DIFFERENTIATION BETWEEN BENIGN AND MALIGNANT THYROID NODULE WITH DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING AND APPARENT DIFFUSION COEFFICIENT MEASUREMENTS AND ITS HISTOPATHOLOGICAL CORRELATION

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ABSTRACT

BACKGROUND

The aetiology of thyroid nodules is diverse. Benign causes include the colloid nodule and the classical multinodular goiter. Occasionally, Hashimoto's thyroiditis and Grave's disease may present with nodularity. Malignant causes include thyroid cancer, lymphoma as well as metastasis to the thyroid glands.

The objectives of the study were to compare ADC value of indeterminate thyroid nodules (includes TIRADS 3, 4 & 5) with their histopathology and then evaluate its role in differentiating malignant from benign thyroid nodules.

MATERIALS AND METHODS

The prospective study was conducted in Department of Radiology and Imaging Sciences, Malabar Institute of Medical Sciences Ltd, Calicut, Kerala between 1st October 2015 to 30th March 2017, for a period of 18 months. The study population for analysis is the patients undergoing ultrasound thyroid, detected to have TIRADS 3, 4 and 5 lesions**.** All patients presenting with indeterminate thyroid nodule on ultrasonography in our hospital are subjected to MRI DW sequences the ADC was calculated.

RESULTS

A total of 80 patients with USG diagnosis of indeterminate thyroid nodule (TIRADS 3, 4 & 5) that came to the department before undergoing surgery were included in the study. For all these patients, T2 weighted MRI, diffusion weighted imaging and ADC mapping was done. Histopathology findings of each patient is collected and correlated with MRI findings to finalize the diagnosis. The sensitivity and specificity for various ADC values were calculated from ROC curve and it was noted the best ADC value for differentiating benign from malignant thyroid nodules according to our study is 1.745 with the highest sensitivity and specificity to qualify it as a screening test. The positive predictive value and negative predictive value when taking 1.745 as cut off ADC are 89.5% & and 98.4% respectively. The mean ADC of the malignant thyroid nodules ($1.52\pm 0.23 \times 10^{-3}$ mm^2/s) was significantly lower than that of the mean ADC of the benign thyroid nodules ($2.25\pm 0.41 \times 10^{-3}$ mm^2/s). Range of mean ADC value for benign lesions was 1.56 – 3.33 and for malignant lesions was 0.96 – 1.87. The proportion of cases with malignancy increases with decreasing ADC value. 17 out of 18 malignant cases were having an ADC value of less than 1.745 (Sensitivity - 94.4%).

CONCLUSION

The study showed MRI with diffusion weighted imaging and ADC mapping is a promising tool in the armamentarium for the differentiation of benign and malignant thyroid nodules.

KEYWORDS

Thyroid Nodule, Malignant, Goiter, Radio Imaging, Histopathology, Thyroiditis.

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BACKGROUND

Thyroid nodules are the most common disorder of thyroid gland. Thyroid nodules are reported to be found in 33% of unselected adults between the age of 18 and 65 years and in 50% of the population over 65 years of age.[(1)] Thyroid nodules are found in 4%–8% of adults by palpation, 41% by sonography, and 50% by pathologic post-mortem examination.[(2)] Although in the general population, most thyroid nodules are benign, the prevalence of thyroid cancer is as high as 5%– 10%.[(3)]The prevalence of thyroid nodules may vary with age, gender, and population studied. Thyroid nodules are frequently seen in adults and women.

