADC values could be appropriate and safe methods for investigating thyroid nodules on MRI. However, further studies with a larger sample size are needed to confirm these findings.

Declarations

All manuscripts must contain the following sections under the heading 'Declarations', to be placed before ‘References’. If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

i. Funding : Not applicable
ii. Conflicts of interest/Competing interests : The authors declare no conflict of interest.
iii. Ethics approval : This study was approved by the committee of biomedical research ethics of Isfahan University of Medical Sciences, Isfahan, Iran.
iv. Consent to participate : All the patient’s written consent was obtained for participating in the study.
v. Consent for publication : Patient’s written consent was obtained for publication purposes.
vi. Availability of data and material : Data available on request.
vii. Code availability : Not applicable
viii. Authors' contributions :

Azin Shayganfar: Design, acquisition of data, analysis and interpretation, manuscript writing, manuscript editing

Neda Azin: Acquisition of data, manuscript writing

Peyman Hashemi: Acquisition of data, analysis and interpretation, manuscript writing, manuscript editing

AmirMohammad Ghanei: Acquisition of data, analysis and interpretation, manuscript writing

Somayeh Hajiahmadi: Design, acquisition of data, analysis and interpretation, manuscript writing, manuscript editing, intellectual content

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Figures

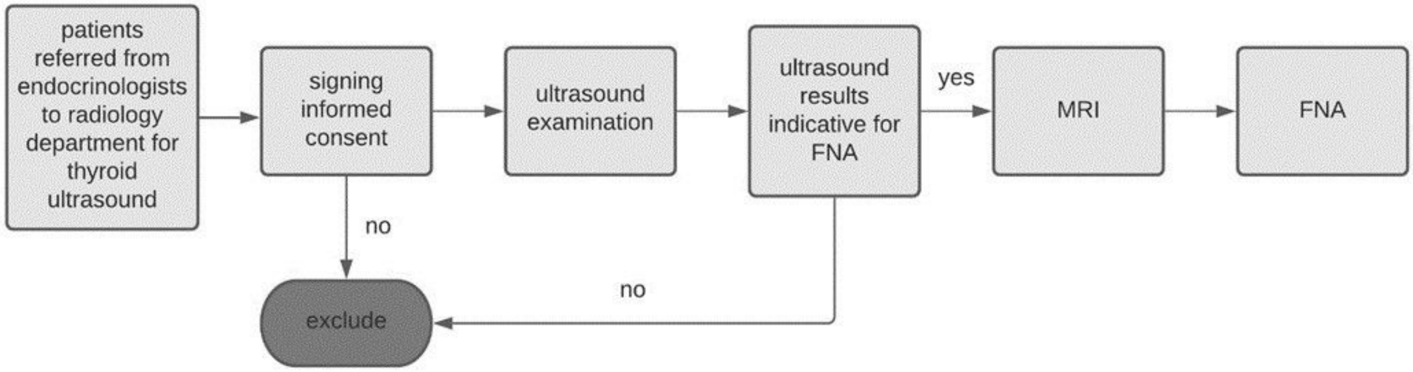


Figure 1

Flow diagram of the study procedure.