Because of the suspicion of malignancy, thyroid nodules require a detailed examination and Investigation. Clinical examination, ultrasonography (US), radionuclide scintigraphy, and fine-needle aspiration cytology (FNAC) are the common methods to evaluate thyroidal nodularity. The

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prevalence of non-palpable nodules detected by ultrasonography is 30% in patients younger than 50 years of age and 50% in patients older than 60 years of age.[4] Many studies have been published to predict whether a thyroid nodule is benign or malignant on the basis of US findings. Several US features have been found to be associated with an increased risk of thyroid cancer including the presence of calcifications, hypo echogenicity, irregular margins, absence of a halo, predominantly solid composition, and intranodular vascularity. However Ultrasound sensitivity and specificity in characterising thyroid nodules vary considerably from study to study and a range between 52 and 97% and 26.6 and 83% respectively.[5] No US feature has both high sensitivity and high positive predictive values for thyroid cancer [6].According to American Thyroid Association guidelines, no single US feature or combination of features is adequately sensitive or specific for identification of all malignant nodules [7].US with fine-needle aspiration biopsy (FNAB, cytology) is considered an effective method for differentiating between benign and malignant thyroid nodules and almost exclusively used for de novo diagnosis. In practice, most of these indeterminate nodules undergo FNAC which is an invasive procedure. However, all does not need FNAC since the malignant potential varies from 5%- 80%. FNAC has inherent limitations with specificity of 60-98% and a sensitivity of 54-90% in various studies due to indeterminate and non-diagnostic results.[8] As a result, a significant number of patients eventually receive unnecessary thyroid surgery.

Despite great improvement in diagnostic techniques there is still a large problem to use a non-invasive and reliable technique to differentiate benign from malignant thyroid nodules.[9] To date, little information is available about the use of MR imaging in the diagnosis of thyroid cancer.

Conventional MR imaging cannot differentiate benign from malignant thyroid nodules or assess the functional status of the thyroid nodule.[10] In order to decrease the risk of unnecessary surgery, as well as financial burden to the community, there is a need for a new non-invasive pre-surgical diagnostic test.[11] Rapid improvements in MRI techniques have resulted in MR images with excellent spatial resolution and soft tissue contrast, which contribute to the differentiation of suspected tumours. Diffusion-weighted MR imaging (DWI) is a noninvasive technique with no radiation exposure, which has the potential to differentiate benign from malignant tissues.[12] During the last 2 decades, DWI has evolved as a helpful diagnostic tool for assessing in vivo tumor characterization, not only in neural lesions but also in extraneural tissue, such as bone marrow pathologies, lymph nodes, and liver tumours. Diffusion weighted imaging (DWI) provides insight into biological and histological characteristics of tissues and may distinguish brain tumor grades, between malignant and benign tumours presumably mainly due to differences in tumor cellularity and biochemical properties of extra-cellular space. Structural changes characteristic of malignancies or benign tissue may result in different signals on DWI, which may be quantified by calculating the apparent diffusion coefficient (ADC). The ADC is an objective parameter that reflects the tissue-specific diffusion capacity and is already being used for tissue characterization and follow-up measurements in therapeutic monitoring.[13] The present study is conducted to compare ADC value of indeterminate thyroid nodules (includes TIRADS 3, 4 & 5) with their histopathology and then evaluate its role in differentiating malignant from benign thyroid nodules.

MATERIALS AND METHODS

Study Area

The prospective, observational research study was conducted in the department of radiology and imaging sciences, Malabar institute of medical sciences ltd, Calicut, Kerala. The study was conducted after taking approval from the ethics committee of MIMS hospital.

Study Population

The study population for analysis is the patients undergoing Ultrasound thyroid detected to have TIRADS 3, 4 and 5 lesions. All participants gave written consent for the study either by themselves or by their close relatives, if they were unable to provide consent. Study samples are selected based on clearly defined criteria as given below.

All patients included presenting with indeterminate thyroid nodule (TIRADS 3, 4 & 5) in ultrasound in Department of Radiology and Imaging sciences, Malabar Institute of Medical Sciences Calicut during the study period 1st October 2015 to 30th March 2017, for a period of 18 months. Patients Excluded from the study were Normal thyroid, TIRADS 1 and 2, Patients not giving consent, those lost to follow up, Contraindications to MRI studies, such as patients with pacemakers, metallic implants, aneurysmal clips, Claustrophobia.

Imaging Technique and Evaluation Process

All patients presenting with indeterminate thyroid nodule on ultrasonography in our hospital are subjected to MRI DW sequences according to our department protocol.

MRI studies are done using 1.5 TESLA whole-body system (OPTIMA 450 W) with same protocol for all patients.

All patients are asked to get rid of any metallic subjects as well as they are asked about any contraindication to MRI examination (artificial heart valve, cardiac pacemaker, metallic stents or joint prosthesis except that made of titanium. The patients are informed about the duration of the examination, the position of the patient and the importance of being motionless). Patients were in supine position and were instructed not to swallow or move during the examination. Circularly polarized surface coil was placed over the neck. The imaging protocol includes axial T2*WI (3446/130/90/3) sequences and Diffusion weighted imaging sequences.

Diffusion Weighted MR Imaging (DWI)

The imaging sequence for DWI is a multi-section, fat suppression spin-echo-type multi-shot echo-planar imaging (EPI) in the axial sequence. Sensitizing diffusion gradients are applied sequentially in the phase encoding direction with b values of 0 and 500 s/mm^2. Sequential sampling of the K space is used with TR/TE, 2500/95 ms; acquisition matrix 120.120 thickness 5 mm, interslice gap 1 mm, FOV26· 26 cm. ADC was calculated by the following formula: ADC = (lnSI1/SI2)/ (b2-b1), where SI1 and SI2 are signal intensities of sequences S1 and S2 respectively and b1 and b2 are motion probing gradient factors (diffusion factors) of sequences S1 and S2 respectively.

The ADC value is calculated automatically by a standard MRI software imager and included in the sequence. In order to measure the ADC of the lesions, a circular region of interest (ROI) ranging from 10 to 30 mm^2 according to the size of the nodule, and were placed in the center of the lesion in cases of solid nodules and on the solid portion of the lesion in cases of mixed solid-cystic thyroid nodules. ADC value was obtained with b values 0 and 500 s/mm^2. The ADC values are expressed in square millimetres per second (mm^2/s).

Statistical Method
Histopathology findings of each patient is collected and correlated with DW and ADC values to finalize the diagnosis. Data will be analysed using SPSS 17.0 (statistical package for social science). Continuous data measurement will be represented as mean with SD or median with inter quantile range according to the distribution of the data. Categorical data will be expressed in frequencies with percentage. Association between categorical variable will be test using Chi Square test or Fishers exact test. Continuous data between two groups will be compared using independent sample t-test or Mann Whitney test. Sensitivity, specificity, accuracy, positive predictive value, negative predictive value will be evaluated in comparison. Ideal cut of will be obtained by Receiver Operator Characteristic Curve (ROC). For all tests a p value less than 0.05 will be considered as a statistically significant difference. Microsoft word and excel have been used to generate tables and graphs.

RESULTS
Over a period of 18 months, a total of 80 patients with USG diagnosis of indeterminate thyroid nodule (TIRADS 3, 4 &5) that came to the department before undergoing surgery were included in the study after explaining about the study and getting informed consent. Those thyroid nodules those were smaller than 5 mm was excluded from the study. For all these patients, T2 weighted MRI, diffusion weighted imaging and ADC mapping was done. Histopathology findings of each patient is collected and correlated with MRI findings to finalize the diagnosis.

Demographic Profile of the Patients
Gender distribution of thyroid nodules
Of the 80 patients in the study, 67 (83.8%) were females. This finding is in accordance with the available literature, as thyroid nodules are more common among females, with a male: female ratio of around 1:5 to 1:2. In this study the ratio is approximately 1:5.

Percentage of Thyroid Nodules in different Age Groups
The commonest age group of thyroid nodules was between 41-50 yrs. (28.7%). The 22.5% of thyroid nodules are seen in 31-40 yrs. age group and 21.3% in 51-60 age groups. The percentage of nodules in <20 years, 21-30 years, 61-70 years and >70 years are 1.3%, 12.5%, 113% and 2.5% respectively.

Percentage of Malignancy among Age Groups
The percentage of malignancy is more in the 21-30 years age group and above 70 years age group (50% of the nodules in the age group) followed by 31-40 years (44.4% of the nodules in the age group). 22.2% of thyroid nodules are malignant in 61-70 years age group and less than 10% (8.7%) in 41-50 years age group. No malignant nodule was detected in less than 20 years and 51-60 years in this study.