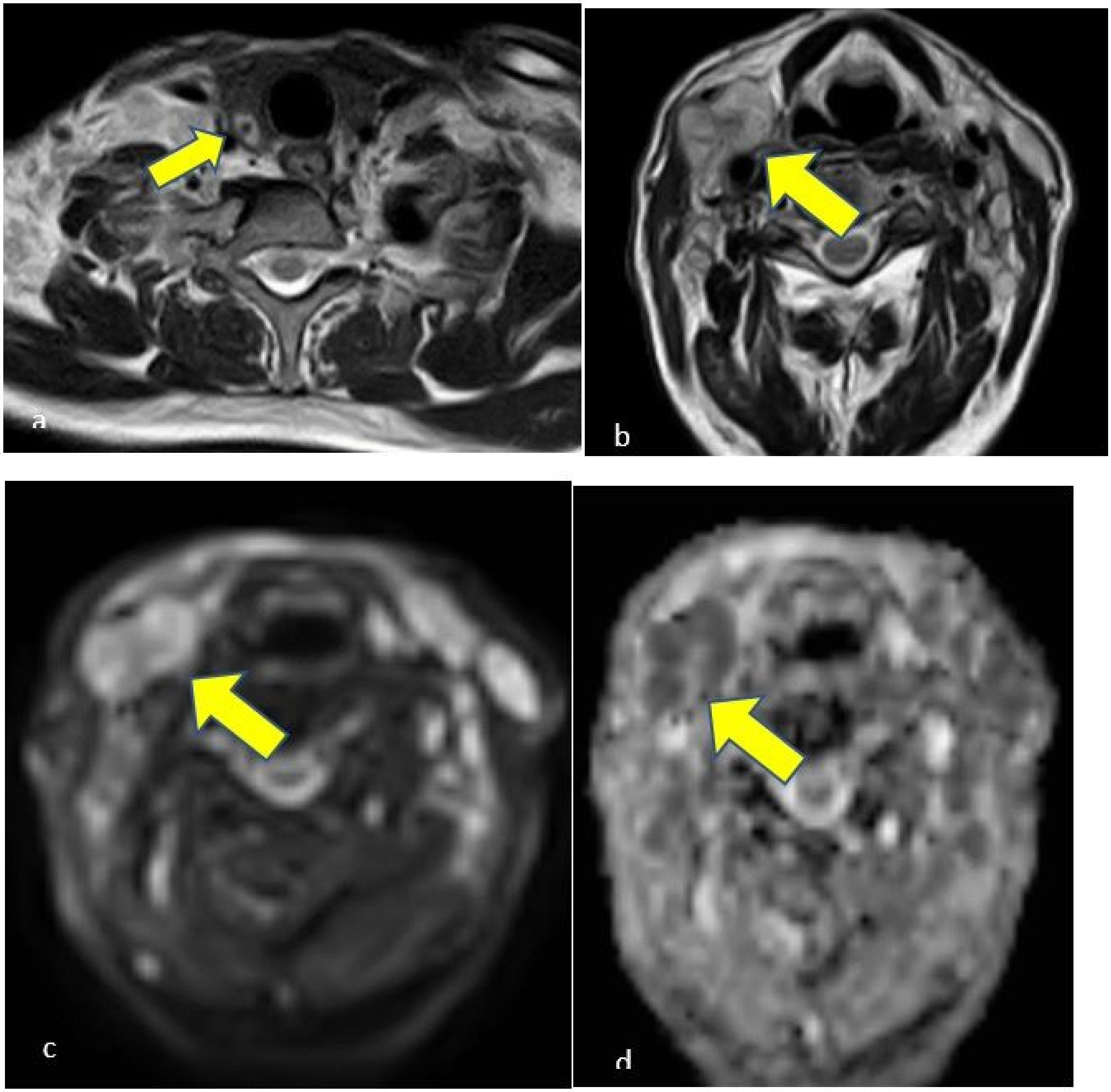


Figure 2

57 years old man with papillary thyroid nodule and nodal metastasis: a) Axial T2-weighted image shows small hyperintense thyroid nodule in right lobe with central calcification(arrow), with TIRADS4 in sonography (not shown here). b) Axial T2-weighted image of same patient with lymphadenopathy(arrow) in right side of neck. C, D) Axial DWI and ADC images of lymph adenopathy show restriction on DWI(c) and ADC value 1.14×10-3mm2/s(d) (arrows).