Gender difference in Malignant Nodule
The gender difference among malignant nodules showed significant difference. Around 46% (6 out of 13) of nodules were malignant in males and 18% (12 out of 67) in case of females. Thyroid nodules were seen malignant in case of males more than two times compared with that of females.

Ultrasound Features in Thyroid Nodules
Echogenicity
On ultrasound majority (52) of the nodules were hyperechoic (65%). The nodules which were hypoechoic constitute around 16(20%) and isoechoic nodules around 12(15%).

Margin
On ultrasound the majority (43) of nodules were having smooth margins (53.8%). The nodules which were having ill defined, lobulated margin constitute 8.8% (7), irregular around 22.5% (18) and with extra thyroidal extension around 6.3% (5).

Composition
On ultrasound the majority (42) of nodules were solid (52.5%). The nodules which were solid and cystic constitute around 36 (45%) and spongiform nodules around 2 (2.5%).

Echogenic Foci
Micro calcifications are detected in 15 out of 80 (18.8%) and macro calcifications in 21 out of 80 (26.3%). No calcification is visualised in 39 out of 80 (48.8%) nodules. Rim calcification and peripheral calcification were noted in 3 (3.8%) and 2 (2.5%) nodules respectively.

Distribution of TIRADS Categorization
Categorization of cases into TIRADS is an important process in the study. All patients (80) who underwent the Ultrasound examination were categorized appropriately. Out of 80 patients examined 46 cases (57.5%) were included in TIRADS III category, 17 patients each in IV and V categories (21.3% each). The below table (Table-6) explain the observation based on TIRADS.

Distribution of Cytology / Histopathology
The distribution of thyroid nodules is shown in Table-7. The most common nodules were colloid nodule, which accounted for around 2/3rd (53.75). Out of the 80 patients 18 patients (22.5%)were diagnosed with malignancy. 16 patients were diagnosed with papillary carcinoma (20%), 1 patient with follicular neoplasm (1.3%)and 1 with anaplastic carcinoma (1.3%). Follicular adenoma was diagnosed in 6 patients (7.5%) and thyroiditis among 13 patients (16.3%).

Bivariate Analysis of Ultrasound Characteristics of Thyroid Nodules
Bivariate on Echogenicity and Histopathology
Out of 18 malignant cases, 10 nodules were hypoechoic while 5 were isoechoic and 3 were hyperechoic. Majority of the hyperechoic nodules were benign (49 out of 52). P value <0.001 (Table- 1).

Bivariate on Margins and Histopathology

All the nodules (5/5) with extra thyroidal extension are malignant. 7 out of 18 and 6 out of 7 nodules with irregular and lobulated margins respectively are malignant. All the nodules with smooth and ill-defined margins are benign. P value <0.001 (Table- 2).

Bivariate on Composition and Histopathology

13 out of 42 solid and 5 out of 36 solid and cystic nodules were malignant. All the spongiform nodules were benign. P value <0.001 (Table- 3).

Bivariate on Echogenic foci and Histopathology

14 out of 15 nodules with micro calcification are malignant. 2 out of 3 and 2 out of 39 nodules with rim and no calcification respectively are malignant. None of the nodules with macro and peripheral calcification are malignant. P value <0.001 (Table- 4).

Bivariate on ACR-TIRADS and Histopathology

Out of 17 TIRADS V (Highly suspicious of malignancy) nodules 16 were malignant one was benign. 2 out of 17 TIRADS IV (Moderately suspicious of malignancy) nodules were malignant. None of the TIRADS III (Mildly suspicious of malignancy) nodules were malignant in our study. P value <0.001(Table- 5).

Area under the Curve

Receiver Operating Curve (ROC) (Fig. 1) for ADC value for differentiating benign from malignancy has a very good area under the curve value of 0.980. Also, from the ROC curve, the sensitivity and specificity for various ADC value were calculated and the result is as follows (Table -6). It was noted that for the ADC values from 1.655-1.745, the specificity was remaining relatively constant with sensitivity showing an increase from 72.2% to 94.4% and with 1.745 as the cut off value of ADC, sensitivity, specificity and accuracy of the study was 94.4%, 96.8% and 96.25 respectively.

Sensitivity and Specificity for different ADC Values

The best ADC values for differentiating benign from malignant thyroid nodules is 1.745. With 1.745 as the cut off value of ADC, sensitivity, specificity and accuracy of the study was 94.4%, 96.8% and 96.25% respectively. The positive predictive value and negative predictive value when taking 1.745 as cut off of ADC are 89.5% & and 98.4% respectively. This value as a cut-off in differentiation of malignant from benign nodules shows a good sensitivity and acceptable specificity.

The proportion of cases with malignancy increases with decreasing ADC value. 17 out of 18 malignant cases were having an ADC value of less than 1.745 (Sensitivity - 94.4%). Two false positive cases were detected in our study (3.2%), i.e. 2 out of 62 benign cases have values less than 1.745.60 out of 62 benign cases were having a value more than 1.745 (Specificity – 96.8%). One false negative case also detected in our study (5.6%).

Crosstab

			Benign/Malignant		Total
			Benign	Malignant	
Echogenicity	Hyperechoic	Count	49	3	52
		% within Benign/ Malignant	79.0%	16.7%	65.0%
	Hypoechoic	Count	6	10	16
		% within Benign/ Malignant	9.7%	55.6%	20.0%
	Isoechoic	Count	7	5	12
		% within Benign/ Malignant	11.3%	27.8%	15.0%
Total		Count	62	18	80
		% within Benign/ Malignant	100.0%	100.0%	100.0%

Table 1. Bivariate table on Echogenicity and Histopathology

			Benign/malignant		Total
			Benign	Malignant	
Margin	Extra-thyroidal extension	Count	0	5	5
		% within Benign/ Malignant	0.0%	27.8%	6.2%
	Ill-defined	Count	7	0	7
		% within Benign /Malignant	11.3%	0.0%	8.8%
	Irregular	Count	11	7	18
		% within Benign/ Malignant	17.7%	38.9%	22.5%
	Lobulated	Count	1	6	7
		% within Benign /Malignant	1.6%	33.3%	8.8%
	Smooth	Count	43	0	43
		% within Benign/ Malignant	69.4%	0.0%	53.8%
Total		Count	62	18	80
		% within Benign/ Malignant	100.0%	100.0%	100.0%

Table 2. Bivariate table on Margins and Histopathology

Crosstab

			Benign/Malignant		Total
			Benign	Malignant	
Composition	Solid	Count	29	13	42
		% within Benign/ Malignant	46.8%	72.2%	52.5%
	Solid and cystic	Count	31	5	36
		% within Benign/ Malignant	50.0%	27.8%	45.0%
	Spongiform	Count	2	0	2
		% within Benign/ Malignant	3.2%	0.0%	2.5%

Total	Count	62	18	80
	% within Benign/ Malignant	100.0%	100.0%	100.0%

Table 3. Bivariate table on Composition and Histopathology

Crosstab					
			Benign/Malignant		Total
			Benign	Malignant	
Echogenic foci	Nil	Count	37	2	39
		% within Benign/ Malignant	59.7%	11.1%	48.8%
	Macro calcification	Count	21	0	21
		% within Benign/ Malignant	33.9%	0.0%	26.2%
	Micro calcification	Count	1	14	15
		% within Benign/ Malignant	1.6%	77.8%	18.8%
	Peripheral calcification	Count	2	0	2
		% within Benign/ Malignant	3.2%	0.0%	2.5%
	Rim calcification	Count	1	2	3
		% within Benign/ Malignant	1.6%	11.1%	3.8%
Total		Count	62	18	80
		% within Benign/ Malignant	100.0%	100.0%	100.0%