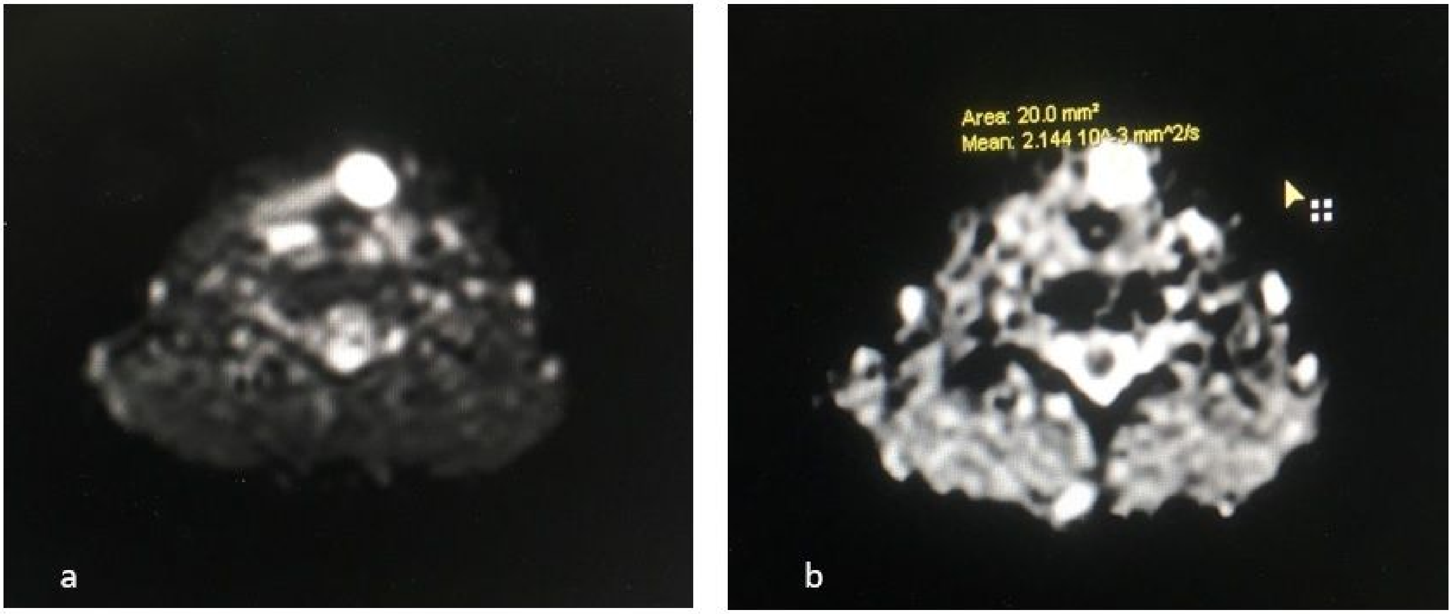
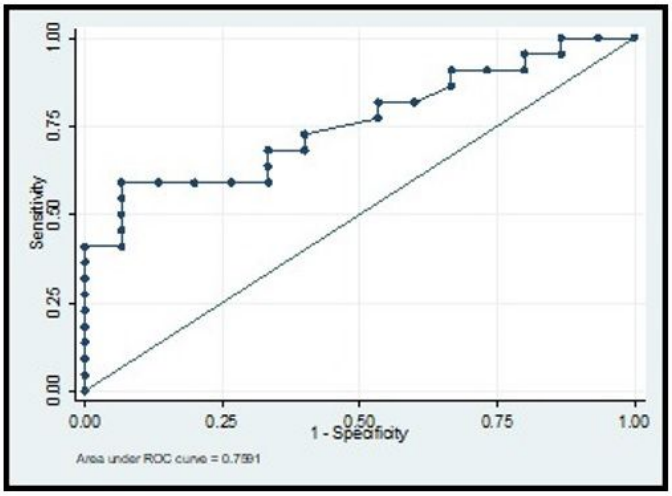


Figure 3

35 years old woman with benign pathology for left thyroid nodule: a, b Axial DWI and ADC of nodule which show no restriction on apparent diffusion coefficient (ADC) map.