Table 4. Bivariate table on Echogenic foci and Histopathology

Crosstab					
			Benign/Malignant		Total
			Benign	Malignant	
ACR TI-RADS	III	Count	46	0	46
		% within Benign/Malignant	74.2%	0.0%	57.5%
	IV	Count	15	2	17
		% within Benign/Malignant	24.2%	11.1%	21.2%
	V	Count	1	16	17
		% within Benign/Malignant	1.6%	88.9%	21.2%
Total		Count	62	18	80
		% within Benign/Malignant	100.0%	100.0%	100.0%

Table 5. Bivariate table on ACR-TIRADS and Histopathology

Area Under the Curve				
Test Result Variable(s): ADC VALUE (B 500)				
Area	**Std. Error**[a]	**P VALUE**	**Asymptotic 95% Confidence Interval**	
			Lower Bound	Upper Bound
.980	.013	**<0.001**	.954	1.000

Table 6. Area under the Curve

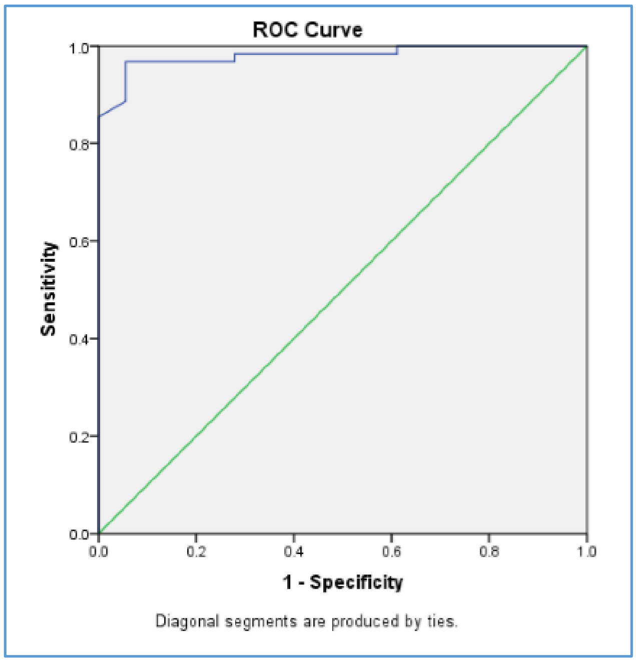

Figure 1. ROC Curve

DISCUSSION

The improved detection of thyroid nodules with Ultrasound has resulted in an increase in the number of thyroid FNABs and, thus, an increase in the number of thyroid cancers diagnosed [14]. Appropriate criteria are necessary to avoid an increase of rather unnecessary benign cytological results and surgery in thyroid nodules. Thyroid Imaging Reporting and Data System (TIRADS) has been developed based on the concepts of Breast Imaging Reporting and Data System (BIRADS), which established different categories according to the percentage of malignancy. Since its publication by Hovarth in JCEM9,[15] its clinical use is still very limited and its practicability in clinical practice is questioned. The Ultrasound patterns described were not applicable to all thyroid nodules and this stereotypic Ultrasound application is difficult for Ultrasound performers to use. All TIRADS 3 and 4 nodules does not need FNAC since the malignant potential varies from 2%- 85%.[16] Alternative imaging techniques like Diffusion MRI can be used to improve the diagnostic accuracy.

This is a prospective study to analyse the diagnostic benefit of diffusion-weighted magnetic resonance imaging (DWI) in the differentiation of malignant from benign thyroid nodules and to avoid unnecessary biopsies.

In our study, a total of 80 patients with age range 19 to 79 year were included. The commonest age group of thyroid nodules was between 41-50 yrs. (28.7%). The 22.5% of thyroid nodules are seen in 31-40 yrs. age group and 21.3% in 51-60 age groups. The percentage of nodules in <20 years, 21-30 years, 61-70 years and >70 years are 1.3%, 12.5%, 113% and 2.5% respectively. The percentage of malignancy is more in 21-30 years. age group and above 70 years age group (50% of the nodules in the age group). The cohort of population we studied contained more of younger age group. So that may be reason why we picked up more malignant lesions in younger age groups.

Majority of the patients were females (83.8%) in our study with a male to female ratio of 1:5 that correspond to that in reported literature [17]. Also, more number of malignant thyroid nodules were found in males (46%) compared to females (18%).

Histopathologically, the most common nodules were colloid nodule, which accounted for around 2/3rd (53.75). Out of the 80 patients 18 patients (22.5%)were diagnosed with malignancy. 16 patients were diagnosed with papillary carcinoma (20%), 1 patient with follicular neoplasm (1.3%)and 1 with anaplastic carcinoma (1.3%). Follicular adenoma were diagnosed in 6 patients (7.5%) and thyroiditis among 13 patients (16.3%).

Out of 18 malignant cases, 10 nodules were hypoechoic while 5 were isoechoic and 3 were hyperechoic. Majority of the hyperechoic nodules were benign (49 out of 52).

All the nodules (5/5) with extrathyroidal extension are malignant. 7 out of 18 and 6 out of 7 nodules with irregular and lobulated margins respectively are malignant. All the nodules with smooth and ill-defined margins are benign.

13 out of 42 solid and 5 out of 36 solid and cystic nodules were malignant. All the spongiform nodules were benign.

14 out of 15 nodules with microcalcification were malignant. 2 out of 3 and 2 out of 39 nodules with rim and no calcification respectively are malignant. None of the nodules with macro and peripheral calcification are malignant.

Out of 17 TIRADS V (Highly suspicious of malignancy) nodules 16 were malignant one was benign. 2 out of 17 TIRADS IV (Moderately suspicious of malignancy) nodules were malignant. None of the TIRADS III (Mildly suspicious of malignancy) nodules were malignant in our study.

The sensitivity and specificity for various ADC values were calculated from ROC curve and it was noted that for the ADC values from 1.655-1.745, the specificity was remaining relatively constant with sensitivity showing an increase from 72.2% to 94.4% and with 1.745 as the cut off value of ADC, sensitivity, specificity and accuracy of the study was 94.4%, 96.8% and 96.25 respectively. The best ADC value for differentiating benign from malignant thyroid nodules according to our study is 1.745 with the highest sensitivity and specificity to qualify it as a screening test. The positive predictive value and negative predictive value when taking 1.745 as cut off ADC are 89.5% & and 98.4% respectively. The mean ADC of the malignant thyroid nodules (1.52± 0.23 x 10^{-3} mm^2/s) was significantly lower than that of the mean ADC of the benign thyroid nodules (2.25± 0.41 x 10^{-3} mm^2/s). Range of mean ADC value for benign lesions was 1.56 – 3.33 and for malignant lesions was 0.96 – 1.87.

The proportion of cases with malignancy increases with decreasing ADC value. 17 out of 18 malignant cases were having an ADC value of less than 1.745 (Sensitivity - 94.4%). Two false positive cases were detected in our study (3.2%), 1) Follicular adenoma (ADC-1.56 X 10^{-3}) 2) Nodular colloid goiter (ADC-1.65 X 10^{-3}). The false positivity may be due to high cellularity of the lesion. 60 out of 62 benign cases were having a value more than 1.745 (Specificity – 96.8%). One false negative case was detected in our study (Papillary carcinoma – ADC- 1.87 x 10^{-3}) and on histopathology necrosis with haemorrhage was detected within the lesion. The results are in par with the meta-analysis done by Chen L.[18]

The result is comparable with Shi HF et al [19] who did a comparative study of Utility of diffusion-weighted imaging in differentiating malignant from benign thyroid nodules with magnetic resonance imaging and pathologic correlation. The majority (65%) of malignant thyroid nodules showed slightly hyperintense, and the majority (69%) of benign nodules were hyperintense on DWI (P < 0.01). The ADC values were lower in the thyroid cancer than in the adenoma and nodular goiter (P < 0.05). When the b factor was 500 s/mm, an ADC value of 1.704 × 10 mm/s can be threshold differentiating malignant from benign nodules, with 92% sensitivity, 88% specificity, and 87% accuracy. The higher cell density and more severe desmoplastic response were the causes of the lower ADC value of thyroid cancer.