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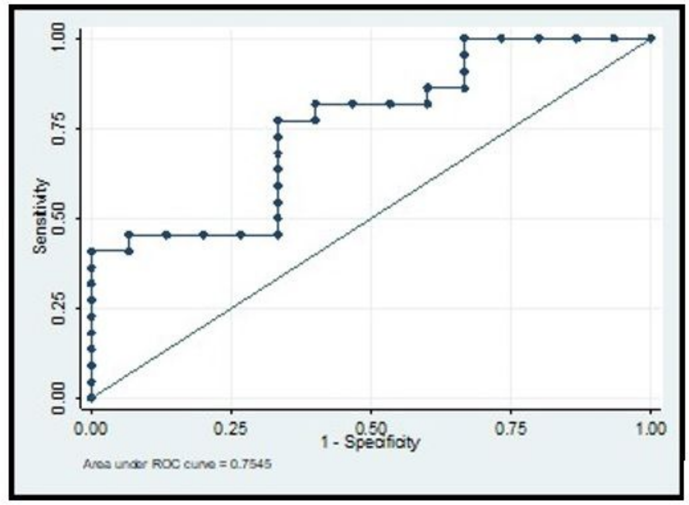

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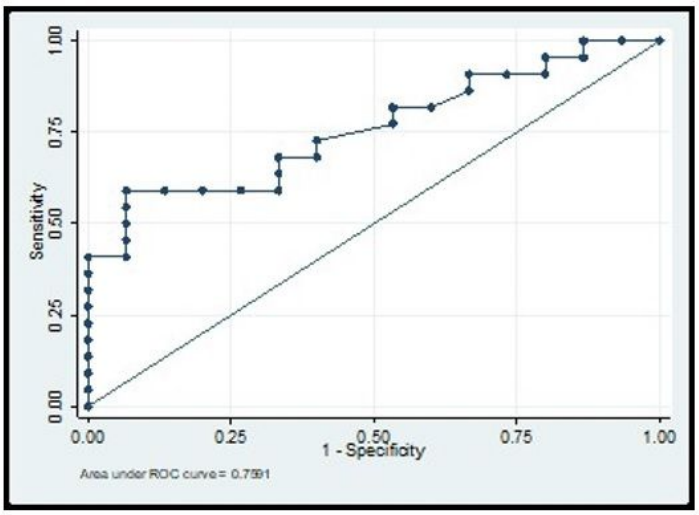

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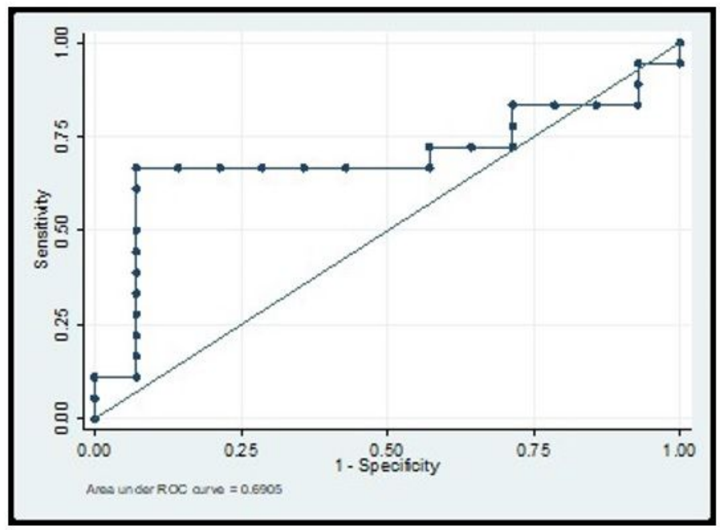

4d

Figure 4

ROC analysis optimal thresholds of T2-weighted signal intensity(a), T2 SIR(b), Z value(c) and ADC value(d).