The result is also comparable with Yan et al [20] who did a study to assess the application of ADC value in differentiating benign and malignant thyroid nodules with MR DWI. The ADC values of 40 thyroid nodules from 27 patients confirmed pathologically were analysed retrospectively. Routine MR T1W, T2W and contrast enhanced fat suppression scan were performed to confirm the solidity of thyroid nodules. DWI were acquired using single shot spin echo-planner imaging (SS SE-EPI) sequence with diffusion-sensitizing gradients using b factors of 0 and 500 s/mm^2. Thyroid nodules were divided into malignant and benign groups based on the pathological findings. ADC values of both groups were compared, and ROC curves were drawn to determine the diagnostic threshold and assess the screening test. Fifteen of 40 thyroid nodules were malignant and 25 were benign. The mean ADC value for benign thyroid nodules was (2.20±0.40) ×10-3 mm^2/s, 95% confidence interval was (2.04—2.37) ×10-3 mm^2/s. The mean ADC value for thyroid malignancy was(1.22±0.27)×10-3 mm^2/s, 95% confidence interval was(1.07—1.37)×10-3 mm^2/s significantly lower than that of benign thyroid nodules (P 0.05).When the area under the ROC curve was 0.98, the diagnostic threshold was 1.49×10-3 mm^2/s the sensitivity, specificity and accuracy was 86.70%, 100% and 95.00%, respectively.

In January 2012, study by El-Hariri, et al[21]showed that the mean ADC of the malignant thyroid nodules (0.89± 0.27 x 10^{-3} mm^2/s) was significantly lower than that of the mean ADC of the benign thyroid nodules (1.85± 0.24 x 10^{-3} mm^2/s). ADC value of 1.5 x 10^{-3} mm^2/s was used as a cut-off value for differentiation benign from malignant thyroid nodules. The sensitivity, specificity, PPV & NPV of DWI in differentiating benign from malignant thyroid nodules were 94%, 95%, 94% & 95%, respectively.

All the above studies are in par with our study showing significant difference in ADC value between the malignant tumours and benign lesions with reduced ADC value in malignant lesions compared to benign lesions.

C. Schueller-Weidekamm et al [22] done a study of Quantitative Diffusion-Weighted MR Imaging to Differentiate Benign and Malignant Cold Thyroid Nodules. Histologically, there were 20 carcinomas with a minimum size of 8 mm and 5 adenomas. The mean ADC values (in 10^{-3} mm^2/s) differed significantly among carcinoma, adenoma, and normal parenchyma (P<.05). The ranges (95% confidence interval) of the ADC values for carcinoma (2.43–3.037), adenoma (1.626–2.233), and normal parenchyma (1.253–1.602) showed no overlap. When an ADC value of 2.25 or higher was used for predicting malignancy, the highest accuracy of 88%, with 85% sensitivity and 100% specificity, was obtained. This study was not in accordance with our study.

Hence findings of our study and other studies quoted above suggest that the ADC values can well be used in the differentiation of benign and malignant thyroid nodules.

Different studies showed difference in the ADC cut off values for predicting thyroid carcinoma which is evident from several different studies quoted above. Hence each MRI unit should determine the exact threshold value for predicting malignancy in thyroid nodules as there are variations in MRI systems, coils and pulse sequences. Zhu and his colleagues,[23] mentioned that at lower b-values, there is risk of perfusion contamination, so the measured ADC will not be reliable to assess diffusion of tissues by mixed effects of perfusion and diffusion that could not be separated at these levels while at high b-values, there is risk of noise contamination and bad images resolution with subsequent non-reliable ADC measurement. They added that at least two b-values should be used to obtain an accurate quantitative analysis of diffusion-weighted images and consequently reliable ADC maps as well as the ADC measurement.

CONCLUSION

MRI with diffusion weighted imaging and ADC mapping is a promising tool in the armamentarium for the differentiation of benign and malignant thyroid nodules. It is superior to other modalities by using no ionizing radiation, its ability to probe the microstructure, its short acquisition time, its high repeatability, its safety, its affordability and the absence of intravenous administration of contrast

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